Influence of randomness in mathematical models for diffraction and T-cell recognition

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Preface

Stochastic models play an important part in many fields of science like physics and biology. In this thesis the influence of randomness in two such models is considered. It is therefore divided into two parts.

The first part deals with diffraction. Starting from a deterministic model we analyze the influence of randomness. The main result is the proof of the absence of singular continuous parts in the diffraction measure of particle gases with short range interaction.

The second part deals with recognition in the immune system. In this part the main focus lies in the probabilistic modeling itself, preparation of the mathematical tools, and the analysis to show the ability of the models to explain the reliable recognition of foreign invaders by certain white blood cells.

Outline

Due to better and better measuring techniques, deterministic models often do not suffice to describe the reality. During the last years an improvement of measuring techniques also occured in the framework of diffraction experiments. Within the framework of experiments concerning T-cell recognition, the observations in the last decades have shown that deterministic models are highly idealized. Therefore, stochastic methods become more and more important and are hence used in this thesis.

The Chapters 1 to 3 are concerned with the mentioned problem from physics, namely (kinematic) diffraction. Chapter 1 explains why the Fourier transform of an autocorrelation function is the relevant quantity. We start with a short derivation of an approximation of the scattering amplitude of a single unit which is then expanded to a bounded object consisting of many units. After that, we show that the practically observed scattering intensity is given by the Fourier transform of the autocorrelation of the function (or measure) which describes the object.

In the second chapter, the standard deterministic model for kinematic diffraction is considered. We start with the recapitulation of the essential mathematical tools in order to expand our consideration to unbounded objects. Then, we state the important results for the diffraction of pointlike scatterers, particularly of crystals.

The third chapter is the main part with the new results. There, we are concerned with the influence of randomness on the diffraction. We consider particle gases on fixed point sets and certain dynamical systems. In the first instance, we prove general results concerning the diffraction. Afterwards, we construct Gibbs measures. These are employed to ensure ergodicity which we need for more explicit results concerning the diffraction.

Chapters 4 to 6 are concerned with the biological problem. The problem itself is presented in Chapter 4. As already mentioned, it deals with the recognition of foreign invaders by certain white blood cells called T-cells. In Chapters 5 and 6, probabilistic models are analyzed to show that they make recognition possible.

In Chapter 5, the problem is considered without taking into account a learning process of the T-cells. We start with a model proposed by van den Berg, Rand and Bourroughs and then present a generalized version. Since the relevant events are rare, we need large deviation results. These are recapitulated and used to derive approximations, which later are applied to the analysis of the generalized model. At last we look at a reduced model in order to get exact results. The bottom line is that, in all three models, recognition is possible but only if there are many invaders present.

In the last chapter, the afore mentioned learning process is included. Again we start from the model proposed by van den Berg, Rand and Bourroughs and pass on to the generalized version. We then draw on novel insights into the learning process, leading to presenting and analyzing an alternative model.

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Introduction

Mathematical models in general describe systems in a mathematical way (i.e., with the help of mathematical language). They are used with great success in the natural sciences, particularly in physics and biology.

The first requirement for mathematical modeling is the extraction of the essential aspects of the system. Then, one has to choose the appropriate mathematical methods to analyze the model. In the end, one must check whether the results are in agreement with the experimental observations.

Mathematical models may be classified in various ways. One possibility is to distinguish between deterministic and probabilistic (stochastic) models. In the former the states of the system are uniquely determined by parameters. In contrast, in the latter randomness is allowed. The states of the systems are then described by probability distributions.

It is clear that stochastic models are more realistic than deterministic ones since real systems can never be exactly determined. However, one often uses deterministic models (as a start) since they are easier to deal with. This may be done since the discrepancy of the results is often lower than the precision of measurements. (For example, quantum mechanics is exact. However, the discrepancy between forecasts of quantum mechanics and those of classical mechanics is often less than the precision of measurements; therefore one may also use classical mechanics.)

In this thesis we are concerned with mathematical models for two different systems, one arising in physics, the other in biology.

In the first part (devoted to the physical problem) we start with a deterministic model and then introduce randomness. This corresponds to the development sketched above. In the second part (concerning the biological problem) we directly consider a probabilistic model but vary the degree of randomness.

Part I

The considered system in physics is an arbitrary solid (given by its atoms) and one is interested in its diffraction. As we will see in the first chapter, kinematic diffraction may be described by the Fourier transform of the autocorrelation of the solid.

In mathematical diffraction theory (i.e., the mathematical model for diffraction), the objects are no longer described by functions but by measures and distributions, respectively. The reason is that one can generalize the considerations of the first chapter to unbounded objects. This will be done for deterministic objects in the second chapter.

However, objects are never perfect (for instance due to impurities and other random influences). Therefore, the influence of disorder (i.e., a random object) is analyzed afterwards (in Chapter 3).

In practice, one usually observes only a slight modification of the Bragg peaks (i.e., the pure point part of the diffraction measure) and additional diffuse scattering (i.e., an absolutely continuous part) compared to the diffraction predicted by deterministic models. (For some examples of diffuse scattering compare [61].) A probabilistic modeling should be in agreement with this observation. In particular, it is interesting to investigate whether a stochastic description will predict the absence of singular continuous components. This is the aim of the first part of this thesis.

We consider so-called particle gases with finitely many different scatterers. These are objects defined by point sets and measures specifying the occupation of the individual points by the possible particles. In this context, we have to distinguish between particle gases defined by a fixed point set and those defined by a dynamical system of point sets. Both cases are considered in this thesis.

One interesting class of particle gases are those where the different types of particles occupy the points according to some random process described by a Gibbs measure. The relevance of Gibbs measures, in turn, stems from the assumption that the structure under consideration is in thermal equilibrium. Clearly, this need not always be the case, but we only consider equilibrium systems here since the equilibrium assumption is good for many solids.

The special case of a particle gas where the underlying point set is a lattice is called a lattice gas. In two recent publications [8, 36], it was shown that certain binary lattice gases, such as those based upon a ferromagnetic Ising model with short range interaction, additionally inherit an absolutely continuous spectral component, but no singular continuous one. The natural question arises whether this situation is more general.

The answer to this question is affirmative, and it is the aim of this contribution to extend the results of [8] to increase the evidence for the rather natural conjecture that non-trivial singular continuous diffraction spectra are the exception, at least as the result of stochastic deviations from systems with a strongly ordered ground state, which are of special interest (see [26]).

The extension refers on the one hand to the generalization of binary lattice gases to those with finitely many types of particles (compare [9]). On the other hand we generalize the theorems to a broader class of point sets than lattices. The beginning may be found in [9]. However, in this case we have to consider certain dynamical systems (each of them arising from a fixed point set) instead of the point sets themselves.

This is the reason why we have to construct Gibbs measures on dynamical systems (see Sect. 3.3). In the end we get the main result in Corollary 5.

Result. *In the case of a regular model set, a translation invariant finite or short range potential and sufficiently high temperature there occurs no singular continuous part in the diffraction spectrum of the particle gas given by the corresponding Gibbs measure.*

This has already been stated in [9, Cor. 5.5], but without correct proof and restricted to a finite range potential.

Part II

The biological system considered here is the immune system, particularly the set of encounters between so-called T-cells and antigen-presenting cells (two kinds of white blood cells). The task of the T-cells is the recognition of foreign invaders like bacteria or viruses (into an individual) and, in succession, the initiation of an immune response that eliminates the intruders. The recognition takes place on the occasion of the mentioned encounters and this is what we are going to look at. It is clear that two properties have to be guaranteed. On the one hand, at least one T-cell has to be activated if there is a foreign invader present. On the other hand, no activation should occur if no invader is present.

In practice, T-cells are normally (in a healthy individual) able to recognize invaders in the sense that they successfully distinguish between foreign and self-molecules. As in the first part, a realistic modeling should be in agreement with this observation.

In Chapter 4 it will become clear that the set of encounters cannot be modeled deterministically without severe limitations. We therefore directly start with probabilistic models. The aim of the second part of this thesis then is the analysis of these models in order to show that they are able to explain a reliable recognition.

The starting point is a model of van den Berg, Rand and Burroughs [11] (henceforth referred to as BRB) which is able to perform this task. In the leading sections of Chapter 5 this model is reconsidered and its analyis refined (compare [65]). In particular, the analysis is put on a solid mathematical basis by stating and applying the necessary large deviation result. This is an asymptotic result for the limit of an infinite system, which leads to an approximation for the true finite system. Moreover, we put forward and analyze numerically a generalization of the model, which is biologically more realistic.

We then complement these results for exact bounds for the finite system in order to understand which features ensure the reliable recognition of foreign invaders. This is developed in the last section of Chapter 5 for a reduced model, which consists of the essential features of the BRB model.

As in the original model, for both the generalization and the reduced model, a reliable recognition is guaranteed only under certain assumptions on the abundance of the invader. But in reality, these assumptions are not always fulfilled. Therefore, we have to take into account an additional learning process called negative selection.

This was already done in the context of the original model. There, it was shown that the recognition then already works under less restrictive assumptions. In the first section of Chapter 6 (compare [65]) we show that the same is true in the generalized version, too. However, we have to resort to simulations.

The desire for analytical results, in combination with novel insights into immunobiology, have been the reasons to develop a new (so-called emulation) model for negative selection which is introduced in the second section of Chapter 6. For the analysis of this model we use the bounds developed for the reduced model. As in the previous model of negative selection, recognition now works under less restrictive assumptions. However, in both models the invader has to be present in an adequate amount.

A model that does not even require this assumption is presented in the third section of Chapter 6. In contrast to the above models it relies on a highly idealized all-or-none law

of stimulation.

In the end we get the following result.

Result. *Either an abundance of the invader is required or an all-or-none law of stimulation.*

In the latter case the question remains whether enough T-cells survive negative selection. We shortly comment on this in the fourth section of Chapter 6.

Part I

Mathematical diffraction theory

Chapter 1

Physical background

The term *diffraction* is used in different ways in the literature. In general, one means a form of scattering which occurs whenever electromagnetic radiation interacts with matter. Following, we restrict ourselves to the kinematical approximation of diffraction in the far field. Our goal is to derive the relevant formulas for diffraction phenomenons in the presence of objects consisting of several scattering units.

1.1 Scattering from a single unit

We start from the fact that monochromatic plane waves hit a scattering unit. Since for our purposes the vector nature of the wave amplitudes is not important (the only consequence is a polarization factor; compare [20, Sect. 1.2.2]), we consider them as scalar.

Under the assumption that the scattering unit is described by a potential field $\varphi \in L^1(\mathbb{R}^d)$, we have to consider scattering of particles by such a field (compare [63, Chap. 4]). This can be done starting with the time-independent Schrödinger equation

$$[\triangledown^2 + \frac{4\pi^2}{\lambda^2} + \mu\varphi(r)]\psi = 0 \ ,$$

where λ is the wavelength and μ the parameter specifying the strength of the interaction with the potential field. Alternatively, one may consider the (equivalent) integral equation

$$\psi_{k_{\text{in}}}(r) = \exp\left(-2\pi i k_{\text{in}} r\right) + \mu \int \frac{\exp\left(-2\pi i |r - r'|/\lambda\right)}{4\pi|r - r'|}\varphi(r')\psi_{k_{\text{in}}}(r')\mathrm{d}r' \ ,$$

where the first part represents the incident wave with wavevector k_{in} ($|k_{\text{in}}| = 1/\lambda$) and the second one the scattered radiation resulting from the spherical waves emitted from all the points in the scattering field. The spherical waves are given by the Green function

$$\frac{\exp\left(-2\pi i |r - r'|/\lambda\right)}{4\pi|r - r'|} \ .$$

For the first Born approximation one assumes that the amplitude of the scattered wave is much less than the incident wave amplitude. Therefore one sets

$$\psi_{k_{\text{in}}}(r') = \exp\left(-2\pi i k_{\text{in}} r'\right) \ .$$

This scenario, in which the scattered wave is made up of contributions scattered directly from the incident wave, is known as *kinematical approximation*[1]. It is good for weakly scattering fields such as that from X-rays or neutrons.

On the Fraunhofer condition that the overall dimensions of the scattering field are much smaller than the distances to the observation point ($|r'| \ll |r|$), one yields the so-called *far field approximation*

$$\psi_{k_{\text{in}}}(r) \approx \exp\left(-2\pi i k_{\text{in}} r\right) + \frac{\exp\left(-2\pi i |r|/\lambda\right)}{|r|} \frac{\mu}{4\pi} \int \exp(-2\pi i (k_{\text{in}} - k_{\text{out}}) r') \varphi(r') \mathrm{d}r'$$

$$=: \exp\left(-2\pi i k_{\text{in}} r\right) + \frac{\exp\left(-2\pi i |r|/\lambda\right)}{|r|} f(k_{\text{in}}, k_{\text{out}}) \, .$$

Here, we used the approximation

$$\frac{\exp\left(-2\pi i |r - r'|/\lambda\right)}{|r - r'|} \approx \frac{\exp\left(-2\pi i |r|\sqrt{1 - 2rr'/|r|^2 + |r'|^2/|r|^2}/\lambda\right)}{|r|}$$

$$\approx \frac{\exp\left(-2\pi i |r|/\lambda\right) \exp\left(2\pi i \frac{r}{|r|\lambda} r'\right)}{|r|}$$

$$=: \frac{\exp\left(-2\pi i |r|/\lambda\right) \exp(2\pi i k_{\text{out}} r')}{|r|} \, .$$

Thus, in the end, we get a formula for the *scattering amplitude* (also called *factor*) of a unit (e.g., an atom) defined by the potential field φ (in the case of an atom defined by its electrons or its nucleus – depending on the matter of radiation):

$$f(q) = f(k_{\text{in}}, k_{\text{out}}) = \frac{\mu}{4\pi} \int \exp(-2\pi i (k_{\text{in}} - k_{\text{out}}) r') \varphi(r') \mathrm{d}r'$$

$$= \frac{\mu}{4\pi} \int \exp(-2\pi i q r') \varphi(r') \mathrm{d}r' \, .$$

We see that the scattering amplitude is given by a constant times the Fourier transform of the potential field (well-defined due to integrability of the potential). Such factors are tabulated in the international tables of crystallography (see e.g. [60]).

1.2   Scattering from an object consisting of several units

We proceed with an object consisting of two scattering units (unit 1 at the origin and 2 at position r_2).

Let us figure the object as a new unit with potential $\varphi(r) = \varphi_1(r) + \varphi_2(r - r_2)$, where φ_1 and φ_2 are the potentials of the two single units if they were located at the origin. Here, one assumes once more that the dimensions of the scattering field are much smaller than the distances to the observation point.

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[1] alternatively called single or elastic scattering

This results in the scattering amplitude

$$
\begin{aligned}
F(q) &= \frac{\mu}{4\pi} \int \exp(-2\pi i q r) \varphi(r) \mathrm{d}r \\
&= \frac{\mu}{4\pi} \int \exp(-2\pi i q r) \varphi_1(r) \mathrm{d}r + \frac{\mu}{4\pi} \int \exp(-2\pi i q r) \varphi_2(r - r_2) \mathrm{d}r \\
&= \frac{\mu}{4\pi} \int \exp(-2\pi i q r') \varphi_1(r') \mathrm{d}r' + \frac{\mu}{4\pi} \int \exp(-2\pi i q r') \varphi_2(r') \mathrm{d}r' \exp(-2\pi i q r_2) \,.
\end{aligned}
$$

The obtained equation may be written as

$$
F(q) = f_1(q) + f_2(q) \exp(-2\pi i q r_2) \,. \tag{1.1}
$$

We will shortly illustrate how this comes about. Let $f_1(k_{\mathrm{in}}, k_{\mathrm{out}})$ be the factor of the scattering unit at the origin and analogously $f_2(k_{\mathrm{in}}, k_{\mathrm{out}})$ the one of the second unit. In order to derive the scattering amplitude for the whole object one has to calculate the phase difference between the emitted waves (see Fig. 1.1).
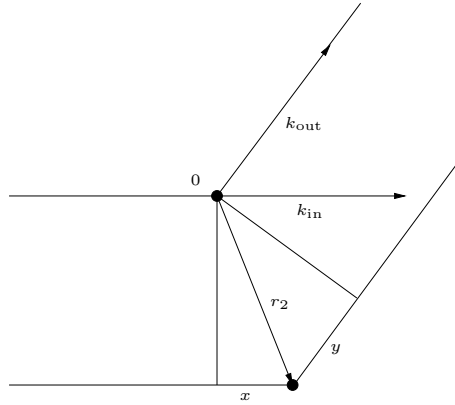
Figure 1.1: Phase difference between two emitted waves

The distance x is given by the scalar product of k_{in} and r_2 divided by the norm of k_{in}. In analogy, y is given by the negative scalar product of k_{out} and r_2 divided by the norm of k_{out}. Therefore the phase difference is

$$
\frac{2\pi}{\lambda}(x + y) = \frac{2\pi}{\lambda} \lambda (k_{\mathrm{in}} - k_{\mathrm{out}}) r_2 = 2\pi (k_{\mathrm{in}} - k_{\mathrm{out}}) r_2 \,,
$$

and setting $k_{\mathrm{in}} - k_{\mathrm{out}} = q$, one gets (1.1).

Generalization to an object consisting of n units yields

$$
F(q) = \sum_{j=1}^{n} f_j(q) \exp(-2\pi i q r_j) = \frac{\mu}{4\pi} \int \exp(-2\pi i q r) \varphi(r) \mathrm{d}r, \tag{1.2}
$$

where $\varphi(r) = \sum_{j=1}^{n} \varphi_j(r - r_j)$.

1.3   Scattering intensity of bounded objects

We have seen that the scattering amplitude is given by the Fourier transform of the potential describing the object.

However, in diffraction experiments, one only observes the *scattering intensity*. It is proportional to the product of the complex amplitude with its complex conjugate (see [20, 33]), i.e.,

$$I(q) = F(q)\overline{F(q)} \ .$$

Applying the convolution theorem (compare [54, Thm. 1.2.4]) yields

$$I(q) = \widehat{\varphi * \widetilde{\varphi}} \ ,$$

with $\widetilde{\varphi}(r) = \overline{\varphi(-r)} = \overline{\varphi \circ \iota(r)}$ where $\iota(r) = -r$.

Up to now, we considered only real functions φ. Since in this case $\widetilde{\varphi}(r) = \varphi \circ \iota(r)$, the convolution $\varphi * \widetilde{\varphi}$ complies with the autocorrelation

$$P(s) = \int \varphi(r)\varphi(r - s)\mathrm{d}r \ . \tag{1.3}$$

In this way, we realize the significance of the Fourier transform of the autocorrelation.

In the case of an object consisting of n units we have

$$\begin{aligned}
I(q) &= \left(\frac{\mu}{4\pi}\right)^2 \int \exp(-2\pi i q r')\varphi(r')\mathrm{d}r' \int \exp(2\pi i q r)\varphi(r)\mathrm{d}r \\
&= \left(\frac{\mu}{4\pi}\right)^2 \int\int \exp(-2\pi i q(r' - r))\varphi(r)\varphi(r')\mathrm{d}r\mathrm{d}r' \\
&= \left(\frac{\mu}{4\pi}\right)^2 \int \left(\int \varphi(r')\varphi(r' - s)\mathrm{d}r'\right) \exp(-2\pi i q s)\mathrm{d}s \\
&= \left(\frac{\mu}{4\pi}\right)^2 \int P(s) \exp(-2\pi i q s)\mathrm{d}s \ .
\end{aligned}$$

Due to (1.2), this is the same as

$$I(q) = \sum_{j=1}^{n} \sum_{k=1}^{n} f_j(q)f_k(-q) \exp\left(-2\pi i q(r_j - r_k)\right) \ . \tag{1.4}$$

The latter form of the scattering intensity illustrates in a clearer way that it is the intensity of an object consisting of n units with scattering factors f_j at the positions r_j, $1 \leqslant j \leqslant n$, $n \in \mathbb{N}$.

Chapter 2

Mathematical model for deterministic objects

We start with a mathematical description of deterministic objects. For this reason we recapitulate the essential aspects of measure and distribution theory (compare [25, Sect. 13] and [40]).

2.1 Measure and distribution theory

Let $\mathcal{K} = \mathcal{K}\left(\mathbb{R}^d\right)$ be the space of complex-valued continuous functions with compact support.

Definition 1.
1. *A (complex) measure μ on $\mathbb{R}^d$ is a linear functional on $\mathcal{K}$ which fulfills the condition that for every compact subset $K \subset \mathbb{R}^d$ there is a constant a_K such that $|\mu(g)| \leqslant a_K \|g\|_\infty$ for all $g \in \mathcal{K}$ with support in K.*

2. *The measure $\overline{\mu}$ defined by $\overline{\mu}(g) := \overline{\mu(\overline{g})}$ is the conjugate of μ. In an analogous way $\widetilde{\mu}$ is defined by $\widetilde{\mu}(g) := \overline{\mu(\widetilde{g})}$.*

3. *A measure μ is positive if $\mu(g) \geqslant 0$ for all $g \geqslant 0$.*

4. *The smallest positive measure $|\mu|$ such that $|\mu(g)| \leqslant |\mu|(g)$ for all non-negative $g \in \mathcal{K}$ is the total variation (or absolute value) of μ.*

5. *A measure is finite if $|\mu|(\mathbb{R}^d)$ is finite, and translation bounded if for every compact set $K \subset \mathbb{R}^d$ there is a constant b_K such that $\sup_{x \in \mathbb{R}^d} |\mu|(K + x) \leqslant b_K$ (which means that the measure is (b_K, K)-translation bounded).*

Remark.
1. The vector space of measures on $\mathbb{R}^d$ is denoted by $\mathcal{M}\left(\mathbb{R}^d\right)$. It is given the vague topology, i.e., a sequence of measures μ_n converges vaguely to μ if $\lim_{n \to \infty} \mu_n(g) = \mu(g)$ for all $g \in \mathcal{K}$.

2. Taking Lebesgue's measure as a reference, a measure μ admits a unique decomposition into three parts,

$$\mu = \mu_{\mathrm{pp}} + \mu_{\mathrm{sc}} + \mu_{\mathrm{ac}} ,$$

where pp, sc and ac stand for pure point, singular continuous and absolutely continuous.

3. The convolution $\mu * \nu$ of two measures μ and ν with at least one of the two measures having compact support or being finite, while the other is translation bounded, is given by

$$(\mu * \nu)(g) := \int \int g(x + y)\mathrm{d}\mu(x)\mathrm{d}\nu(y) . \qquad (2.1)$$

It is well-defined due to [10, Prop. 1.13].

The advantage of a description by distributions is the possibility to define the Fourier transform of infinite objects. Since all the objects in our context can be described by translation bounded measures, we may restrict ourselves to a special subclass of distributions, the so-called tempered distributions. They are linear functionals on the space $\mathcal{S} = \mathcal{S}\left(\mathbb{R}^d\right)$ of Schwartz functions. These are rapidly decreasing C^∞ functions (for an exact definition see Sect. VII.3 in [56]).

Definition 2. *The Fourier transform of a Schwartz function $\Phi \in \mathcal{S}$ is given by*

$$\widehat{\Phi}(k) := \int_{\mathbb{R}^d} \Phi(x)\mathrm{e}^{-2\pi ikx}\mathrm{d}x ,$$

where kx denotes the Euclidean inner product in $\mathbb{R}^d$.

Remark. The Fourier transform of a Schwartz function is again a Schwartz function and the inverse operation

$$\check{\Phi}(x) := \int_{\mathbb{R}^d} \Phi(k)\mathrm{e}^{2\pi ixk}\mathrm{d}k$$

exists, meaning that $\check{\widehat{\Phi}} = \widehat{\check{\Phi}} = \Phi$ for all $\Phi \in \mathcal{S}$.

On the basis of these facts, a tempered distribution and its Fourier transform can be defined.

Definition 3. *A tempered distribution T is a continuous linear functional on $\mathcal{S}$. The Fourier transform $\widehat{T}$ of a tempered distribution T is given by $\widehat{T}(\Phi) := T(\widehat{\Phi})$ for all $\Phi \in \mathcal{S}$.*

Theorem 1. *If there exists some $\ell \in \mathbb{N}$ such that*

$$\int \frac{\mathrm{d}|\mu|(x)}{(1 + |x|)^\ell} < \infty ,$$

the measure μ is a tempered distribution.

Proof. See [56, Thm. VII.VII]. □

Corollary 1. *Every translation bounded measure defines a tempered distribution.*

This corollary is the reason why objects in our context can be described by tempered distributions. However, the Fourier transform of a tempered distribution is again a tempered distribution but it need not be a measure. And since the product of two tempered distributions is not defined in general (compare [58, §3.IV]), the scattering intensity cannot be calculated by the product of the scattering amplitude and its complex conjugate. Instead, one can calculate the Fourier transform of the autocorrelation.

Theorem 2. *If μ is positive definite in the sense that $\mu(\Phi * \widetilde{\Phi}) \geqslant 0$ for all $\Phi \in \mathcal{S}$ then $\widehat{\mu}$ is a positive measure.*

Proof. By Bochner's theorem (see e.g. [56, Thm. VII.XVIII]), the existing inverse Fourier transform $\check{\mu}$ is a positive measure. Since

$$\widehat{\mu}(\Phi) = \widehat{\check{\widehat{\mu}}}(\Phi) = \check{\mu}(\widehat{\widehat{\Phi}}) = \check{\mu}(\Phi \circ \iota) \, ,$$

the Fourier transform is a positive measure, too. $\qquad\square$

Since every autocorrelation measure is translation bounded (see [35, Prop. 2.2]), it is again a tempered distribution, and, therefore, its Fourier transform is defined. Moreover, every autocorrelation is positive definite and due to the last theorem we have

Corollary 2. *The Fourier transform of an autocorrelation measure exists and is a positive, translation bounded measure on $\mathbb{R}^d$, with a unique decomposition*

$$\widehat{\gamma} = \widehat{\gamma}_{\mathsf{pp}} + \widehat{\gamma}_{\mathsf{sc}} + \widehat{\gamma}_{\mathsf{ac}}$$

into its pure point, singular continuous and absolutely continuous parts, relative to Lebesgue measure as reference (being the Haar measure of $\mathbb{R}^d$).

2.2 Change from bounded to unbounded objects

Returning to the considerations of Chapter 1, the (potential of an) object consisting of n units can be described by the absolutely continuous measure

$$\vartheta(g) = \int g(x)\varphi(x)dx$$

or by the discrete (pure point) measure

$$\vartheta(g) = \sum_{j=1}^{n} f_j \delta_{r_j}(g)$$

with scattering factors f_j of the individual units at the positions r_j, $1 \leqslant j \leqslant n$, $n \in \mathbb{N}$. Here, δ_{x_0} is the *Dirac measure* which assigns the function value at x_0 to each (continuous) function. However, the measure can also be understood as a tempered distribution. The only difference is the space, in which g lies.

The autocorrelation measure (analogous and due to (1.3) and (2.1)) is then given by

$$(\vartheta * \widetilde{\vartheta})(g) = \int g(z) \int \varphi(x)\overline{\varphi(x-z)}\mathrm{d}x\mathrm{d}z$$

and

$$(\vartheta * \widetilde{\vartheta})(g) = \sum_{j=1}^{n} \sum_{k=1}^{n} f_j \overline{f_k} \delta_{r_j - r_k}(g) \, , \tag{2.2}$$

respectively.

Fourier transformation of the latter results in

$$\widehat{\vartheta * \widetilde{\vartheta}} = \sum_{j=1}^{n} \sum_{k=1}^{n} f_j \overline{f_k} \exp\left(-2\pi i q(r_j - r_k)\right)$$

(compare (1.4)), and thus gives the scattering intensity.

Up to now, we considered objects consisting of finitely many scattering units. In this context we used a first approximation, namely the kinematical far-field one, assuming that the distance to the observation point is very large (see Subsection 1.1). From now on, we use a second approximation. Since the objects analyzed in diffraction experiments consist of many units, it is common practice to model these objects in the limit of increasing number of scattering units (compare Fig. 2.1).
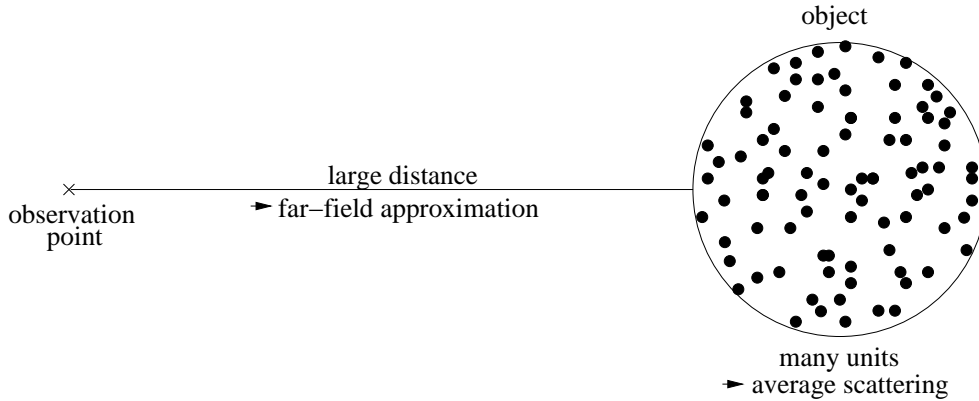
Figure 2.1: The two approximations of kinematic diffraction

For the purpose of convergence one is interested in the scattering intensity per unit or unit volume (compare [20, 35]). That is the reason why one is interested in the vague points of accumulation of

$$\gamma_R := \frac{1}{\mathrm{vol}(B_R)} \vartheta_R * \widetilde{\vartheta_R} \,, \tag{2.3}$$

the normalized autocorrelation measures for bounded regions. Here, B_R denotes the closed ball of radius R with centre 0, $\mathrm{vol}(B_R)$ its volume and μ_R the restriction of a measure μ to the ball B_R. If only one point of accumulation exists, the autocorrelation is unique and called the *natural autocorrelation*. As we have seen above, its Fourier transform (in the sense of distributions) is defined. In our model, this is the scattering intensity measure of the considered object. It can be decomposed in pure point, absolutely and singular continuous parts. The pure point part represents the so-called *Bragg peaks*. The absolutely continuous part describes the *diffuse scattering*, and the singular continuous part represents the rest (compare [26]).

2.3   Diffraction of pointlike scatterers

In the idealization of pointlike scatterers we may restrict ourselves to measures that are concentrated on discrete point sets Γ. In order to derive general results, we consider FLC point sets, characterized in the following (compare [55]).

Definition 4.   *1. A point set $\Gamma \subset \mathbb{R}^d$ is uniformly discrete if $r > 0$ exists such that, for all $x \in \Gamma$, $(x + B_r) \cap \Gamma = \{x\}$.*

   2. A point set $\Gamma \subset \mathbb{R}^d$ is locally finite (closed and discrete) if for any compact set $K \subset \mathbb{R}^d$ the intersection $\Gamma \cap K$ is a finite set.

3. A point set $\Gamma \subset \mathbb{R}^d$ is of finite local complexity (FLC) if and only if $\Gamma - \Gamma$ is locally finite.

Proposition 1. *For a discrete point set $\Gamma \subset \mathbb{R}^d$, the following are equivalent:*

1. *Γ is of finite local complexity.*

2. *For every compact set $K \subset \mathbb{R}^d$, there is a compact set $K' \subset \mathbb{R}^d$ such that, for every $x \in \mathbb{R}^d$, there is some $x' \in K'$ with $(x + \Gamma) \cap K = (x' + \Gamma) \cap K'$.*

Proof. See [55, Prop. 2.3]. $\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\square$

Remark.   1. A point set of finite local complexity is locally finite.

2. A point set of finite local complexity is uniformly discrete (since 0 is an isolated point of $\Gamma - \Gamma$).

3. A point set Γ is of finite local complexity if for any compact set $K \subset \mathbb{R}^d$ there are only finitely many *clusters* $\Gamma \cap (x + K)$, $x \in \mathbb{R}^d$, up to translations (due to Proposition 1).

A fixed unbounded object with underlying FLC point set is then modeled by the measure

$$\delta_\Gamma^{(f)} := \sum_{x \in \Gamma} f_x \delta_x$$

and we have

Proposition 2. *Let $\Gamma \subset \mathbb{R}^d$ be an FLC point set and Γ_R the restriction of Γ to the ball B_R. If the autocorrelation coefficients*

$$\eta_\Gamma^{(f)}(z) := \lim_{R \to \infty} \frac{1}{\mathrm{vol}(B_R)} \sum_{\substack{x \in \Gamma_R \\ x - z \in \Gamma}} f_x \overline{f_{x-z}}$$

exist for all $z \in \Gamma - \Gamma$, the natural autocorrelation is given by

$$\gamma_\Gamma^{(f)} = \sum_{z \in \Gamma - \Gamma} \eta_\Gamma^{(f)}(z) \delta_z \ . \tag{2.4}$$

Proof. Due to (2.3),

$$\gamma_{\Gamma_R}^{(f)} = \frac{1}{\mathrm{vol}(B_R)} \sum_{x,y \in \Gamma_R} f_x \overline{f_y} \delta_{x-y} \ ,$$

compare (2.2). If we choose $N > 0$ and $g \in \mathcal{K}$ with support in B_N, we have

$$\gamma_{\Gamma_R}^{(f)}(g) = \frac{1}{\mathrm{vol}(B_R)} \sum_{\substack{x,y \in \Gamma_R \\ x - y \in B_N}} f_x \overline{f_y} \delta_{x-y}(g) = \frac{1}{\mathrm{vol}(B_R)} \sum_{z \in (\Gamma - \Gamma)_{\min(N, 2R)}} \sum_{\substack{x \in \Gamma_R \\ x - z \in \Gamma}} f_x \overline{f_{x-z}} \delta_z(g) \ .$$

Since the number of terms in the summation over z is finite due to the FLC property (see 3. in Definition 1), the assumption gives

$$\lim_{R \to \infty} \gamma_{\Gamma_R}^{(f)}(g) = \sum_{z \in (\Gamma - \Gamma)_N} \eta_\Gamma^{(f)}(z) \delta_z(g) \ .$$

Because N and g were arbitrary, (2.4) is proven (see [4, 5]). $\qquad\qquad\qquad\qquad\qquad\square$

In the following, we assume the scattering factors f_x to be the same for all units. Thus, we consider measures of the form

$$\delta_\Gamma := \sum_{x \in \Gamma} \delta_x .$$

Proposition 3. *Let $\Gamma \subset \mathbb{R}^d$ be an FLC set for which the frequencies of finite patterns exist uniformly. Then the autocorrelation γ_Γ as well as the diffraction measure exist. The latter is a positive, translation bounded measure on $\mathbb{R}^d$, with a unique decomposition*

$$\widehat{\gamma_\Gamma} = \left(\widehat{\gamma_\Gamma}\right)_{\mathsf{pp}} + \left(\widehat{\gamma_\Gamma}\right)_{\mathsf{sc}} + \left(\widehat{\gamma_\Gamma}\right)_{\mathsf{ac}}$$

into its pure point, singular continuous and absolutely continuous parts, relative to Lebesgue measure as reference (being the Haar measure of $\mathbb{R}^d$).

Proof. Due to the frequency property,

$$\eta_\Gamma(z) := \lim_{R \to \infty} \frac{1}{\mathrm{vol}(B_R)} \sum_{\substack{x \in \Gamma_R \\ x - z \in \Gamma}} 1 ,$$

the frequency of the finite pattern $K = \{0, -z\}$, exists. The claim now follows from Corollary 2. $\square$

Proposition 4. *Let $\Gamma \subset \mathbb{R}^d$ be an FLC set, and consider the complex measure*

$$\vartheta := \sum_{z \in \Gamma - \Gamma} g(z)\, \delta_z .$$

If $\sum_{z \in \Gamma - \Gamma} |g(z)| < \infty$, ϑ is a finite measure, and the Fourier transform $\widehat{\vartheta}$ is a bounded, uniformly continuous function that defines an absolutely continuous measure on $\mathbb{R}^d$.

Proof. ϑ is a pure point measure because $\Gamma - \Gamma$ is discrete and closed by the FLC property, so that $|\vartheta|(\mathbb{R}^d) = \sum_{z \in \Gamma - \Gamma} |g(z)| < \infty$ implies that ϑ is finite.

By the general properties of the Fourier (or Fourier-Stieltjes) transform, compare [54, Theorem 1.3.3], $\widehat{\vartheta}$ is then a bounded and uniformly continuous function on $\mathbb{R}^d$. It is thus locally integrable, and hence defines an absolutely continuous measure on $\mathbb{R}^d$ by the Radon-Nikodym theorem. $\square$

The best studied objects in our setting are lattice periodic ones, so-called *crystals*. In this case, both Γ and $\Gamma - \Gamma$ are lattices, for example $\mathbb{Z}^d$. The autocorrelation coefficients

$$\eta_\Gamma(z) = \lim_{R \to \infty} \frac{1}{\mathrm{vol}(B_R)} \sum_{\substack{x \in \Gamma_R \\ x - z \in \Gamma}} 1 = \lim_{R \to \infty} \frac{1}{\mathrm{vol}(B_R)} \mathrm{card}\left(\Gamma_R \cap (\Gamma_R - z)\right) = \mathrm{dens}(\Gamma)$$

are the same for all $z \in \Gamma - \Gamma = \Gamma$, and the autocorrelation is given by

$$\gamma_\Gamma = \mathrm{dens}(\Gamma) \sum_{z \in \Gamma} \delta_z = \mathrm{dens}(\Gamma)\delta_\Gamma .$$

In order to calculate the Fourier transform of the autocorrelation in the lattice case, *Poisson's summation formula* (PSF) plays an important part.

Theorem 3 (General PSF). *If Γ is a lattice in $\mathbb{R}^d$, with dual lattice*

$$\Gamma^* := \{ y \in \mathbb{R}^d \mid xy \in \mathbb{Z}, \ \text{for all } x \in \Gamma \} \, ,$$

and if $\Phi \in \mathcal{S}$, one has

$$\sum_{m \in \Gamma} \Phi(m) = \mathrm{dens}(\Gamma) \sum_{\ell \in \Gamma^*} \widehat{\Phi}(\ell) \, .$$

Moreover,

$$\widehat{\delta_\Gamma} = \mathrm{dens}(\Gamma) \delta_{\Gamma^*} \, .$$

Proof. See [45, Thm. 2.6 ff]. $\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad$ □

Corollary 3. *The scattering intensity measure in the lattice periodic case is given by*

$$\widehat{\gamma_\Gamma} = \mathrm{dens}(\Gamma)^2 \delta_{\Gamma^*} \, ,$$

which is a pure point measure that describes the Bragg peaks of the crystal.

This can easily be generalized to any measure of the form

$$\vartheta = \rho * \delta_\Gamma$$

with ρ some finite measure. Since the autocorrelation is well-defined, it can be calculated by

$$\gamma_\Gamma^{(\rho)} = \mathrm{dens}(\Gamma)(\rho * \tilde{\rho}) * \delta_\Gamma$$

and the diffraction then gives

$$\widehat{\gamma_\Gamma^{(\rho)}} = |\widehat{\rho}|^2 \cdot (\mathrm{dens}(\Gamma))^2 \cdot \delta_{\Gamma^*}$$

by an application of the convolution theorem. The finite measure ρ can accomodate the distribution of finitely many possibly different atoms over the unit cell of Γ as well as characteristic profiles of the atoms. The result shows up as the continuous modulation factor $|\widehat{\rho}|^2$ in the diffraction measure, see [20] for various applications.

Remark. Besides lattices there are other examples of pure point diffractive systems as regular model sets, also called cut and project sets [51]. In general, however, other spectral types, or mixtures, can occur [4, 36, 39, 61].

Chapter 3

Influence of randomness

In the last chapter, we analyzed the diffraction (scattering intensity) of fixed pointlike scatterers as for example crystals. However, in reality, the objects are never perfect. All systems are thermally, chemically or otherwise disturbed, which results in an uncertainty of the location or the occupation with the different scatterers. This can be modeled by a stochastic modification of perfect structures. (With respect to the location this has been done for example in [34].)

In this context, one is interested in the influence of the randomness (disorder) on the diffraction. In practice, one observes only a slight modification of the pure point part and the diffuse scattering. A realistic modeling should be in agreement with this observation. In particular, it is interesting to investigate whether a stochastic description will predict the absence of singular continuous components.

In this chapter, we will be concerned with the random occupation of point sets by different scatterers, so-called *particle gases*. Let $W := \{c_1, \ldots, c_n\}$, $n \in \mathbb{N}$, with $c_i \in \mathbb{C}$, $1 \leqslant i \leqslant n$, be the set of possible scattering strengths representing the different scatterers.

We start with particle gases on fixed FLC point sets. They may be modeled by random fields.

3.1 Particle gases on fixed point sets

We go on with the crystals considered at the end of the last chapter. Let $\Gamma := \mathbb{Z}^d$ (which results in $\Gamma - \Gamma = \mathbb{Z}^d$), and consider the random field $(H_x)_{x \in \Gamma}$ with $H_x : W^\Gamma \to \mathbb{C}$, $H_x(\omega) = \omega_x$. Since Γ is a lattice, the particle gas is a lattice gas and we have

Lemma 1. *Let μ_Γ be a $\mathbb{Z}^d$-ergodic measure on $(W^\Gamma, \mathcal{W}^\Gamma)$. Then, the autocorrelation of the lattice gas exists μ_Γ-a.s. and is given by*

$$\gamma_\Gamma^{(H)} = |\mu_\Gamma(H_0)|^2 \, \gamma_\Gamma + \mathrm{dens}(\Gamma) \sum_{z \in \Gamma - \Gamma} \mathrm{cov}_{\mu_\Lambda}(H_0, \overline{H_{-z}}) \, \delta_z \, . \tag{3.1}$$

Proof. Let T_x denote the shift map, i.e., let $T_x(H_0\overline{H_{-z}}) := H_x\overline{H_{x-z}}$. Due to Birkhoff's ergodic theorem [41, Chapter 2], one has μ_Γ-a.s.:

$$\eta_\Gamma^{(H)}(z) = \lim_{r \to \infty} \frac{1}{\mathrm{vol}(B_r)} \sum_{\substack{x \in \Gamma_r \\ z \in \Gamma}} T_x(H_0\overline{H_{-z}}) = \lim_{r \to \infty} \frac{\mathrm{card}(\Gamma_r)}{\mathrm{vol}(B_r)} \, \mu_\Gamma(H_0\overline{H_{-z}})$$

$$= \mathrm{dens}(\Gamma) \, \mu_\Gamma(H_0\overline{H_{-z}}) \, .$$

Then, by using the fact that $\mu_\Gamma(\overline{H_{-z}}) = \mu_\Gamma(\overline{H_0})$ for all $z \in \Gamma$, one has

$$
\begin{aligned}
\gamma_\Gamma^{(H)} &= \sum_{z \in \Gamma - \Gamma} \operatorname{dens}(\Gamma) \, \mu_\Gamma(H_0 \overline{H_{-z}}) \, \delta_z \\
&= \sum_{z \in \Gamma - \Gamma} \operatorname{dens}(\Gamma) \, |\mu_\Gamma(H_0)|^2 \, \delta_z + \sum_{z \in \Gamma - \Gamma} \operatorname{dens}(\Gamma) \, \left(\mu_\Gamma(H_0 \overline{H_{-z}}) - |\mu_\Gamma(H_0)|^2 \right) \, \delta_z \\
&= |\mu_\Gamma(H_0)|^2 \, \gamma_\Gamma + \operatorname{dens}(\Gamma) \sum_{z \in \Gamma - \Gamma} \operatorname{cov}_{\mu_\Gamma}(H_0, \overline{H_{-z}}) \, \delta_z \,,
\end{aligned}
$$

which establishes the claim. $\qquad \square$

Theorem 4. *Let μ_Γ be a $\mathbb{Z}^d$-ergodic measure on $(W^\Gamma, \mathcal{W}^\Gamma)$. If*

$$
\sum_{z \in \Gamma - \Gamma} |\operatorname{cov}_{\mu_\Gamma}(H_0, \overline{H_{-z}})| < \infty \,,
$$

the diffraction of the lattice gas μ_Γ-a.s. exists, is $\mathbb{Z}^d$-periodic and consists of a pure point part and an absolutely continuous part with continuous density. No singular continuous part is present.

Proof. Due to Lemma 1, the autocorrelation measure is given by

$$
\gamma_\Gamma^{(H)} = |\mu_\Gamma(H_0)|^2 \, \gamma_\Gamma + \operatorname{dens}(\Gamma) \sum_{z \in \Gamma - \Gamma} \operatorname{cov}_{\mu_\Gamma}(H_0, \overline{H_{-z}}) \, \delta_z \,.
$$

This holds for μ_Γ-almost all elements of our lattice gas ensemble (respectively for μ_Γ-almost all realisations of the corresponding stochastic process).

The first part of the autocorrelation gives, under Fourier transform, the pure point part of the diffraction measure, by means of the Poisson summation formula for lattice Dirac combs (compare Section 2.3). This part is clearly $\mathbb{Z}^d$-periodic.

Furthermore, due to the assumption and Proposition 4, the second part of the autocorrelation, under explicit Fourier transform, gives the absolutely continuous part of the diffraction measure. It is again $\mathbb{Z}^d$-periodic (compare [5, 8] for a more general explanation of this phenomenon), and our claim follows. $\qquad \square$

We have to note that the stated theorem is limited to the lattice case. It can be extended to general periodic objects but periodicity has to be ensured. An exception is the case of independent variables, i.e., μ_Γ being the product measure. In this case, Γ may be any FLC set since one may use the law of large numbers (compare [3, 9]). However, in general, one has to consider particle gases on dynamical systems. These will be introduced in the following.

3.2 Particle gases on dynamical systems

A particle gas on a dynamical system can be defined by a random measure.

Definition 5. *A random measure with phase space $\mathbb{R}^d$ is a measurable mapping from a probability space into $\left(\mathcal{M}(\mathbb{R}^d), \mathcal{B}(\mathcal{M}(\mathbb{R}^d)) \right)$.*

In the following we will consider random measures with respect to different probability spaces. These are specified before we finally determine the diffraction of the random measures.

3.2.1   Dynamical systems

At first, we consider a dynamical system of FLC sets. This is the base of the larger dynamical system of marked FLC sets, considered afterwards.

Proposition 5. *For a point set $\Gamma \subset \mathbb{R}^d$ the following are equivalent:*

1. *Γ is of finite local complexity.*

2. *The orbit $\{x + \Gamma \,|\, x \in \mathbb{R}^d\}$ is precompact in the local topology (LT), where two point sets are close if, after a small translation, they agree on a large ball around $0 \in \mathbb{R}^d$.*

Proof. See [55, Prop. 2.3].   □

Due to Proposition 5, for each FLC set $\Gamma \subset \mathbb{R}^d$, the *hull*

$$\mathbb{X}(\Gamma) := \overline{\{x + \Gamma \,|\, x \in \mathbb{R}^d\}}^{\text{LT}}$$

is compact, and $(\mathbb{X}(\Gamma), \mathbb{R}^d)$ forms a *topological dynamical system*, on which one can define translation invariant probability measures, see [55] for details. The latter, at this point, need neither be unique nor ergodic.

This can be seen by combining $2\mathbb{Z}$ with an arbitrary (e.g., random) subset of $2\mathbb{Z}+1$, which always produces an FLC set. When using a standard Bernoulli process (e.g., coin tossing) to decide on the occupation of the sites from $2\mathbb{Z}+1$, the hull $\mathbb{X}(\Gamma)$ almost surely contains the set $2\mathbb{Z}$ as well as the set $\mathbb{Z}$ (since there are 0- and 1-sequences of arbitrary length in almost all realisations of the Bernoulli process). Therefore different probability measures on $\mathbb{X}(\Gamma)$ clearly exist.

However, in the following, we fix an FLC set Λ such that $(\mathbb{X}(\Lambda), \mathbb{R}^d)$ is uniquely ergodic and denote $\mathbb{X}(\Lambda)$ by $\mathbb{X}$. Due to unique ergodicity, we then have a unique translation invariant probability measure ν on $\mathbb{X}$ and may consider the measurable dynamical system $(\mathbb{X}, \mathbb{R}^d, \nu)$.

Moreover, we may now consider certain marked FLC point sets, more precisely, the space

$$\mathbb{Y} := \bigcup_{\Gamma \in \mathbb{X}} W^\Gamma \,.$$

In accordance to [55] we denote by $\mathfrak{D}$ the set of all closed and discrete subsets of $\mathbb{R}^d$. Instead of these point sets themselves, we consider marked point sets, i.e., the space $\mathfrak{D}_W = \bigcup_{\Gamma \in \mathfrak{D}} W^\Gamma$. Our first task is to define a topology, more specifically a uniformity on $\mathfrak{D}_W$ which makes it a complete uniform Hausdorff space. Analogously to the pure point set case, where two point sets Γ_1 and Γ_2 are close if, after a small translation, they coincide on a large compact region, two marked point sets $\omega_1 = \bigcup_{x \in \Gamma_1} \{x, \omega_x^{(1)}\}$ and $\omega_2 = \bigcup_{x \in \Gamma_2} \{x, \omega_x^{(2)}\}$ are close if this holds also for the marks.

We use the following notation:

- $\omega + y := \bigcup_{x \in \Gamma} \{x + y, \omega_x\}$ for $y \in \mathbb{R}^d$

- $\omega_K := \omega \cap K = \bigcup_{x \in \Gamma \cap K} \{x, \omega_x\}$ is the restriction to a compact set $K \subset \mathbb{R}^d$

- $\omega =: \omega_K \otimes \omega_{\bar{K}}$ with $\bar{K} = \mathbb{R}^d \backslash K$ (the complement of K) and $K \subset \mathbb{R}^d$

- $\Gamma(\omega)$ denotes the underlying point set of ω ($\Gamma(\omega_K)$ alike)

A sequence $\omega^{(n)}$, $n \in \mathbb{N}$, converges to ω if for all $\varepsilon > 0$ and $K \subset \mathbb{R}^d$ there exists an $N \in \mathbb{N}$ such that for all $n > N$ $\tilde{\omega}_K^{(n)} = \omega_K$, where $\tilde{\omega}^{(n)} = \omega^{(n)} + \varepsilon^{(n)}$ with $|\varepsilon^{(n)}| < \varepsilon$.

As in the pure point set case in [55], the set

$$U_{K,V} := \{(\omega_1, \omega_2) \in \mathfrak{D}_W \times \mathfrak{D}_W \mid \exists s \in V : \omega_1 \cap K = (s + \omega_2) \cap K\} \qquad (3.2)$$

forms a base of a uniform structure $\mathfrak{U}$ on $\mathfrak{D}_W$. The topology on $\mathfrak{D}_W$ (LT') induced by this uniformity is given by taking the sets $U_{K,V}[\omega]$ as a base of neighbourhoods of $\omega \in \mathfrak{D}_W$. The uniformity and likewise the topology are chosen such that we are able to generalize the main theorems of the pure point set case. First of all, the uniform structure separates points. Hence $\mathfrak{D}_W$ becomes a uniform Hausdorff space. Moreover, we have the two following statements.

Proposition 6. $\mathfrak{D}_W$ *is complete in the uniformity defined by* (3.2).

Proof. Clear, since every Cauchy net in $\mathfrak{D}_W$ has an equivalent in $\mathfrak{D}$; $\mathfrak{D}$ is complete due to [55, Prop. 2.1] and the limit point with all possible marks is in $\mathfrak{D}_W$. $\qquad\square$

Proposition 7.

$$\mathbb{Y} = \overline{\bigcup_{\Gamma \in \{x + \Lambda \mid x \in \mathbb{R}^d\}} W^\Gamma}^{LT'}$$

Proof. Clear, since $\omega \in \mathfrak{D}_W$ is an accumulation point with respect to LT' if and only if the underlying point set is an accumulation point with respect to LT. $\qquad\square$

It follows

Theorem 5. *If Λ is of finite local complexity, $\mathbb{Y}$ is a compact Hausdorff space.*

Proof. Analogously to the proof of Proposition 5, one can show that $\bigcup_{\Gamma \in \{x + \Lambda \mid x \in \mathbb{R}^d\}} W^\Gamma$ is precompact since Λ is of finite local complexity and W is finite. Due to Propositions 6 and 7, $\mathbb{Y}$ is complete as a closed subset of $\mathfrak{D}_W$, and precompact. Thus, $\mathbb{Y}$ is compact (compare [42, Chap. 6, Thm. 32]). $\qquad\square$

Remark. The critical part in the compactness analysis is the compactness of $\mathbb{X}$ (shown in [55]). The compactness of $\mathbb{Y}$ then follows immediately.

Proposition 8. $\mathfrak{D}_W$ *with the uniformity defined by* (3.2) *is metrizable.*

Proof. We define an alternative base of the uniform structure given by (3.2):

$$\tilde{U}_{B_{1/\varepsilon}, B_\varepsilon} := \{(\omega_1, \omega_2) \in \mathfrak{D}_W \times \mathfrak{D}_W \mid \exists s, t \in B_\varepsilon : (\omega_1 + s) \cap B_{1/\varepsilon} = (\omega_2 + t) \cap B_{1/\varepsilon}\}$$

Analogously to the arguments in [55], one can prove that the $\tilde{U}_{B_{1/\varepsilon}, B_\varepsilon}$, $\varepsilon \in \mathbb{N} \cup 1/\mathbb{N}$, form a countable base of $\mathfrak{U}$ since for any $U_{K,V}$ there is a $\tilde{U}_{B_{1/\varepsilon}, B_\varepsilon}$ such that $\tilde{U}_{B_{1/\varepsilon}, B_\varepsilon} \subset U_{K,V}$ (compare [42, Chap. 6]). In combination with the Hausdorff property of $\mathfrak{D}_W$, this results in the applicability of the metrization theorem (see [42, Chap. 6, Thm. 13]). Hence, $(\mathfrak{D}_W, \mathfrak{U})$ is metrizable. $\qquad\square$

So far we have defined the dynamical systems $(\mathbb{X}, \mathbb{R}^d)$ as well as $(\mathbb{Y}, \mathbb{R}^d)$. Moreover we have fixed the measure ν such that $(\mathbb{X}, \mathbb{R}^d)$ is uniquely ergodic. We now consider a measure on the second dynamical system.

Theorem 6. *Let $\mathcal{B}$ denote the Borel sets. Every translation invariant measure μ on $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}))$ can be disintegrated with respect to $(\mathbb{X}, \mathcal{B}(\mathbb{X}), \nu)$ and therefore has the representation*

$$\mu(A) = \int_{\mathbb{Y}} \mathbb{1}_A(\omega) \, \mathrm{d}\mu(\omega) = \int_{\mathbb{X}} \int_{W^\Gamma} \mathbb{1}_A(\omega) \, \mathrm{d}\mu_\Gamma(\omega) \, \mathrm{d}\nu(\Gamma) \ .$$

Proof. $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}), \mu)$ is a regular measure space since $\mathbb{Y}$ is a compact metric space (due to Proposition 8 and Theorem 5) and $\mathcal{B}(\mathbb{Y})$ consists of all Borel sets in $\mathbb{Y}$ (compare [28, Def. 5.5]). Moreover, the function $\Gamma \colon \mathbb{Y} \to \mathbb{X}$ which maps each marked point set on its underlying point set defines a homomorphism from $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}), \mu)$ to $(\mathbb{X}, \mathcal{B}(\mathbb{X}), \nu)$ since the image measure given by $\mu\left(\Gamma^{-1}(A)\right)$ equals $\nu(A)$ for all $A \in \mathcal{B}(\mathbb{X})$. This follows from the fact that the image measure is translation invariant (due to the translation invariance of μ) and there is only one translation invariant probability measure on $(\mathbb{X}, \mathcal{B}(\mathbb{X}))$ due to the unique ergodicity of ν. (Compare [28, Chap. 5].) Due to the disintegration theorem (see [28, Thm. 5.8]) we get the representation. $\qquad\square$

We have now defined two probability spaces. In the following we consider the diffraction of random measures with respect to these probability spaces.

3.2.2 Diffraction of particle gases

At first, the diffraction of a random measure with respect to $(\mathbb{X}, \mathcal{B}(\mathbb{X}), \nu)$ is analyzed.

We allow the scattering strengths at the various positions of the objects to be different but fixed. They are defined by functions f_x with certain restrictions. The restrictions ensure that

$$\delta^{(f)} : (\mathbb{X}, \mathcal{B}(\mathbb{X}), \nu) \to \left(\mathcal{M}(\mathbb{R}^d), \mathcal{B}(\mathcal{M}(\mathbb{R}^d))\right), \quad \Gamma \mapsto \sum_{x \in \Gamma} f_x(\Gamma) \, \delta_x \ ,$$

is a random measure. We are interested in the autocorrelation of this random measure.

Proposition 9. *Let $(f_x)_{x \in \mathbb{R}^d}$ be a family of functions $f_x : \mathbb{X} \to \mathbb{C}$ such that for all $z \in \mathbb{R}^d$*

$$\delta^{(f,z)} : (\mathbb{X}, \mathcal{B}(\mathbb{X}), \nu) \to \left(\mathcal{M}(\mathbb{R}^d), \mathcal{B}(\mathcal{M}(\mathbb{R}^d))\right), \quad \Gamma \mapsto \sum_{x, x-z \in \Gamma} f_x(\Gamma)\overline{f_{x-z}(\Gamma)} \, \delta_x$$

are stationary random measures. Then, the autocorrelation of $\delta^{(f)}$ exists ν-a.s. and is given by the coefficients

$$\eta^{(f)}(z) = \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} f_x(\Gamma)\overline{f_{x-z}}(\Gamma) \, \mathrm{d}\nu(\Gamma) \ ,$$

where $\mathbb{U}^d$ is the unit cube in $\mathbb{R}^d$.

Proof. We may apply the ergodic theorem ([21, Cor. 12.2.V]):

$$\eta^{(f)}(z) = \lim_{r \to \infty} \frac{1}{\mathrm{vol}(B_r)} \sum_{\substack{x \in \Gamma_r \\ x-z \in \Gamma}} f_x \overline{f_{x-z}} = \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} f_x(\Gamma)\overline{f_{x-z}}(\Gamma) \, \mathrm{d}\nu(\Gamma) \quad \nu\text{-a.s.}$$

$\qquad\square$

One can easily show that the assumptions of Proposition 9 are fulfilled if the scattering strengths are the same at all positions. Moreover, one has

Proposition 10. *Each $\Gamma \in \mathbb{X}$ has the same autocorrelation and diffraction.*

Proof. Due to [55, Cor. 3.3], $(\mathbb{X}, \mathbb{R}^d)$ is uniquely ergodic if and only if the frequencies of finite patterns exist in every $\Gamma \in \mathbb{X}$ and are independent of the particular choice of Γ. $\square$

Remark. The existence of the frequencies of finite patterns in every $\Gamma \in \mathbb{X}$ and the independence of the choice of Γ is tantamount to uniform frequencies for a fixed point set.

From now on, the diffraction of a random measure with respect to $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}), \mu)$ is analyzed. In this case, the scattering strengths at the various positions of the objects are no longer fixed. Instead, we are concerned with a random occupation of the positions with the scattering strengths. The resulting particle gas is defined by

$$\delta^{(H)} := \sum_{x \in \Gamma} H_x \, \delta_x$$

with random variables Γ specifying the point set (i.e., $\Gamma \colon \mathbb{Y} \to \mathbb{X}$, $\omega \mapsto \Gamma(\omega)$) and H_x, $x \in \mathbb{R}^d$, specifying the scattering strengths at the various positions (i.e., $\forall x \in \mathbb{R}^d$, $H_x \colon \mathbb{Y} \to \mathbb{C}$, $H_x(\omega) = \omega_x$).

Lemma 2. *The function $\delta^{(H)} \colon \mathbb{Y} \to \mathcal{M}(\mathbb{R}^d)$, $\omega \mapsto \sum_{x \in \Gamma(\omega)} \omega_x \, \delta_x$ is $\mathcal{B}(\mathbb{Y})$-measurable and thus defines a random measure (compare Definition 5).*

Proof. We show the continuity of $\delta^{(H)}$, i.e., for any $\varepsilon > 0$ there must be found an $N \in \mathbb{N}$ such that for all $n \geqslant N$

$$\left| \sum_{y \in \mathrm{supp}\, f \cap \Gamma(\omega^{(n)})} \omega_y^{(n)} f(y) - \sum_{x \in \mathrm{supp}\, f \cap \Gamma(\omega)} \omega_x f(x) \right| < \varepsilon$$

with $\left(\omega^{(n)} \right)_{n \in \mathbb{N}}$ a sequence of marked point sets converging to ω and $f \in \mathcal{K}$ with support $\mathrm{supp}(f)$.

Due to convergence of $\left(\omega^{(n)} \right)_{n \in \mathbb{N}}$, for arbitrary $\tilde{\varepsilon} > 0$ and $K \supset \mathrm{supp}\, f$ there exists an $N \in \mathbb{N}$ such that for all $n > N$ $\tilde{\omega}_K^{(n)} = \omega_K$, where $\tilde{\omega}^{(n)} = \omega^{(n)} + \varepsilon^{(n)}$ with $|\varepsilon^{(n)}| < \tilde{\varepsilon}$. Moreover,

$$\left| \sum_{y \in \mathrm{supp}\, f \cap \Gamma(\omega^{(n)})} \omega_y^{(n)} f(y) - \sum_{x \in \mathrm{supp}\, f \cap \Gamma(\omega)} \omega_x f(x) \right|$$

$$= \left| \sum_{x \in \mathrm{supp}\, f \cap \Gamma(\omega)} \left(\tilde{\omega}_x^{(n)} f\left(x - \varepsilon^{(n)} \right) - \omega_x f(x) \right) \right|$$

$$= \left| \sum_{x \in \mathrm{supp}\, f \cap \Gamma(\omega)} \left(\tilde{\omega}_x^{(n)} \left(f\left(x - \varepsilon^{(n)} \right) - f(x) \right) + f(x) \left(\tilde{\omega}_x^{(n)} - \omega_x \right) \right) \right|$$

$$= \left| \sum_{x \in \mathrm{supp}\, f \cap \Gamma(\omega)} \tilde{\omega}_x^{(n)} \left(f\left(x - \varepsilon^{(n)} \right) - f(x) \right) \right| .$$

Since f is continuous and the sum is finite, for any $\varepsilon > 0$, $\tilde{\varepsilon}$ can be chosen such that

$$\left| \sum_{x \in \mathrm{supp}\, f \cap \Gamma(\omega)} \tilde{\omega}_x^{(n)} \left(f\left(x - \varepsilon^{(n)} \right) - f(x) \right) \right| < \varepsilon .$$

Measurability then follows from continuity. $\square$

Furthermore, ergodicity of the measure μ ensures the existence of the autocorrelation (as we will see in the next proposition).

Proposition 11. *Let μ be an $\mathbb{R}^d$-ergodic measure on $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}))$. Then, the autocorrelation measure of $\delta^{(H)}$ exists μ-a.s. and is given by the coefficients*

$$\eta^{(H)}(z) = \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mu_\Gamma(H_x \overline{H_{x-z}}) \, d\nu(\Gamma) \ .$$

Moreover, if (for all $z \in \mathbb{R}^d$) $\delta^{(\mathbb{E},z)}, \delta^{(\mathbb{E})} : \mathbb{X} \to \mathcal{M}(\mathbb{R}^d)$, $\Gamma \mapsto \sum_{x, x-z \in \Gamma} \mu_\Gamma(H_x) \mu_\Gamma(\overline{H_{x-z}}) \, \delta_x$ and $\Gamma \mapsto \sum_{x \in \Gamma} \mu_\Gamma(H_x) \, \delta_x$, respectively, are stationary random measures,

$$\eta^{(H)}(z) = \eta^{(\mathbb{E})}(z) + \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mathrm{cov}_{\mu_\Gamma}(H_x, \overline{H_{x-z}}) \, d\nu(\Gamma)$$

with $\eta^{(\mathbb{E})}(z)$ the autocorrelation coefficients of $\delta^{(\mathbb{E})}$.

Proof. The function $\delta^{(H,z)} : \mathbb{Y} \to \mathcal{M}(\mathbb{R}^d)$, $\omega \mapsto \sum_{x, x-z \in \Gamma(\omega)} \omega_x \overline{\omega_{x-z}} \, \delta_x$ is $\mathcal{B}(\mathbb{Y})$-measurable and hence defines a random measure (analogously to Lemma 2). It is clearly stationary (compare [21, Def. 12.1.II]). Therefore, we may apply the ergodic theorem ([21, Cor. 12.2.V]):

$$\eta^{(H)}(z) = \lim_{r \to \infty} \frac{1}{\mathrm{vol}(B_r)} \sum_{\substack{x \in \Gamma_r \\ x-z \in \Gamma}} H_x \overline{H_{x-z}} = \mu\bigg(\sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} H_x \overline{H_{x-z}} \bigg) \quad \mu\text{-a.s.}$$

Due to the structure of disintegration (see Theorem 6) this results μ-a.s. in

$$\eta^{(H)}(z) = \int_{\mathbb{Y}} \sum_{\substack{x \in \Gamma(\omega) \cap \mathbb{U}^d \\ x-z \in \Gamma(\omega)}} \omega_x \overline{\omega_{x-z}} \, d\mu(\omega) = \int_{\mathbb{X}} \int_{W^\Gamma} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \omega_x \overline{\omega_{x-z}} \, d\mu_\Gamma(\omega) \, d\nu(\Gamma)$$

$$= \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \int_{W^\Gamma} \omega_x \overline{\omega_{x-z}} \, d\mu_\Gamma(\omega) \, d\nu(\Gamma) = \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mu_\Gamma(H_x \overline{H_{x-z}}) \, d\nu(\Gamma)$$

Under the additional assumption that (for all $z \in \mathbb{R}^d$) $\delta^{(\mathbb{E},z)}$ and $\delta^{(\mathbb{E})}$ are stationary random measures, the autocorrelation of $\delta^{(\mathbb{E})}$ exists ν-a.s. due to Proposition 9 and

$$\eta^{(H)}(z) = \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mu_\Gamma(H_x \overline{H_{x-z}}) \, d\nu(\Gamma)$$

$$= \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mu_\Gamma(H_x) \mu_\Gamma(\overline{H_{x-z}}) \, d\nu(\Gamma) + \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mathrm{cov}_{\mu_\Gamma}(H_x, \overline{H_{x-z}}) \, d\nu(\Gamma)$$

$$= \eta^{(\mathbb{E})}(z) + \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mathrm{cov}_{\mu_\Gamma}(H_x, \overline{H_{x-z}}) \, d\nu(\Gamma) \quad \mu\text{-a.s.}$$

$\square$

Moreover, under additional assumptions, we can show the absence of a singular continuous part in the diffraction of the particle gas $\delta^{(H)}$.

Theorem 7. *Let μ be an $\mathbb{R}^d$-ergodic measure on $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}))$. If $\delta^{(\mathbb{E})}$ and $\delta^{(\mathbb{E},z)}$ (for all $z \in \mathbb{R}^d$) define stationary random measures and there is no singular continuous part present in the diffraction of $\delta^{(\mathbb{E})}$ and*

$$\sum_{z \in \Gamma - \Gamma} \left| \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma' \cap \mathbb{U}^d \\ x - z \in \Gamma'}} \mathrm{cov}_{\mu_{\Gamma'}}(H_x, \overline{H_{x-z}}) \, \mathrm{d}\nu(\Gamma') \right| < \infty \,,$$

for all $\Gamma \in \mathbb{X}$, no singular continuous part will occur in the diffraction of $\delta^{(H)}$.

Proof. Due to Propositions 2 and 11, the autocorrelation of $\delta^{(H)}$ is μ-a.s. given by

$$\gamma^{(H)} = \sum_{z \in \Gamma - \Gamma} \eta^{(\mathbb{E})}(z) \, \delta_z + \sum_{z \in \Gamma - \Gamma} \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma' \cap \mathbb{U}^d \\ x - z \in \Gamma'}} \mathrm{cov}_{\mu_{\Gamma'}}(H_x, \overline{H_{x-z}}) \, \mathrm{d}\nu(\Gamma') \, \delta_z \,.$$

Since the diffraction is given by the Fourier transform of $\gamma^{(H)}$, it consists of the diffraction of $\delta^{(\mathbb{E})}$ in addition to the Fourier transform of the second sum. The latter, however, defines an absolutely continuous measure on $\mathbb{R}^d$ (due to the assumption and Proposition 4). Therefore, the diffraction of $\delta^{(H)}$ equals the diffraction of $\delta^{(\mathbb{E})}$ except for an additional absolutely continuous part, but there is no singular continuous part present. $\qquad\square$

Hence, under the assumptions of Theorem 7, the stochastic description predicts the absence of singular continuous components. In order to get some examples satisfying the assumptions we will consider so-called Gibbs measures.

3.3   Gibbs measures

A *Gibbs measure* is "a mathematical idealization of an equilibrium state of a physical system which consists of a very large number of interacting components" ([31, p. 5]). Such a measure is appropriate to define the random occupation of point sets by different scatterers. In order to deal with the corresponding particle gases, it is necessary to define Gibbs measures on the dynamical system of FLC sets. Therefore, we will recapitulate the theory of Gibbs states (compare [31, 53]) and use it to construct ergodic measures on $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}))$.

Remark. In general, Gibbs measures arise as limits of Boltzmann distributions. However, due to possible ambiguity, a powerful formalism is required. This is already the case for Gibbs measures on point sets and becomes more extensive in the case of Gibbs measures on dynamical systems.

Let Ω be a set representing the basic phase space and $\mathcal{A}$ a σ-field of subsets of Ω representing the observables. Moreover, let $\mathcal{I}$ be a partially ordered index set such that the sub-σ-fields $\{\mathcal{T}_K\}_{K \in \mathcal{I}}$ are decreasing, i.e., $\mathcal{T}_{K_2} \subset \mathcal{T}_{K_1}$ whenever $K_1 \leqslant K_2$, and $\{\mathcal{A}_K\}_{K \in \mathcal{I}}$ are increasing.

Definition 6. *A collection $V = \{\kappa_K\}_{K \in \mathcal{I}}$ of probability kernels is a specification if*

- $\kappa_K(A \,|\, \cdot)$ *is $\mathcal{T}_K$-measurable for all $A \in \mathcal{A}$, $K \in \mathcal{I}$,*

- $\kappa_K(C \mid \cdot) = \mathbb{1}_C$ for all $C \in \mathcal{T}_K$, $K \in \mathcal{I}$,

- $\kappa_{K_2}\kappa_{K_1} = \kappa_{K_2}$ whenever $K_1 \leqslant K_2$.

The Gibbs states $G(V)$ with respect to a given specification V are then given due to the following definition.

Definition 7. Let V be a specification. $G(V)$ is the set of all measures on $(\Omega, \mathcal{A})$ for which the following condition holds. For all $K \in \mathcal{I}$, $A \in \mathcal{A}$ and $C \in \mathcal{T}_K$,

$$\mu(A \cap C) = \int_C \kappa_K(A \mid \omega) \, \mathrm{d}\mu(\omega) \,. \tag{3.3}$$

In the following, we consider Gibbs states on different phase spaces. We start with the phase space $(\Omega, \mathcal{A}) := (W^\Gamma, \mathcal{W}^\Gamma) = (W, \mathcal{W})^\Gamma$ defined by the finite discrete state space $(W, \mathcal{W})$ and a countably infinite set of sites Γ. Later on we consider the phase space $(\Omega, \mathcal{A}) := (\mathbb{Y}, \mathcal{B}(\mathbb{Y}))$.

In both cases $\mathcal{I}$ is the set of compact subsets of $\mathbb{R}^d$. Moreover, we consider a special class of Gibbs states. They are given by an interaction potential Φ.

Definition 8. Let $\mathcal{F}$ be the set of all non-empty finite subsets of $\mathbb{R}^d$. An (interaction) potential $\Phi = (\Phi_S)_{S \in \mathcal{F}}$ is a family of $\mathcal{W}^S$-measurable functions $\Phi_S : \Omega \mapsto \mathbb{R}$ such that, for all $\omega \in \Omega$ and $K \in \mathcal{I}$, the total energy

$$\mathcal{H}_K^\Phi(\omega) = \sum_{\substack{S \in \mathcal{F} \\ S \cap K \neq \varnothing, S \subset \Gamma(\omega)}} \Phi_S(\omega)$$

of ω in K for Φ exists. The partition function for a subsystem K is given by

$$Z_K^\Phi(\omega) = \sum_{\lambda \in W^{\Gamma(\omega_K)}} \mathrm{e}^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})} \,.$$

Regarding the phase space $(W, \mathcal{W})^\Gamma$, for all $K \in \mathcal{I}$, $\mathcal{A}_K := \mathcal{W}_K^\Gamma := \mathcal{W}^{\Gamma \cap K}$ is the sigma field consisting of those events which only depend on the coordinates of Γ in K and $\mathcal{T}_K^\Gamma := \mathcal{W}_{\mathbb{R}^d \setminus K}^\Gamma$ the sigma field consisting of those events which only depend on the coordinates of Γ outside of K.

Proposition 12. Let Φ be a potential and Γ a point set such that $Z_K^\Phi(\omega)$ is finite for all $K \in \mathcal{I}$ and $\omega \in W^\Gamma$. The family $V^{\Phi,\Gamma} = (\kappa_K^\Phi)_{K \in \mathcal{I}}$, defined by

$$\kappa_K^\Phi(A^\Gamma \mid \omega) := \frac{1}{Z_K^\Phi(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} \mathbb{1}_{A^\Gamma}(\lambda \otimes \omega_{\bar{K}}) \, \mathrm{e}^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})}$$

is a specification.

Proof. Due to [31, Prop. 2.5 and Remark 1.32]. $\square$

Remark. The measures μ_Γ^Φ satisfying $\mu_\Gamma^\Phi(A^\Gamma \cap C^\Gamma) = \int_{C^\Gamma} \kappa_K^\Phi(A^\Gamma \mid \omega) \, \mathrm{d}\mu_\Gamma^\Phi(\omega)$ for all $A^\Gamma \in \mathcal{W}^\Gamma$ and $C^\Gamma \in \mathcal{T}_K^\Gamma$ (for any $K \in \mathcal{I}$) are the Gibbs states on $(W, \mathcal{W})^\Gamma$ with respect to the potential Φ (compare Definition 7).

The next proposition gives a condition on the potential which ensures the uniqueness of the Gibbs measure.

Proposition 13. *Let $V^{\Phi,\Gamma}$ be a specification. For $S \in \mathcal{F}$, let $\mathrm{diam}(S)$ denote the diameter of S with respect to any metric $\mathrm{d}(x,y)$ and*

$$\mathcal{D}(\Phi_S) = \sup_{\zeta, \lambda \in W^\Gamma} |\Phi_S(\zeta) - \Phi_S(\lambda)| \,.$$

On the condition that

$$\sup_{u \in \Gamma} \sum_{\substack{S \in \mathcal{F} \cap \Gamma \\ u \in S}} \mathrm{e}^{\mathrm{diam}(S)}(|S|-1)\,\mathcal{D}(\Phi_S) \;<\; 2 \,, \tag{3.4}$$

the corresponding Gibbs measure μ_Γ^Φ is unique. Moreover, for all $x \in \Gamma$, and functions $H_x, \overline{H_x} : W^\Gamma \to \mathbb{C}$, $H_x(\omega) = \omega_x$ and $\overline{H_x}(\omega) = \overline{\omega_x}$,

$$\sum_{y \in \Gamma} \left|\mathrm{cov}_{\mu_\Gamma^\Phi}(H_x, \overline{H_y})\right| \leqslant \frac{\left(\sup_{i,j} |c_i - c_j|\right)^2}{4(1-\alpha)}$$

with

$$0 \leqslant \alpha \leqslant \sup_{u \in \Gamma} \sum_{\substack{S \in \mathcal{F} \cap \Gamma \\ u \in S}} \mathrm{e}^{\mathrm{diam}(S)}(|S|-1)\,\mathcal{D}(\Phi_S)/2 < 1 \,. \tag{3.5}$$

Proof. Due to (3.4) and [31, Prop. 8.8], $V^{\Phi,\Gamma}$ satisfies Dobrushin's condition. From Dobrushin's uniqueness theorem ([31, Thm. 8.7]), the uniqueness of μ_Γ^Φ follows. This is the reason why we may apply [31, Prop. 8.34] which states that

$$|\mathrm{cov}_{\mu_\Gamma^\Phi}(f,g)| \leqslant \tfrac{1}{4} \sum_{u,v \in \Gamma} \mathcal{D}_u(f) D_{uv}^\Gamma \mathcal{D}_v(g) \,, \tag{3.6}$$

where f and g are bounded quasilocal functions on W^Γ,

$$\mathcal{D}_u(f) = \sup\{|f(\zeta) - f(\lambda)| \,|\, \zeta = \lambda \text{ off } u\}$$

and $D_{uv}^\Gamma := \left(\sum_{n=0}^\infty \left(C^\Gamma\right)^n\right)_{uv}$ with Dobrushin's interaction matrix C^Γ defined by

$$C_{uv}^\Gamma = \sup_{A^\Gamma \in \mathcal{W}^\Gamma} \left\{ |\kappa_{B_\varepsilon(u)}^\Phi(A^\Gamma \,|\, \zeta) - \kappa_{B_\varepsilon(u)}^\Phi(A^\Gamma \,|\, \lambda)| \,|\, \zeta = \lambda \text{ off } v \right\}$$

for all $u, v \in \Gamma$ and ε such that $\Gamma \cap B_\varepsilon(u) = \{u\}$. Recall that a measurable function is called *quasilocal* when

$$\lim_{F \in \mathcal{F}} \sup_{\substack{\zeta, \lambda \in W^\Gamma \\ \zeta_{|F} = \lambda_{|F}}} |f(\zeta) - f(\lambda)| = 0 \,.$$

Here, the notation $\lim_{F \in \mathcal{F}}$ means that the limit is taken along sets, where more and more points are added, so that $|F| \nearrow \infty$.

Let $f(\omega) = \omega_x$ and $g(\omega) = \overline{\omega_y}$. This results in

$$\mathcal{D}_u(\omega_x) = \begin{cases} \sup_{i,j} |c_i - c_j|, & \text{if } u = x, \\ 0, & \text{otherwise,} \end{cases} \quad \text{and} \quad \mathcal{D}_v(\overline{\omega_y}) = \begin{cases} \sup_{i,j} |c_i - c_j|, & \text{if } v = y, \\ 0, & \text{otherwise.} \end{cases}$$

Then, (3.6) implies

$$\sum_{y \in \Gamma} |\operatorname{cov}_{\mu_\Gamma^\Phi}(f,g)| \leqslant \sum_{y \in \Gamma} \frac{\left(\sup_{i,j} |c_i - c_j|\right)^2}{4} D_{xy}^\Gamma \leqslant \frac{\left(\sup_{i,j} |c_i - c_j|\right)^2}{4(1-\alpha)} ,$$

since [31, Remark 8.26] states that, for all $x \in \Gamma$, $\sum_{y \in \Gamma} D_{xy}^\Gamma \leqslant 1/(1-\alpha)$ with

$$\alpha := \sup_{u \in \Gamma} \sum_{v \in \Gamma} C_{uv}^\Gamma \mathrm{e}^{\mathrm{d}(u,v)} \leqslant \sup_{u \in \Gamma} \sum_{\substack{S \in \mathcal{F} \cap \Gamma \\ u \in S}} \mathrm{e}^{\operatorname{diam}(S)} (|S| - 1)\, \mathcal{D}(\Phi_S)/2 < 1$$

(due to the proof of [31, Remark 8.26]). $\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\square$

In order to get examples of potentials satisfying the assumptions of the last theorem we now restrict ourselves to potentials of finite or short range.

Definition 9. *A potential $(\Phi_S)_{S \in \mathcal{F}} = (\beta \Phi_S^*)_{S \in \mathcal{F}}$ with $\beta := 1/(k_B T)$ (the inverse temperature) is called a finite range potential if for each point $x \in \mathbb{R}^d$ there is a ball with radius R such that $\Phi_S = 0$ unless $S \subset B_R(x)$. The smallest R fulfilling this condition is called the range of the potential.*

Definition 10. *A short range (pair) interaction potential for a point set $\Gamma \subset \mathbb{R}^d$ is given by*

$$\Phi_S(\omega) = \begin{cases} \beta\phi(\omega_{|\{x,y\}})J(x-y), & \text{if } S = \{x,y\}, \\ 0, & \text{otherwise,} \end{cases}$$

with $\phi : W \times W \to \mathbb{R}$ and bounded function J satisfying either

$$\sum_{z \in \Gamma - \Gamma} \mathrm{e}^{t\|z\|}|J(z)| = const < \infty \quad or \quad \sum_{z \in \Gamma - \Gamma} \|z\|^p |J(z)| = const < \infty \qquad (3.7)$$

for some positive constant t and $p > 1$.

Remark. It can be shown that Condition (3.7) holds if $\Gamma - \Gamma$ is uniformly discrete and $|J(z)| = \mathcal{O}\left(\mathrm{e}^{-s\|z\|}\right)$ for $\|z\| \to \infty$ and some positive constant s or $|J(z)| = \mathcal{O}\left(\|z\|^{-\tilde{p}}\right)$ for $\|z\| \to \infty$ and some $\tilde{p} > d + 1$.

Proposition 14. *In the case of a finite or short range potential and sufficiently high temperature, Condition (3.4) holds for all $\Gamma \in \mathbb{X}$. Therefore, μ_Γ^Φ is unique (for all $\Gamma \in \mathbb{X}$). Moreover, α in (3.5) may be chosen independently of the point set.*

Proof. We start with the finite range potential. For sufficiently small β, we have

$$\sup_{x \in \Gamma} \sum_{\substack{S \in \mathcal{F} \cap \Gamma \\ x \in S}} \mathrm{e}^{\operatorname{diam}(S)} (|S|-1)\, \mathcal{D}(\Phi_S) \leqslant \mathrm{e}^R \sup_{x \in \Gamma} \sum_{\substack{S \in \mathcal{F} \cap \Gamma \\ x \in S}} (|S|-1)\, \mathcal{D}(\Phi_S) \leqslant c\beta < 2 ,$$

where c is a constant. Indeed, the finite number of $S \ni x$ with $\Phi_S \neq 0$ results in a finite sum. Moreover, because of the finite range, there is a maximum of $|S|$ and $\mathcal{D}(\Phi_S)$ for all S with $\operatorname{diam}(S) \leqslant R$. Thus, for sufficiently high temperatures, Condition (3.4) holds.

In the short range potential case we fix the metric $\mathrm{d}(x, y) := t\|x - y\| \wedge \lfloor p \rfloor \log(1 + \|x - y\|)$ with some constants $t > 0$ and $p > 1$, where $a \wedge b$ means the minimum of a and b. It is not difficult to check that this is indeed a metric. Then, (3.7) results in the estimates

$$\sup_{x \in \Gamma} \sum_{\substack{S \in \mathcal{F} \cap \Gamma \\ x \in S}} \mathrm{e}^{\mathrm{diam}(S)} (|S| - 1) \mathcal{D}(\Phi_S) \leqslant \beta \sup_{x \in \Gamma} (|\phi(\zeta_{|x,0}) - \phi(\lambda_{|x,0})|) \sum_{z \in \Gamma - \Gamma} \mathrm{e}^{t\|z\|} |J(z)|$$

$$\leqslant \beta \sup_{x \in \Gamma} (|\phi(\zeta_{|x,0}) - \phi(\lambda_{|x,0})|) \sum_{z \in \Lambda - \Lambda} \mathrm{e}^{t\|z\|} |J(z)| \leqslant c\beta$$

and

$$\sup_{x \in \Gamma} \sum_{\substack{S \in \mathcal{F} \cap \Gamma \\ x \in S}} \mathrm{e}^{\mathrm{diam}(S)} (|S| - 1) \mathcal{D}(\Phi_S) \leqslant \tilde{c}\beta \sup_{x \in \Gamma} (|\phi(\zeta_{|x,0}) - \phi(\lambda_{|x,0})|) \sum_{z \in \Gamma - \Gamma} \|z\|^p |J(z)|$$

$$\leqslant \tilde{c}\beta \sup_{x \in \Gamma} (|\phi(\zeta_{|x,0}) - \phi(\lambda_{|x,0})|) \sum_{z \in \Lambda - \Lambda} \|z\|^p |J(z)| \leqslant c\beta \ .$$

Note that, in addition to $\mathrm{diam}(S) \leqslant t\|x - y\|$, one has $\mathrm{diam}(S) \leqslant \lfloor p \rfloor \log(1 + \|x - y\|)$ in this metric, which implies the estimate

$$\mathrm{e}^{\mathrm{diam}(S)} \leqslant (1 + \|z\|)^{\lfloor p \rfloor} = \sum_{k=0}^{\lfloor p \rfloor} \binom{\lfloor p \rfloor}{k} \|z\|^{\lfloor p \rfloor} \leqslant \sum_{k=0}^{\lfloor p \rfloor} \binom{\lfloor p \rfloor}{k} \|z\|^p = \tilde{c} \|z\|^p.$$

Thus, for sufficiently high temperatures, $c\beta$ is bounded away from 2 such that $\alpha < 1$ independent of the point set. $\square$

Moreover, we have

Theorem 8. *Let μ_Γ^Φ be a unique Gibbs measure on $(W^\Gamma, \mathcal{W}^\Gamma)$ given by a finite or short range potential Φ and sufficiently high temperature. Then,*

$$\mu_\Gamma^\Phi(A^\Gamma) = \lim_{K_n \nearrow \mathbb{R}^d} \kappa_{K_n}^\Phi(A^\Gamma \mid \omega)$$

holds for all $\omega \in W^\Gamma$.

Proof. See [31, Prop. 7.11]. $\square$

After defining Gibbs states on $(W, \mathcal{W})^\Gamma$ for a fixed FLC set Γ we now consider Gibbs states on the larger phase space $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}))$. We suppose

$$\kappa_K^{\Phi, \mathbb{Y}}(A \mid \omega) := \frac{1}{Z_K^\Phi(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} \mathbb{1}_A(\lambda \otimes \omega_{\bar{K}}) \mathrm{e}^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})} = \kappa_K^\Phi \left(A \cap W^{\Gamma(\omega)} \mid \omega \right)$$

to act as specification (with $A \in \mathcal{B}(\mathbb{Y})$, $\omega \in \mathbb{Y}$). Therefore, we have to define sub-σ-fields $\{\mathcal{T}_K\}_{K \in \mathcal{I}}$ and $\{\mathcal{A}_K\}_{K \in \mathcal{I}}$. In contrast to the afore considered case, we cannot define the sub-σ-fields consisting of those events, which only depend on the inside and outside of K, respectively. The reason is that, in this case, the $\mathcal{T}_K$-measurability is not ensured. In order to show this, we consider ω_1 and ω_2 matching on the complement of K but living on different point sets inside K and satisfying

$$a = \kappa_K^{\Phi, \mathbb{Y}}(A \mid \omega_1) \neq \kappa_K^{\Phi, \mathbb{Y}}(A \mid \omega_2) = a + c$$

with $c \neq 0$. Then, the preimage of $[a, a+c-\varepsilon]$ (for arbitrary $\varepsilon > 0$) is a set, which contains ω_1 but not ω_2. However, such a set is not contained in the assumed sigma field.

Therefore, we have to define other sigma fields such that the $\mathcal{T}_K$-measurability is guaranteed. At first, we choose

$$\tilde{\mathcal{T}}_K := \left\{ \bigcup_{\Gamma \in \mathbb{X}} C^\Gamma \,|\, C^\Gamma \in \mathcal{T}_K^\Gamma \right\} \,.$$

The reason is the next lemma.

Lemma 3. $\kappa_K^{\Phi, \mathbb{Y}}(A \,|\, \cdot)$ is $\tilde{\mathcal{T}}_K$-measurable for all $A \in \mathcal{B}(\mathbb{Y})$.

Proof. It is clear that for any intervall $I \subset \mathbb{R}$

$$\kappa_K^{\Phi, \mathbb{Y}}(A \,|\, \cdot)^{-1}(I) = \bigcup_{\Gamma \in \mathbb{X}} \left\{ \omega \in W^\Gamma \,|\, \kappa_K^\Phi \left(A \cap W^\Gamma \,|\, \omega \right) \in I \right\}$$

lies in $\tilde{\mathcal{T}}_K$ since $\left\{ \omega \in W^\Gamma \,|\, \kappa_K^\Phi \left(A \cap W^\Gamma \,|\, \omega \right) \in I \right\} \in \mathcal{T}_K^\Gamma$. $\qquad\qquad\square$

Remark. It is easy to check that $\tilde{\mathcal{T}}_K$ as well as

$$\tilde{\mathcal{A}} := \left\{ \bigcup_{\Gamma \in \mathbb{X}} A^\Gamma \,|\, A^\Gamma \in \mathcal{W}^\Gamma \right\}$$

are sigma fields.

$\{\tilde{\mathcal{T}}_K\}_{K \in \mathcal{I}}$ are sub-σ-fields of $\tilde{\mathcal{A}}$, and it is clear that $\mathcal{B}(\mathbb{Y}) \subset \tilde{\mathcal{A}}$ since every neighborhood $U_{K,V}[\omega]$ is contained in $\tilde{\mathcal{A}}$. Therefore, every $A \in \mathcal{B}(\mathbb{Y})$ has a representation $\bigcup_{\Gamma \in \mathbb{X}} A^\Gamma$ and $A \cap W^\Gamma = A^\Gamma$. However, it is not ensured that $\{\tilde{\mathcal{T}}_K\}_{K \in \mathcal{I}}$ are sub-σ-fields of $\mathcal{B}(\mathbb{Y})$. This is the reason why we define the sigma fields

$$\mathcal{T}_K := \left\{ \bigcup_{\Gamma \in \mathbb{X}} C^\Gamma \,|\, C^\Gamma \in \mathcal{T}_K^\Gamma \right\} \cap \mathcal{B}(\mathbb{Y}) = \tilde{\mathcal{T}}_K \cap \mathcal{B}(\mathbb{Y}) \,,$$

which are well-defined since the intersection of two sigma fields is again a sigma field. In order to show that $\kappa_K^{\Phi, \mathbb{Y}}(A \,|\, \cdot)$ is $\mathcal{T}_K$-measurable for all $A \in \mathcal{B}(\mathbb{Y})$, we have to show the $\mathcal{B}(\mathbb{Y})$-measurability. If we restrict ourselves to translation invariant finite or short range potentials and sufficiently high temperature, this follows from the next proposition. But, first, we note a statement about the continuity of the potential.

Lemma 4. *Let Φ be a finite or short range potential and β large enough. Moreover, let $\omega^{(n)} \in \mathbb{Y}$ be a sequence of elements converging to $\omega \in \mathbb{Y}$. Then, for each $\varepsilon > 0$, and $K_1 \subset \mathbb{R}^d$, there exist $K_2 \supset K_1$, $\tilde{\varepsilon} > 0$ and $N \in \mathbb{N}$ such that for all $n > N$ $\tilde{\omega}_{K_2}^{(n)} = \omega_{K_2}$, where $\tilde{\omega}^{(n)} = \omega^{(n)} + \varepsilon^{(n)}$ with $|\varepsilon^{(n)}| < \tilde{\varepsilon}$ and*

$$\left| \mathcal{H}_{K_1}^\Phi \left(\lambda \otimes \omega_{\bar{K}_1} \right) - \mathcal{H}_{K_1}^\Phi \left(\lambda \otimes \tilde{\omega}_{\bar{K}_1}^{(n)} \right) \right| < \varepsilon \quad \text{for all } \lambda \in W^{\Gamma(\omega_{K_1})} \,.$$

Proof. In the case of a finite range potential this is clear, since one may choose $K_2 \supset \bigcup_{x \in K_1} B_R(x)$ (with R the range of the potential). This results in

$$\left| \mathcal{H}_{K_1}^\Phi \left(\lambda \otimes \omega_{\bar{K}_1} \right) - \mathcal{H}_{K_1}^\Phi \left(\lambda \otimes \tilde{\omega}_{\bar{K}_1}^{(n)} \right) \right| = 0 \quad \text{for all } \lambda \in W^{\Gamma(\omega_{K_1})} \,.$$

In the case of a short range potential

$$\left| \mathcal{H}_{K_1}^{\Phi}\left(\lambda \otimes \omega_{\bar{K}_1}\right) - \mathcal{H}_{K_1}^{\Phi}\left(\lambda \otimes \tilde{\omega}_{\bar{K}_1}^{(n)}\right)\right|$$

$$= \left| \sum_{x \in \Gamma(\omega_{K_1})} \left(\sum_{y \in \Gamma(\omega_{\bar{K}_2})} \beta\phi\left(\omega_{|_{\{x,y\}}}\right) J(x-y) - \sum_{z \in \Gamma(\tilde{\omega}_{\bar{K}_2}^{(n)})} \beta\phi\left(\tilde{\omega}_{|_{\{x,y\}}}^{(n)}\right) J(x-y) \right)\right|$$

becomes arbitrarily small for growing sets K_2 and all $\lambda \in W^{\Gamma(\omega_{K_1})}$ since the inner differences converge, and the outer sum is finite. $\qquad\square$

Proposition 15. *For a translation invariant finite or short range potential Φ and sufficiently high temperature, $\kappa_K^{\Phi,\mathbb{Y}} \colon \mathcal{B}(\mathbb{Y}) \times \mathbb{Y} \to \mathbb{R}$, with*

$$\kappa_K^{\Phi,\mathbb{Y}}(A \,|\, \omega) = \kappa_K^{\Phi}\left(A \cap W^{\Gamma(\omega)} \,|\, \omega\right) ,$$

is a probability kernel.

Proof. For any $\omega \in \mathbb{Y}$, $\kappa_K^{\Phi,\mathbb{Y}}(\cdot \,|\, \omega)$ is a probability measure. Moreover, for each $A \in \mathcal{B}(\mathbb{Y})$ $\kappa_K^{\Phi,\mathbb{Y}}(A \,|\, \cdot)$ is $\mathcal{B}(\mathbb{Y})$-measurable as we will show in the following.

Let $f \colon \mathbb{Y} \to \mathbb{R}$, $\omega \mapsto f(\omega)$ be continuous. We first show the continuity of

$$\kappa_K^f \colon \mathbb{Y} \to \mathbb{R}, \ \omega \mapsto \frac{1}{Z_K^{\Phi}(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} f\left(\lambda \otimes \omega_{\bar{K}}\right) e^{-\mathcal{H}_K^{\Phi}(\lambda \otimes \omega_{\bar{K}})} .$$

Let $\omega^{(n)}$ be a sequence of elements converging to ω. Then, for each $\varepsilon > 0$, and $K \subset \mathbb{R}^d$, there exist $\tilde{K} \supset K$ and $N \in \mathbb{N}$ such that for all $n > N$ $\tilde{\omega}_{\tilde{K}}^{(n)} = \omega_{\tilde{K}}$, where $\tilde{\omega}^{(n)} = \omega^{(n)} + \varepsilon^{(n)}$ with $|\varepsilon^{(n)}| < \varepsilon$.

Due to the translation invariance of the potential, we have

$$\left| \kappa_K^f(\omega) - \kappa_K^f\left(\omega^{(n)}\right) \right|$$

$$= \left| \frac{1}{Z_K^\Phi(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} f\left(\lambda \otimes \omega_{\bar{K}}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})} \right.$$

$$\left. - \frac{1}{Z_K^\Phi(\omega^{(n)})} \sum_{\lambda \in W^{\Gamma(\omega_K^{(n)})}} f\left(\lambda \otimes \omega_{\bar{K}}^{(n)}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}}^{(n)})} \right|$$

$$\leqslant \left| \frac{1}{Z_K^\Phi(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} f\left(\lambda \otimes \omega_{\bar{K}}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})} \right.$$

$$\left. - \frac{1}{Z_K^\Phi(\tilde{\omega}^{(n)})} \sum_{\lambda \in W^{\Gamma(\omega_K)}} f\left(\left(\lambda - \varepsilon^{(n)}\right) \otimes \omega_{\bar{K}}^{(n)}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)})} \right|$$

$$\leqslant \frac{1}{Z_K^\Phi(\omega)} \left| \sum_{\lambda \in W^{\Gamma(\omega_K)}} \left(f\left(\lambda \otimes \omega_{\bar{K}}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})} - f\left(\left(\lambda - \varepsilon^{(n)}\right) \otimes \omega_{\bar{K}}^{(n)}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)})} \right) \right| +$$

$$\frac{1}{Z_K^\Phi(\omega)} \left| \sum_{\lambda \in W^{\Gamma(\omega_K)}} f\left(\left(\lambda - \varepsilon^{(n)}\right) \otimes \omega_{\bar{K}}^{(n)}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)})} \right| \times$$

$$\frac{1}{Z_K^\Phi(\tilde{\omega}^{(n)})} \left| \sum_{\lambda \in W^{\Gamma(\omega_K)}} \left(e^{-\mathcal{H}_K^\Phi(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)})} - e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})} \right) \right|$$

$$\leqslant \sup_{\lambda \in W^{\Gamma(\omega_K)}} \left| f\left(\lambda \otimes \omega_{\bar{K}}\right) - f\left(\left(\lambda - \varepsilon^{(n)}\right) \otimes \omega_{\bar{K}}^{(n)}\right) e^{\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}}) - \mathcal{H}_K^\Phi(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)})} \right| +$$

$$\sup_{\lambda \in W^{\Gamma(\omega_K)}} \left| f\left(\left(\lambda - \varepsilon^{(n)}\right) \otimes \omega_{\bar{K}}^{(n)}\right) e^{\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}}) - \mathcal{H}_K^\Phi(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)})} \right| \times$$

$$\sup_{\lambda \in W^{\Gamma(\omega_K)}} \left| 1 - e^{\mathcal{H}_K^\Phi(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)}) - \mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})} \right| ,$$

which becomes arbitrarily small for growing $\tilde{K}$ and N since f is continuous and $|\mathcal{H}_K^\Phi\left(\lambda \otimes \omega_{\bar{K}}\right) - \mathcal{H}_K^\Phi\left(\lambda \otimes \tilde{\omega}_{\bar{K}}^{(n)}\right)|$ becomes small due to Lemma 4. Due to continuity, κ_K^f is $\mathcal{B}(\mathbb{Y})$-measurable.

The indicator function $\mathbb{1}_A$ for a closed set A may be approximated by continuous functions f_n, $n \in \mathbb{N}$ (compare [14, Thm. 1.2]). Since

$$\kappa_K^{\Phi, \mathbb{Y}}(A \,|\, \omega) = \frac{1}{Z_K^\Phi(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} \mathbb{1}_A(\lambda \otimes \omega_{\bar{K}}) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})}$$

$$= \frac{1}{Z_K^\Phi(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} \lim_{n \to \infty} f_n\left(\lambda \otimes \omega_{\bar{K}}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})}$$

$$= \lim_{n \to \infty} \frac{1}{Z_K^\Phi(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} f_n\left(\lambda \otimes \omega_{\bar{K}}\right) e^{-\mathcal{H}_K^\Phi(\lambda \otimes \omega_{\bar{K}})}$$

$$= \lim_{n \to \infty} \kappa_K^{f_n}(\omega) ,$$

for all closed sets A, $\kappa_K^\Phi(A \,|\, \omega)$ is $\mathcal{B}(\mathbb{Y})$-measurable as a limit of $\mathcal{B}(\mathbb{Y})$-measurable functions

$\kappa_K^{f_n}(\omega)$.

Next, we show that

$$D := \{A \in \mathcal{B}(\mathbb{Y}) \mid \kappa_K^{\Phi,\mathbb{Y}}(A \mid \omega) \text{ is } \mathcal{B}(\mathbb{Y})\text{-measurable}\}$$

is a Dynkin system.

$\mathbb{Y}$ is closed and therefore lies in D. Moreover, for a closed set $A \in \mathcal{B}(\mathbb{Y})$,

$$\kappa_K^{\Phi,\mathbb{Y}}\left(\bar{A} \mid \omega\right) = \frac{1}{Z_K^{\Phi}(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} \left(1 - \mathbb{1}_A(\lambda \otimes \omega_{\bar{K}})\right) \mathrm{e}^{-\mathcal{H}_K^{\Phi}(\lambda \otimes \omega_{\bar{K}})} = 1 - \kappa_K^{\Phi,\mathbb{Y}}\left(A \mid \omega\right)$$

is $\mathcal{B}(\mathbb{Y})$-measurable and, for a disjoint union of elements of D,

$$\kappa_K^{\Phi,\mathbb{Y}}\left(\bigcup_{n \in \mathbb{N}} A_n \mid \omega\right) = \frac{1}{Z_K^{\Phi}(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} \lim_{m \to \infty} \sum_{n=1}^{m} \mathbb{1}_{A_n}(\lambda \otimes \omega_{\bar{K}}) \mathrm{e}^{-\mathcal{H}_K^{\Phi}(\lambda \otimes \omega_{\bar{K}})}$$

$$= \lim_{m \to \infty} \sum_{n=1}^{m} \frac{1}{Z_K^{\Phi}(\omega)} \sum_{\lambda \in W^{\Gamma(\omega_K)}} \mathbb{1}_{A_n}(\lambda \otimes \omega_{\bar{K}}) \mathrm{e}^{-\mathcal{H}_K^{\Phi}(\lambda \otimes \omega_{\bar{K}})}$$

$$= \lim_{m \to \infty} \sum_{n=1}^{m} \kappa_K^{\Phi,\mathbb{Y}}(A_n \mid \omega)$$

is $\mathcal{B}(\mathbb{Y})$-measurable as a limit of $\mathcal{B}(\mathbb{Y})$-measurable functions.

Let $\mathcal{E}$ be the set of all closed sets. On the one hand, we have $\mathcal{E} \subset D \subset \mathcal{B}(\mathbb{Y})$. Since $\mathcal{E}$ is closed under intersections, the generated Dynkin system $D(\mathcal{E})$ equals the generated sigma field $\sigma(\mathcal{E})$. Therefore, on the other hand, $\mathcal{B}(\mathbb{Y}) = \sigma(\mathcal{E}) = D(\mathcal{E}) \subset D$. It follows that $D = \mathcal{B}(\mathbb{Y})$, i.e., $\kappa_K^{\Phi,\mathbb{Y}}(A \mid \omega)$ is $\mathcal{B}(\mathbb{Y})$-measurable for all $A \in \mathcal{B}(\mathbb{Y})$.

$\square$

Due to this lemma we get

Proposition 16. *For a translation invariant finite or short range potential Φ and sufficiently high temperature the collection $V^{\Phi} = \left(\kappa_K^{\Phi,\mathbb{Y}}\right)_{K \in \mathcal{I}}$ of probability kernels is a specification.*

Proof. We have to verify the three points of Definition 6.

- $\kappa_K^{\Phi,\mathbb{Y}}(A \mid \cdot)$ is $\mathcal{T}_K$-measurable for all $K \in \mathcal{I}$, $A \in \mathcal{B}(\mathbb{Y})$, since it is $\tilde{\mathcal{T}}_K$-measurable due to Lemma 3 and $\mathcal{B}(\mathbb{Y})$-measurable due to Proposition 15.

- $\kappa_K^{\Phi,\mathbb{Y}}(C \mid \cdot) = \mathbb{1}_C$ for all $C \in \mathcal{T}_K$ since

$$\kappa_K^{\Phi,\mathbb{Y}}(C \mid \omega) = \kappa_K^{\Phi}\left(C \cap W^{\Gamma(\omega)} \mid \omega\right) = \kappa_K^{\Phi}\left(C^{\Gamma(\omega)} \mid \omega\right) = \mathbb{1}_{C^{\Gamma(\omega)}}(\omega) = \mathbb{1}_C(\omega)$$

- For all $A \in \mathcal{B}(\mathbb{Y})$

$$\kappa_{K_2}^{\Phi,\mathbb{Y}} \kappa_{K_1}^{\Phi,\mathbb{Y}} = \kappa_{K_2}^{\Phi,\mathbb{Y}}$$

if $K_1 \subset K_2$, since

$$
\begin{aligned}
\kappa_{K_2}^{\Phi,\mathbb{Y}} \kappa_{K_1}^{\Phi,\mathbb{Y}}(A \,|\, \omega) &= \int_{\mathbb{Y}} \kappa_{K_1}^{\Phi,\mathbb{Y}}(A \,|\, \tilde{\omega}) \kappa_{K_2}^{\Phi,\mathbb{Y}}(\mathrm{d}\tilde{\omega} \,|\, \omega) \\
&= \int_{\mathbb{Y}} \kappa_{K_1}^{\Phi}\left(A \cap W^{\Gamma(\tilde{\omega})} \,|\, \tilde{\omega}\right) \kappa_{K_2}^{\Phi}\left(\mathrm{d}\tilde{\omega} \cap W^{\Gamma(\omega)} \,|\, \omega\right) \\
&= \int_{W^{\Gamma(\omega)}} \kappa_{K_1}^{\Phi}\left(A \cap W^{\Gamma(\omega)} \,|\, \tilde{\omega}\right) \kappa_{K_2}^{\Phi}(\mathrm{d}\tilde{\omega} \,|\, \omega) = \kappa_{K_2}^{\Phi}\left(A \cap W^{\Gamma(\omega)} \,|\, \omega\right) \\
&= \kappa_{K_2}^{\Phi,\mathbb{Y}}(A \,|\, \omega) \, .
\end{aligned}
$$

$\square$

Theorem 9. *Let Φ be a translation invariant finite or short range potential and the temperature sufficiently high. The measure μ^{Φ} on $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}))$ defined by*

$$
\mu^{\Phi}(A) = \int_A \mathrm{d}\mu^{\Phi}(\omega) := \int_{\mathbb{X}} \int_{A^{\Gamma}} \mathrm{d}\mu_{\Gamma}^{\Phi}(\omega) \, \mathrm{d}\nu(\Gamma) = \int_{\mathbb{X}} \int_{W^{\Gamma}} \mathbb{1}_{A \cap W^{\Gamma}}(\omega) \, \mathrm{d}\mu_{\Gamma}^{\Phi}(\omega) \, \mathrm{d}\nu(\Gamma) \quad (3.8)
$$

is well-defined. It is a Gibbs measure given by the specification V^{Φ} from Proposition 16.

Proof. In order to prove that μ^{Φ} is well-defined, we have to show that the well-defined map

$$
f : \mathbb{X} \to \mathbb{C}, \ \Gamma \mapsto \int_{W^{\Gamma}} \mathbb{1}_{A \cap W^{\Gamma}}(\omega) \, \mathrm{d}\mu_{\Gamma}^{\Phi}(\omega) = \mu_{\Gamma}^{\Phi}(A \cap W^{\Gamma}) =
$$
$$
\lim_{K_n \nearrow \mathbb{R}^d} \kappa_{K_n}^{\Phi}(A \cap W^{\Gamma} \,|\, \omega(\Gamma)) = \lim_{K_n \nearrow \mathbb{R}^d} \kappa_{K_n}^{\Phi,\mathbb{Y}}(A \,|\, \omega(\Gamma))
$$

(compare Theorem 8) is $\mathcal{B}(\mathbb{X})$-measurable where $\omega \colon \mathbb{X} \to \mathbb{Y}$ is the function which maps Γ to the marked point set living on Γ and having (arbitrary) identical marks $c \in W$ at all positions. Since the function ω is $\mathcal{B}(\mathbb{X})$-measurable and $\kappa_{K_n}^{\Phi,\mathbb{Y}}$ is $\mathcal{B}(\mathbb{Y})$-measurable due to Proposition 15, the latter is also $\mathcal{B}(\mathbb{X})$-measurable as the composition of measurable functions. It follows that $\Gamma \mapsto \mu_{\Gamma}^{\Phi}(A \cap W^{\Gamma})$ is $\mathcal{B}(\mathbb{X})$-measurable as a limit of measurable functions.

μ^{Φ} fulfills (3.3) since

$$
\begin{aligned}
\mu^{\Phi}(A \cap C) &= \int_{\mathbb{X}} \int_{W^{\Gamma}} \mathbb{1}_{A \cap C}(\omega) \, \mathrm{d}\mu_{\Gamma}^{\Phi}(\omega) \, \mathrm{d}\nu(\Gamma) = \int_{\mathbb{X}} \int_{C^{\Gamma}} \mathbb{1}_{A^{\Gamma}}(\omega) \, \mathrm{d}\mu_{\Gamma}^{\Phi}(\omega) \, \mathrm{d}\nu(\Gamma) \\
&= \int_{\mathbb{X}} \int_{C^{\Gamma}} \kappa_K^{\Phi}\left(A^{\Gamma} \,|\, \omega\right) \, \mathrm{d}\mu_{\Gamma}^{\Phi}(\omega) \, \mathrm{d}\nu(\Gamma) = \int_C \kappa_K^{\Phi,\mathbb{Y}}(A \,|\, \omega) \, \mathrm{d}\mu^{\Phi}(\omega) \, .
\end{aligned}
$$

$\square$

Theorem 10. *For a translation invariant finite or short range potential Φ and sufficiently high temperature the measure μ^{Φ} defined by (3.8) is $\mathbb{R}^d$-ergodic.*

Proof. Let T_x, $x \in \mathbb{R}^d$, denote the $\mathbb{R}^d$-translations. First of all, μ^{Φ} is translation invariant, since

$$
\mu^{\Phi}(T_x(g)) = \int_{\mathbb{X}} \mu_{\Gamma}^{\Phi}(T_x(g)) \, \mathrm{d}\nu(\Gamma) = \int_{\mathbb{X}} \mu_{\Gamma+x}^{\Phi}(T_x(g)) \, \mathrm{d}\nu(\Gamma) = \int_{\mathbb{X}} \mu_{\Gamma}^{\Phi}(g) \, \mathrm{d}\nu(\Gamma) = \mu^{\Phi}(g)
$$

because of the translation invariance of the potential and the stationarity of ν.

Due to Theorem 6, any translation invariant Gibbs measure $\tilde{\mu}^{\Phi}$ with respect to the potential Φ may be represented by

$$\tilde{\mu}^{\Phi}(A) = \int_{\mathbb{Y}} \mathbb{1}_A(\omega)\, \mathrm{d}\tilde{\mu}^{\Phi}(\omega) = \int_{\mathbb{X}} \int_{W^{\Gamma}} \mathbb{1}_A(\omega)\, \mathrm{d}\tilde{\mu}_{\Gamma}^{\Phi}(\omega)\, \mathrm{d}\nu(\Gamma)\ .$$

However there is only one such measure possible since the Gibbs measures μ_{Γ}^{Φ} are unique (due to Proposition 14). Therefore, μ^{Φ} is the unique translation invariant Gibbs measure with respect to the potential Φ.

T_x, $x \in \mathbb{R}^d$, separates $\mathcal{I}$ since $\mathcal{B}(\mathbb{Y})$ is the smallest sigma field containing

$$\bigcup_{n \geqslant 1} \mathcal{A}_{B_n} := \bigcup_{n \geqslant 1} \left\{ \bigcup_{\Gamma \in \mathbb{X}} A_{B_n}^{\Gamma} \mid A_{B_n}^{\Gamma} \in \mathcal{W}_{B_n}^{\Gamma} \right\}\ ,$$

and for any $n \geqslant 1$, $K \in \mathcal{I}$, there exists a translation T_x, $x \in \mathbb{R}^d$, with $T_x(\mathcal{A}_{B_n}) \subset \mathcal{T}_K$ (compare [53, Chap. 4]). With [53, Thm. 4.1] (which states that, under the assumption of separability, uniqueness is equivalent to ergodicity) the claim follows. $\square$

3.4 Examples of particle gases using Gibbs measures

In Theorem 4 of Section 3.1 and Theorem 7 of Section 3.2 it was shown that there is no singular continuous part present in the diffraction of certain particle gases fulfilling some conditions. The main assumption refers to ergodicity of the relevant measure. In the last section we have proven ergodicity for some Gibbs measures. These will be used in the following in order to give some examples of particle gases satisfying the mentioned assumptions. We start with particle gases on fixed point sets (considered in Section 3.1).

3.4.1 On fixed point sets

Let $\Gamma := \mathbb{Z}^d$. We consider the lattice gas defined by a measure on $(W^{\Gamma}, \mathcal{W}^{\Gamma})$.

Corollary 4. *If Φ is a translation invariant finite or short range potential and the temperature sufficiently high, there is no singular continuous part present in the diffraction of the lattice gas defined by the corresponding Gibbs measure.*

Proof. Due to Proposition 14, μ_{Γ}^{Φ} is unique. Moreover it is $\mathbb{Z}^d$-translation invariant. Thus it is $\mathbb{Z}^d$-ergodic and the result follows from Proposition 13 together with Theorem 4. $\square$

We proceed with the particle gases on dynamical systems (considered in Section 3.2).

3.4.2 On dynamical systems

Let us first look at an *interaction-free particle gas*, i.e., for a randomly chosen point set $\Gamma \in \mathbb{X}$, the scattering strengths at the various points are i.i.d. random variables. It is clear that, analogously to the construction in the last section one may define an ergodic Gibbs measure on $\mathbb{Y}$ such that the measures on the various point sets $\Gamma \in \mathbb{X}$ are the product measures.

Let $\mathbb{E}_p := \sum_{i=1}^{n} p_i c_i$ and $\mathbb{V}_p := \sum_{i=1}^{n} p_i |c_i|^2 - |\mathbb{E}_p|^2$.

Clearly, $\delta^{(\mathbb{E})} := \mathbb{E}_p \sum_{x \in \Gamma} \delta_x$ and (for all $z \in \mathbb{R}^d$) $\delta^{(\mathbb{E},z)} := |\mathbb{E}_p|^2 \sum_{x, x-z \in \Gamma} \delta_x$ define stationary random measures. Due to Proposition 11, the autocorrelation of $\delta^{(H)}$ is therefore given by the coefficients

$$\eta^{(H)}(z) = \eta^{(\mathbb{E})}(z) + \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mathrm{cov}_{\mu_\Gamma}(H_x, \overline{H_{x-z}}) \, \mathrm{d}\nu(\Gamma)$$

with $\eta^{(\mathbb{E})}(z) = |\mathbb{E}_p|^2 \eta_\Lambda(z)$ (due to independence and Proposition 10). Moreover, due to independence, we have

$$\int_{\mathbb{X}} \sum_{\substack{x \in \Gamma \cap \mathbb{U}^d \\ x-z \in \Gamma}} \mathrm{cov}_{\mu_\Gamma}(H_x, \overline{H_{x-z}}) \, \mathrm{d}\nu(\Gamma) = \begin{cases} \mathrm{dens}(\Lambda)\mathbb{V}_p, & z = 0, \\ 0, & \text{otherwise.} \end{cases}$$

This results in

$$\gamma^{(H)} = \sum_{z \in \Lambda - \Lambda} |\mathbb{E}_p|^2 \, \eta_\Lambda(z) \, \delta_z + \mathrm{dens}(\Lambda) \, \mathbb{V}_p \, \delta_0$$

$$= |\mathbb{E}_p|^2 \, \gamma_\Lambda + \mathrm{dens}(\Lambda) \, \mathbb{V}_p \delta_0$$

(compare Prop. 2) and since $\widehat{\delta_0} = 1$, the Fourier transform is given by

$$\widehat{\gamma}^{(H)} = |\mathbb{E}_p|^2 \, \widehat{\gamma_\Lambda} + \mathrm{dens}(\Lambda) \, \mathbb{V}_p \,,$$

where the second term on the right hand side is a constant and hence a contribution to the absolutely continuous part of $\widehat{\gamma}^{(H)}$.

We now extend our analysis to more interesting types of disorder, namely dependent random variables controlled by a non-trivial Gibbs measure.

Lemma 5. *Let Φ be a translation invariant finite or short range potential and the temperature sufficiently high. Then, the functions $\delta^{(\mathbb{E},z)}$ (for all $z \in \mathbb{R}^d$) and $\delta^{(\mathbb{E})}\colon \mathbb{X} \to \mathcal{M}(\mathbb{R}^d)$, $\Gamma \mapsto \sum_{x, x-z \in \Gamma} \mu_\Gamma^\Phi(H_x) \mu_\Gamma^\Phi(\overline{H_{x-z}}) \delta_x$ and $\Gamma \mapsto \sum_{x \in \Gamma} \mu_\Gamma^\Phi(H_x) \delta_x$, respectively, are continuous and hence $\mathcal{B}(\mathbb{X})$-measurable.*

Proof. We show the continuity of $\delta^{(\mathbb{E})}$, i.e., for any $\varepsilon > 0$ there must be found an $N \in \mathbb{N}$ such that for all $n \geqslant N$

$$\left| \sum_{y \in \mathrm{supp}\, f \cap \Gamma^{(n)}} \mu_{\Gamma^{(n)}}^\Phi(H_y) f(y) - \sum_{x \in \mathrm{supp}\, f \cap \Gamma} \mu_\Gamma^\Phi(H_x) f(x) \right| < \varepsilon$$

with $(\Gamma^{(n)})_{n \in \mathbb{N}}$ a sequence of point sets converging to Γ and $f \in \mathcal{K}$ with support $\mathrm{supp}(f)$. Due to convergence of $(\Gamma^{(n)})_{n \in \mathbb{N}}$, for arbitrary $\tilde{\varepsilon} > 0$ and $K \supset \mathrm{supp}\, f$ with $x \in K$, there exists an $N \in \mathbb{N}$ such that for all $n > N$ $\tilde{\Gamma}_K^{(n)} = \Gamma_K$, where $\tilde{\Gamma}^{(n)} = \Gamma^{(n)} + \varepsilon^{(n)}$ with

$|\varepsilon^{(n)}| < \tilde{\varepsilon}$. Moreover, we have

$$\left| \sum_{y \in \mathrm{supp}\, f \cap \Gamma^{(n)}} \mu^{\Phi}_{\Gamma^{(n)}}(H_y) f(y) - \sum_{x \in \mathrm{supp}\, f \cap \Gamma} \mu^{\Phi}_{\Gamma}(H_x) f(x) \right|$$

$$= \left| \sum_{x \in \mathrm{supp}\, f \cap \Gamma} \left(\mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(H_x) f\big(x - \varepsilon^{(n)}\big) - \mu^{\Phi}_{\Gamma}(H_x) f(x) \right) \right|$$

$$= \left| \sum_{x \in \mathrm{supp}\, f \cap \Gamma} \left(\mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(H_x) \left(f\big(x - \varepsilon^{(n)}\big) - f(x) \right) + f(x) \big(\mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(H_x) - \mu^{\Phi}_{\Gamma}(H_x) \big) \right) \right|.$$

Since f is continuous, and the sum is finite, we only have to show that $\mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(H_x) - \mu^{\Phi}_{\Gamma}(H_x)$ becomes arbitrarily small.

Let $A_c = \{ \omega \mid H_x(\omega) = \omega_x = c \}$, $\tilde{\omega}^{(n)} = \omega\big(\tilde{\Gamma}^{(n)}\big)$, and $\omega = \omega(\Gamma)$. We have

$$\left| \kappa^{\Phi, \mathbb{Y}}_K(A_c \mid \tilde{\omega}^{(n)}) - \kappa^{\Phi, \mathbb{Y}}_K(A_c \mid \omega) \right|$$

$$= \left| \frac{1}{Z^{\Phi}_K(\tilde{\omega}^{(n)})} \sum_{\lambda \in W^{\Gamma}(\omega_K)} \mathbb{1}_{A_c}(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}}) \, \mathrm{e}^{-\mathcal{H}^{\Phi}_K(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}})} - \right.$$

$$\left. \frac{1}{Z^{\Phi}_K(\omega)} \sum_{\lambda \in W^{\Gamma}(\omega_K)} \mathbb{1}_{A_c}(\lambda \otimes \omega_{\bar{K}}) \, \mathrm{e}^{-\mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{\bar{K}})} \right|$$

$$\leqslant \left| \frac{1}{Z^{\Phi}_K(\tilde{\omega}^{(n)})} \sum_{\lambda \in W^{\Gamma}(\omega_K)} \left(\mathbb{1}_{A_c}(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}}) \, \mathrm{e}^{-\mathcal{H}^{\Phi}_K(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}})} - \mathbb{1}_{A_c}(\lambda \otimes \omega_{\bar{K}}) \, \mathrm{e}^{-\mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{\bar{K}})} \right) \right| +$$

$$\frac{1}{Z^{\Phi}_K(\omega)} \left| \sum_{\lambda \in W^{\Gamma}(\omega_K)} \mathbb{1}_{A_c}(\lambda \otimes \omega_{\bar{K}}) \, \mathrm{e}^{-\mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{\bar{K}})} \right| \times$$

$$\frac{1}{Z^{\Phi}_K(\tilde{\omega}^{(n)})} \left| \sum_{\lambda \in W^{\Gamma}(\omega_K)} \left(\mathrm{e}^{-\mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{\bar{K}})} - \mathrm{e}^{-\mathcal{H}^{\Phi}_K(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}})} \right) \right|$$

$$\leqslant \sup_{\lambda \in W^{\Gamma}(\omega_K)} 2 \left| 1 - \mathrm{e}^{\mathcal{H}^{\Phi}_K(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}}) - \mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{\bar{K}})} \right|,$$

(where the last inequality holds due to the assumption $x \in K$) and hence

$$\left| \mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(A_c) - \mu^{\Phi}_{\Gamma}(A_c) \right|$$

$$\leqslant \left| \mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(A_c) - \kappa^{\Phi}_K(A_c \mid \tilde{\omega}^{(n)}) \right| + \left| \kappa^{\Phi, \mathbb{Y}}_K(A_c \mid \tilde{\omega}^{(n)}) - \kappa^{\Phi, \mathbb{Y}}_K(A_c \mid \omega) \right| + \left| \kappa^{\Phi}_K(A_c \mid \omega) - \mu^{\Phi}_{\Gamma}(A_c) \right|$$

$$\leqslant \sum_{y \in \tilde{\Gamma}^{(n)} \setminus K} D_{xy} + \sup_{\lambda \in W^{\Gamma}(\omega_K)} 2 \left| 1 - \mathrm{e}^{\mathcal{H}^{\Phi}_K(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}}) - \mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{|\bar{K}})} \right| + \sum_{y \in \Gamma \setminus K} D_{xy},$$

where the last inequality holds due to [31, Thm. 8.23].

Altogether, with [31, Remark 8.26], this results in

$$\left| \mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(H_x) - \mu^{\Phi}_{\Gamma}(H_x) \right| = \left| \sum_{i=1}^n c_i \left(\mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(A_{c_i}) - \mu^{\Phi}_{\Gamma}(A_{c_i}) \right) \right| \leqslant \sum_{i=1}^n c_i \left| \mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(A_{c_i}) - \mu^{\Phi}_{\Gamma}(A_{c_i}) \right|$$

$$\leqslant \sum_{i=1}^n c_i \left(\frac{\mathrm{e}^{-\min_{y \in \tilde{\Gamma}^{(n)} \setminus K} \mathrm{d}(x,y)}}{1 - \alpha} + \sup_{\lambda \in W^{\Gamma}(\omega_K)} 2 \left| 1 - \mathrm{e}^{\mathcal{H}^{\Phi}_K(\lambda \otimes \tilde{\omega}^{(n)}_{\bar{K}}) - \mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{\bar{K}})} \right| + \frac{\mathrm{e}^{-\min_{y \in \Gamma \setminus K} \mathrm{d}(x,y)}}{1 - \alpha} \right)$$

which becomes arbitrarily small. The reason is that, firstly, there exists an $N \in \mathbb{N}$ such that, for all $n > N$,

$$\frac{\mathrm{e}^{-\min_{y \in \tilde{\Gamma}^{(n)} \setminus K} \mathrm{d}(x,y)}}{1 - \alpha} < \frac{\varepsilon^*}{3} \quad \text{and} \quad \frac{\mathrm{e}^{-\min_{y \in \Gamma \setminus K} \mathrm{d}(x,y)}}{1 - \alpha} < \frac{\varepsilon^*}{3}$$

for arbitrary $\varepsilon^* > 0$. Moreover, due to convergence of $\left(\Gamma^{(n)}\right)_{n \in \mathbb{N}}$, N and $\tilde{K} \supset K$ may be chosen such that $\tilde{\Gamma}^{(n)}_{\tilde{K}} = \Gamma_{\tilde{K}}$ for all $n > N$ and

$$\sup_{\lambda \in W^{\Gamma}(\omega_K)} 2 \left| 1 - \mathrm{e}^{\mathcal{H}^{\Phi}_K(\lambda \otimes \tilde{\omega}^{(n)}_K) - \mathcal{H}^{\Phi}_K(\lambda \otimes \omega_{\tilde{K}})} \right| < \frac{\varepsilon^*}{3}$$

due to Lemma 4. This results in

$$\left| \mu^{\Phi}_{\tilde{\Gamma}^{(n)}}(H_x) - \mu^{\Phi}_{\Gamma}(H_x) \right| < \varepsilon^* \ .$$

Analogously, the continuity of $\delta^{(\mathbb{E},z)}$ can be shown. $\square$

Theorem 11. *Let Φ be a translation invariant finite or short range potential and the temperature sufficiently high. Then, the autocorrelation of $\delta^{(\mathbb{E})}$ exists. If there is no singular continuous part present in the diffraction of $\delta^{(\mathbb{E})}$, there occurs no singular continuous part in the diffraction spectrum of $\delta^{(H)}$.*

Proof. Due to Lemma 5 both $\delta^{(\mathbb{E})}$ and $\delta^{(\mathbb{E},z)}$ (for all $z \in \mathbb{R}^d$) define random measures. Clearly, they are stationary. Therefore, Proposition 9 ensures the existence of the autocorrelation.

Moreover, the measure μ^{Φ} is $\mathbb{R}^d$-ergodic due to Theorem 10. By the dominated convergence theorem as well as Propositions 13 and 14, we have

$$\sum_{z \in \Gamma - \Gamma} \left| \int_{\mathbb{X}} \sum_{\substack{x \in \Gamma' \cap \mathbb{U}^d \\ x - z \in \Gamma'}} \mathrm{cov}_{\mu_{\Gamma'}}(H_x, \overline{H_{x-z}}) \, \mathrm{d}\nu(\Gamma') \right|$$

$$\leqslant \sum_{z \in \Gamma - \Gamma} \int_{\mathbb{X}} \left| \sum_{\substack{x \in \Gamma' \cap \mathbb{U}^d \\ x - z \in \Gamma'}} \mathrm{cov}_{\mu_{\Gamma'}}(H_x, \overline{H_{x-z}}) \right| \mathrm{d}\nu(\Gamma')$$

$$= \int_{\mathbb{X}} \sum_{z \in \Gamma - \Gamma} \sum_{\substack{x \in \Gamma' \cap \mathbb{U}^d \\ x - z \in \Gamma'}} \left| \mathrm{cov}_{\mu_{\Gamma'}}(H_x, \overline{H_{x-z}}) \right| \mathrm{d}\nu(\Gamma') \leqslant \mathrm{const} \, \frac{\left(\sup_{i,j} |c_i - c_j| \right)^2}{4(1 - \alpha)} < \infty \ .$$

Due to Theorem 7, the result follows. $\square$

On the basis of this result we are able to rectify the proof of [9, Cor. 5.5]. There we used the strong law of large numbers although the considered random variables are not identically distributed. However, we can now prove the result (for the particle gas with probability space $(\mathbb{Y}, \mathcal{B}(\mathbb{Y}), \mu)$).

Corollary 5. *Let Φ be a translation invariant finite or short range potential and the temperature sufficiently high. In the case of a regular model set there occurs no singular continuous part in the diffraction spectrum of $\delta^{(H)}$.*

Proof. We define $\mathbb{X}(\delta^{(\mathbb{E})}(\Gamma)) := \mathbb{X}(\sum_{x \in \Gamma} \mu_\Gamma^\Phi(H_x)\,\delta_x)$ as the orbit closure of $\delta^{(\mathbb{E})}(\Gamma)$ in the vague topology. Due to continuity of $\delta^{(\mathbb{E})}$ (compare Lemma 5), $\delta^{(\mathbb{E})}(\mathbb{X}) \subset \mathbb{X}(\delta^{(\mathbb{E})}(\Gamma))$ (due to [15, Chap. I.2, Thm. 1]).

In the case of FLC sets and $\max_i c_i < \infty$ it suffices to consider $\mathcal{M}_{C,V}(\mathbb{R}^d)$, the set of all (C,V)-translation bounded measures (for appropriately chosen C and V), instead of $\mathcal{M}(\mathbb{R}^d)$. Due to [6, Thm. 2] $\mathcal{M}_{C,V}(\mathbb{R}^d)$ is a compact Hausdorff space. Since, furthermore, $\mathbb{X}$ is a compact metrizable space, $\delta^{(\mathbb{E})}(\mathbb{X})$ is closed in $\mathcal{M}_{C,V}(\mathbb{R}^d)$ (compare [25, 12.3.6]). Since $\delta^{(\mathbb{E})}(\mathbb{X})$ already contains $\{\delta^{(\mathbb{E})}(\Gamma + x)|x \in \mathbb{R}^d\}$, we have $\delta^{(\mathbb{E})}(\mathbb{X}) = \mathbb{X}(\delta^{(\mathbb{E})}(\Gamma))$.

Hence, together with the translations in $\mathbb{R}^d$, $\delta^{(\mathbb{E})}(\mathbb{X})$ is a factor of $\mathbb{X}$. The latter has a pure point diffraction spectrum since Λ is a regular model set (compare [55, Thm. 4.5]). This is inherited by $\delta^{(\mathbb{E})}(\mathbb{X})$ due to [7, Prop. 1 and Thm. 2]. Together with Theorem 11 the result follows. □

3.5 Résumé

As already mentioned, in reality, objects are never perfect, and due to an improvement of measuring techniques, stochastic methods become more and more important. This is the reason why we were interested in the influence of randomness on the diffraction.

In practice, one observes only a slight modification of the pure point part and the diffuse scattering. A realistic modeling should be in agreement with this observation. In particular, it is interesting to investigate whether a stochastic description predicts the absence of singular continuous components.

We have therefore considered particle gases with finitely many different scatterers. The starting point was the paper of Baake and Sing [8], where the absence of a singular continuous part in the diffraction of certain binary lattice gases was shown.

By means of some results concerning Gibbs measures we extended this result to the case of finitely many types of particles (see Corollary 4).

Via the introduction of particle gases on dynamical systems (including Gibbs measures on dynamical systems) the results were also extended to a broader class of point sets than lattices (see Theorem 11).

Altogether, this increases the evidence for the rather natural conjecture that singular continuous diffraction spectra are the exception.

Part II

Theoretical immunobiology

Chapter 4

Biological background

The object of immunobiology is the body's own defense against pathogens like bacteria, viruses or fungi. If one catches a flu for example, the immune system recognizes the pathogen (in this case, the virus) and starts an immune response that finally eliminates the foreign intruder.

The defense mechanisms in the context of such an immune response can be classified into unspecific and specific ones.

Unspecific defense mechanisms recognize the intruders by means of certain surface molecules common to many pathogens (therefore *unspecific*). In this case, the recognition motifs which recognize the surface molecules of the foreign invaders are genetically determined.

Specific defense mechanisms, however, recognize *specific* pathogens. It is known that this recognition is the task of so-called T-cells. In this case, the question arises how the recognition works. The reason is that the recognition motifs which recognize the foreign invaders are not genetically determined. Instead, they are randomly composed of various parts and can, a priori, recognize either foreign or self-components since there is no inherent difference between foreign and self-molecules (like some fundamental difference in molecular structure; see below).

As we will see in the following chapters there are two possibilities to give an answer to the arised question, i.e., to explain how T-cells can distinguish between self-components and foreign invaders. On the one hand, an additional learning process (so-called negative selection) could introduce a difference between foreign and self. On the other hand, the additional assumption of a high abundance of the invader could make the recognition possible.

At first, we briefly describe the essential facts about recognition by T-cells; for more details, see the textbook by Janeway et al. [38].

T-cells. T-cells are produced in the bone marrow and subsequently migrate to the *thymus*[1], where they mature (see below). On leaving the thymus, each T-cell is characterized by a specific type of T-cell receptor (TCR), which is displayed in many *identical* copies on the surface of the particular T-cell (see Fig. 4.1). These TCRs play an important part in the recognition of intruders (see below). It is important to note that all TCRs on one

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[1] a lymphatic organ

T-cell are of the same type. However, a large number (roughly 10^7 up to 10^8; see [2, 50]) of different receptors, and hence different T-cell types, are present in an individual.
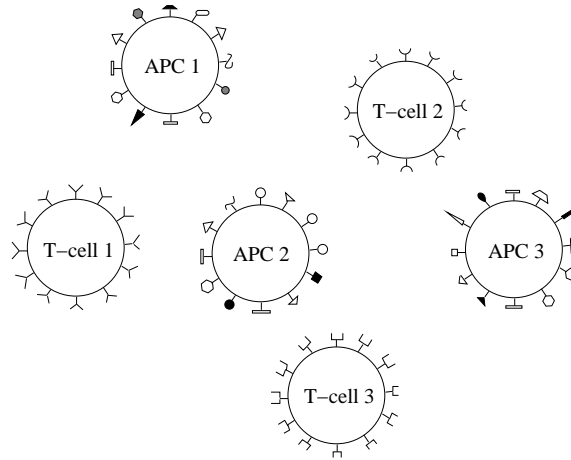

Figure 4.1: A sample of different T-cells and APCs: Each T-cell shows many identical copies of its specific TCR; each APC a large variety of pMHCs - some (e.g., the three circles on APC 2) occuring in many and some (e.g., the hexagon on APC 2) in few copies

Antigen-presenting cells. The partners of the T-cells are the antigen-presenting cells (APCs), each producing so-called MHC molecules of different types. These molecules can be classified into MHC I and MHC II[2] molecules. (Within the two classes further discrimination is possible.) MHC I molecules are important for the activation of cytotoxic T-cells (also called CD8 T-cells due to their CD8 coreceptor). MHC II molecules are important for the activation of CD4 T-cells[3].

An APC absorbs *antigens*[4] from its vicinity and breaks them down. In the cell the emerging fragments, so-called peptides (short sequences of amino acids), are bound to the MHC molecules. The resulting complexes, composed of an MHC molecule and a peptide (abbreviated by pMHC), are displayed on the surface of the cell (compare Fig. 4.1; the MHC molecules serve as "carriers" or "anchors" to the cell surface). Since most of the peptides in the vicinity of an APC are the body's own peptides, every APC displays a large variety of different types of self-peptides and, possibly, one (or a small number of) foreign types. The various types of peptides occur in various copy numbers, as will be detailed below. For the moment, we merely note that foreign peptides are often present at elevated copy numbers. This is because pathogens multiply within the body and flood it with their antigens, before an immune response is initiated.

Interactions between T-cells and APCs. The presentation of peptides on the surface of the APCs is of great importance for the immune system, because T-cells will only be activated when they recognize foreign peptides on the surface of an APC. The contact between a T-cell and an APC is established by a temporary bond between the cells, through which a so-called immunological synapse (see Fig. 4.2) is formed, in which the TCRs and the pMHCs interact with each other. If a T-cell recognizes a foreign peptide

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[2] denoted by MHC without addition

[3] denoted by T-cell without addition

[4] derived from *anti*body *gen*erating; substances (in our case proteins) which can elicit an immune reaction

through its receptors, then it is activated to reproduce, and the resulting clones of T-cells will initiate an immune reaction against the intruder.
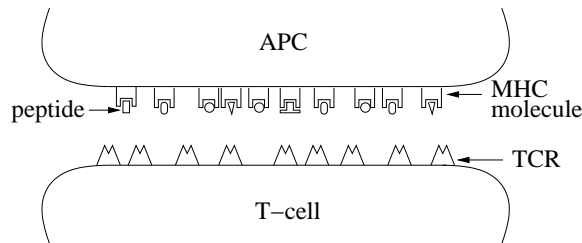

Figure 4.2: An immunological synapse (with a variety of pMHCs on the surface of the APC and many identical TCRs on the surface of the T-cell)

Maturation. During the maturation of a T-cell, several processes take place in the thymus. Initially, the T-cell starts to display the TCRs on its surface. After this, two selective processes take place. During positive selection, those T-cells that hardly interact with the MHC molecules of the individual are removed. Furthermore, negative selection causes the removal of those T-cells that react too strongly to self-peptides (see Chapter 6). Thus, both useless and dangerous T-cells are removed.

Recognition. As mentioned above, the main task of T-cells is the recognition of intruders in the form of foreign peptides presented by APCs. The recognition takes place during the lifetime of an immunological synapse in the *periphery*[5]. The question is which event causes the activation of the T-cell. The answer is unknown up to now because there are many different models and experimental results. Textbooks like [38] and also recent papers avoid to go into this question. But there are two possibilities:

(A1) Activation depends on a single (or few) pMHC(s).

(A2) Activation depends on all pMHCs in an immunological synapse.

Problem. There cannot be an a priori difference between foreign and self-peptides (like some fundamental difference in molecular structure). After all, even tissues of a different individual of the same species are recognized as foreign (this is the basic problem of transplant rejection). Therefore, the question comes up how the T-cells can distinguish between foreign and self. At first sight, the task seems hopeless, since there are vastly more different peptides (roughly 10^{13}; see Mason [49]) than TCRs (roughly 10^7, as noted earlier), which makes specific recognition (where one TCR recognizes exactly one pMHC) impossible; this is known as the Mason paradox. However, there are possibilities to explain the so-called *foreign-self distinction* (the ability of the T-cells to distinguish between foreign and self). This is shown in the next chapters.

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[5] the entire body except for the thymus

Chapter 5

Recognition without negative selection

In the last chapter we have presented two hypotheses, how a T-cell may become activated, namely (A1) and (A2).

If one proceeds on assumption (A1), foreign-self distinction cannot be explained without taking into account negative selection (which will be done in the next chapter). The reason is that foreign and self-peptides do not differ a priori. A T-cell therefore cannot, without any previous learning process, distinguish between a single (or few) foreign and a single (or few) self-peptide(s). However, if one proceeds on assumption (A2), the foreign-self distinction is possible without taking into account negative selection (as we will see in the following). Certainly, in this case, another difference between foreign and self-peptides has to be assumed. This could be the copy number of the foreign peptides in the immunological synapse as we will see on the basis of a model proposed in 2001.

We start with this model and then analyze a generalized version. In order to do so we need a result from large deviation theory. It is a limit theorem that will be stated and applied in terms of an approximation. However, we do not know how good this approximation is. Therefore we additionally consider exact results for a reduced model containing the essential components.

5.1 The original BRB model and a generalized version

One possibility to explain how foreign-self distinction of T-cells works can be given on the basis of a model by van den Berg, Rand and Burroughs [11] (henceforth referred to as BRB).

Instead of the individual quantities characterizing the TCR-pMHC complexes (which would be decisive under assumption (A1)), the relevant quantities are the sums of the individual quantities. More precisely, the relevant quantities are the sums of the individual stimulation rates of all complexes in the immunological synapse. The individual stimulation rates might, in principle, be determined experimentally. However, owing to the diversity of complexes, it is neither possible nor necessary to specify all these quantities (as in statistical physics). Therefore, a probabilistic approach is required. The BRB model is the first such approach. There, the total stimulation rates characterizing the

encounters between an APC and a T-cell are assumed to be i.i.d. random variables; the distribution of these is the essential quantity. It will be derived in the following.

5.1.1   The total stimulation rate

As we have seen in the last chapter, an immunological synapse (formed during an encounter between a randomly chosen APC and a randomly chosen T-cell) consists of various types of self-pMHCs on the side of the APC (if there is no foreign invader present). We assume that the number n_s of different types of self-peptides is fixed for all immunological synapses.

Let us consider a randomly chosen immunological synapse. We assume that each of the n_s different pMHC types in the synapse occurs in a certain number Z_j ($j \in \{1, \ldots, n_s\}$) of copies such that the expected number of pMHCs in an immunological synapse is fixed, i.e.,

$$n_M = \mathbb{E} \left(\sum_{j=1}^{n_s} Z_j \right).$$

Moreover, each pMHC type is characterized by its individual stimulation rate (with respect to the TCR of the chosen T-cell). It is assumed to be a random variable denoted by W_j, where j characterizes the pMHC type. (In principle, W_j depends also on the TCR type. However, we suppress additional notation due to the i.i.d. assumption of all individual stimulation rates.) Thus, the total stimulation rate in the immunological synapse reads

$$G(z_f) = \left(\sum_{j=1}^{n_s} q Z_j W_j \right) + z_f W_{n_s+1} . \tag{5.1}$$

It depends on the number z_f of foreign peptides in the synapse, and the factor

$$q = \frac{n_M - z_f}{n_M}$$

appears here since the expected number of peptide molecules on the APCs is assumed to be constant (n_M).

The total stimulation rate G (a random variable) is the relevant quantity. A T-cell is assumed to be activated if G exceeds a certain threshold g_{act}. The probability of T-cell activation is therefore given by

$$\mathrm{P}\left(G(z_f) \geqslant g_{\mathrm{act}}\right) .$$

We now specify (5.1), strictly speaking, the distribution of the individual stimulation rates W_j, $1 \leqslant j \leqslant n_s + 1$, and the distribution of the copy numbers Z_j, $1 \leqslant j \leqslant n_s$.

5.1.2   Individual stimulation rates

The binding and unbinding of a TCR and a pMHC may, in chemical shorthand notation, be symbolized as

$$\mathrm{TCR} + \mathrm{pMHC} \underset{\rho}{\overset{\lambda}{\rightleftharpoons}} \mathrm{TCR\text{-}pMHC\ complex} ,$$

where λ and ρ are the association and dissociation rates, respectively. Due to the theory of elementary reaction kinetics, the duration T of a contact between a TCR and a pMHC is then exponentially distributed with mean binding time $\tau = 1/\rho$. Hence, the probability of

T to exceed t^* is $\mathrm{e}^{-t^*/\tau}$, which we refer to as the *stimulation probability* (of the TCR-pMHC complex).

It is assumed that the T-cell receives a stimulus every time a complex dissociates that has existed for at least time $t^* = 1$. (The reason is that certain reactions of signal transduction have to be completed.) Therefore, the average stimulation rate of a randomly chosen complex is given by

$$\rho\,\mathrm{P}(T > 1) = w(\tau) \quad \text{with} \quad w(\tau) = \frac{1}{\tau}\mathrm{e}^{-\frac{1}{\tau}}\,. \tag{5.2}$$

In Fig. 5.1, $w(\tau)$ is depicted as a function of τ. This curve can be interpreted as follows.

1. If $\tau \ll 1$, then the complex will typically dissociate before stimulation.

2. If $\tau \gg 1$, then the TCR and the pMHC will typically be associated for a long time. Therefore, the T-cell will get a stimulus through practically every binding event, but the pMHC keeps the receptor occupied for a long time, so only few stimuli are expected per time unit.
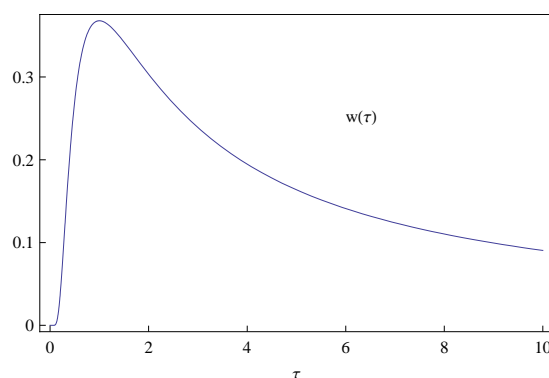

Figure 5.1: Average stimulation rate as a function of the average waiting time

The dissociation rates of the TCR-pMHC complexes in a randomly chosen immunological synapse are assumed to be i.i.d. random variables. (Of course, the same holds for the mean binding times $\mathcal{T}_j$, $j \in \{1, \dots, n_s + 1\}$.) This is justified by the same rationale as in statistical physics - the huge amount of complexes. Note: We make the i.i.d. assumption both for foreign and self-peptides. In particular, this assumption means that no distinction between foreign and self is built into the interaction between receptors and antigens. This reflects the fact that there is no a priori difference between the peptides.

The individual stimulation rates are then given by $W_j := w(\mathcal{T}_j)$, $j \in \{1, \dots, n_s + 1\}$, (compare (5.2)).

In the original BRB model, the mean binding times $\mathcal{T}_j$, $1 \leqslant j \leqslant n_s + 1$, are i.i.d. exponentially distributed with mean $\bar{\tau} := 0.04\,t^* = 0.04$. The resulting distribution of the individual stimulation rates (i.e., the distribution of W_1) is called ω-distribution. Note that there are two exponential distributions involved here. First, $\mathcal{T}_j$ ($1 \leqslant j \leqslant n_s + 1$), the mean binding times of the pMHCs and the TCR are exponential random variables. Second, the duration of the individual bindings of a pMHC and the TCR is $\mathrm{Exp}(1/\mathcal{T}_j)$ distributed (compare [47]).

Remark. The exponential distribution of the mean binding times is poorly founded. To show that the qualitative behavior does not rely on this particular probability distribution, we will, as an alternative, use the log-normal distribution (with parameters $\mu = -3.3$ and $\sigma = 0.5$) in Subsection 5.3.3. This has a justification in terms of binding/unbinding kinetics (see BRB [11] and Zint [64]).

The density f of W_1 is obtained via the transformation function for densities and depicted in Fig. 5.2 (on a logarithmic scale). Due to the missing monotonicity of w, one has to consider the two branches $[0,1]$ and $(1,\infty)$, separately. However, since $P(\mathcal{T}_1 \geqslant 1) = 1.34 \cdot 10^{-11}$, only the first branch is relevant. This becomes clear by plotting its contribution to f. The resulting curve does not differ visibly from f itself.
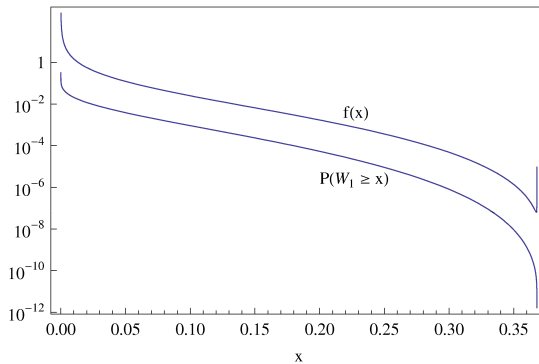

Figure 5.2: Density and activation curve of W_1

The density has two singularities (at 0 and 1/e) since $w'(0) = 0$ and $w'(1/e) = 0$ with much mass $(P(0 \leqslant W_1 \leqslant 0.01) = 0.98)$ close to the first singularity and little mass $(P(1/e - 0.01 \leqslant W_1 \leqslant 1/e) = 2.17 \cdot 10^{-9})$ close to the second singularity. We also depicted the so-called *activation curve* $1 - F_{W_1}(x)$ with $F_{W_1}(x) := 1 - P(W_1 \geqslant x)$. On the logarithmic scale it has a very similar form as the density. The reason is that the density is approximately linear on the logarithmic scale in the central range. The same holds for the activation curve since the activation curve of an exponentially distributed random variable (density $f(x) = \lambda e^{-\lambda x}$) is an exponential function $(P(X \geqslant x) = e^{-\lambda x})$. The only difference is the constant (λ) which results in the vertical shift of the curve.

Remark. As we stated in the last remark, the distribution of the mean binding time is not so decisive. The reason is the well founded function w resulting from the reaction kinetics. It ensures that for many distributions of the mean binding time the density and activation curve of W_1 is similar to that in Fig. 5.2.

Note that the flat central part of the activation curve of W_1 suggests an approximation by a scaled Bernoulli distribution. This is done in [12]. Instead of the ω-distribution for the individual stimulation rates, the authors choose $W_j \sim a \operatorname{Ber}(p)$ with $a = 1/e$ $(j \in \{1, \ldots, n_s + 1\})$. However, the choice of the parameters remains debatable. We get back to this below. But first we look into the distribution of Z_j, $j \in \{1, \ldots, n_s\}$.

5.1.3 Presentation of antigens

The genes of an organism can be classified as constitutive ones and inducible ones. The former encode proteins that are always present in every cell (e.g., proteins of the basic

metabolism). In contrast, the latter encode proteins that only exist in some cells (like for example muscle proteins) and/or occur only temporarily, i.e., they are variable.

Accordingly, in the original BRB model, the types of self-peptides on each APC are partitioned into constitutive and variable ones. The constitutive types are the same on each APC, whereas there is a different sample of variable types on each APC (depending on the tissues the APC has seen).

It is assumed that there are constant numbers n_c and n_v of constitutive and variable types of peptides, respectively, on each APC (such that $n_c + n_v = n_s$). Moreover, the copy numbers Z_j, $1 \leqslant j \leqslant n_c$ and $n_c + 1 \leqslant j \leqslant n_c + n_v$, respectively, of the constitutive and variable types are fixed (z_c and z_v, respectively). The parameter values $n_M = 10^5$, $n_c = 50$, $n_v = 1500$, $z_c = 500$ and $z_v = 50$ have been chosen on the grounds of experimental data (see BRB [11] and Zint [64]).

Due to (5.1), the total stimulation rate with respect to a conjunction of a randomly chosen T-cell and a randomly chosen APC is then given by

$$G(z_f) = \left(\sum_{j=1}^{n_c} qz_c W_j \right) + \left(\sum_{j=n_c+1}^{n_c+n_v} qz_v W_j \right) + z_f W_{n_c+n_v+1} \tag{5.3}$$

with W_j, $1 \leqslant j \leqslant n_c + n_v + 1$, i.i.d. ω-distributed. (5.3) is the original BRB model. But let us now consider a generalized version of the model.

5.1.4 Generalized BRB model

As a generalization of BRB [11] and Zint [64], in [65] we allowed the copy numbers of the individual types within each class (constitutive and variable, respectively) to vary. That is, we assume the random variables Z_j ($1 \leqslant j \leqslant n_s$) to be i.i.d. within each of the two classes (referred to as $Z_j^{(c)}$, $1 \leqslant j \leqslant n_c$, and $Z_j^{(v)}$, $n_c + 1 \leqslant j \leqslant n_c + n_v$).

Remark. The i.i.d. assumption is made for simplicity; we do not model a particular biological mechanism here. Realistic models would be based on an explicit consideration of how antigens are loaded onto MHC molecules (cf. BRB [11, Appendix C]).

Due to (5.1), the total stimulation rate with respect to a conjunction of a randomly chosen T-cell and a randomly chosen APC is then given by

$$G(z_f) = \left(\sum_{j=1}^{n_c} qZ_j^{(c)} W_j \right) + \left(\sum_{j=n_c+1}^{n_c+n_v} qZ_j^{(v)} W_j \right) + z_f W_{n_c+n_v+1} \ . \tag{5.4}$$

For ease of exposition we maintain the ω-distribution as in the original model as well as the parameter values for n_M, n_c and n_v. Furthermore, we use binomial distributions $\mathrm{Bin}(m_c, p)$ and $\mathrm{Bin}(m_v, p)$ for $Z_j^{(c)}$, $1 \leqslant j \leqslant n_c$, and $Z_j^{(v)}$, $n_c + 1 \leqslant j \leqslant n_c + n_v$, with parameters $m_c = 1000$, $m_v = 100$ and $p = 0.5$, so that the means $\mathbb{E}(Z_1^{(c)}) = 500$ and $\mathbb{E}(Z_1^{(v)}) = 50$ correspond to the values $z_c/n_M = 0.005$ and $z_v/n_M = 0.0005$ in the BRB-model. (Apart from the expectation, the probability distribution is an ad-hoc choice.) It should be mentioned that moderate changes of the values of the parameters (like for example n_c, n_v, $\mathbb{E}(Z_1^{(c)})$ and $\mathbb{E}(Z_1^{(v)})$) do not qualitatively alter the results.

5.1.5   Foreign-self distinction

As already seen in Chapter 4, for the immune system to work, two conditions are essential: (a) if a foreign antigen is present, then at least one T-cell will be activated; (b) there will be no activation when only self-antigens are present.

It is helpful to recast this into a hypothesis testing framework, in the following way. The immune system performs a test of the null hypothesis

$$H_0: \ z_f = 0 \tag{5.5}$$

against the alternative hypothesis

$$H_A: \ z_f > 0\,. \tag{5.6}$$

The test is performed via N independent encounters between a T-cell and an APC. H_0 is then rejected (and H_A assumed) if at least one encounter leads to the event $\{G \geqslant g_{\mathrm{act}}\}$; otherwise, H_0 is retained. The type I error is therefore

$$\alpha = \mathrm{P}(H_A \text{ assumed} \mid H_0 \text{ true}) = 1 - (1 - \mathrm{P}\left(G(0) \geqslant g_{\mathrm{act}}\right))^N,$$

and the type II error is

$$\beta = \mathrm{P}(H_0 \text{ assumed} \mid H_A \text{ true}) = (1 - \mathrm{P}\left(G(z_f) \geqslant g_{\mathrm{act}}\right))^N\,.$$

Here, $G(z_f)$ is as in Equation (5.1). In particular, $G(0)$ denotes the total stimulation rate in the absence of foreign peptides.

Remark. The parameter g_{act} can be fine-tuned by the cell; for more on activation threshold tuning, see van den Berg and Rand [13].

Clearly, α is the probability of an autoimmune response, whereas β is the probability that a foreign antigen goes unnoticed. By (b) and (a) above, both α and β must be small for foreign-self distinction to work.

Both $\{G(0) \geqslant g_{\mathrm{act}}\}$ and $\{G(z_f) \geqslant g_{\mathrm{act}}\}$ are rare events (since at most a tiny fraction of the T-cell population reacts to a given APC). Therefore, α is close to 0 (close to 1) and β is close to 1 (close to 0) for N small (N very large). We have no good knowledge of the value of N (except that it is bounded above by the number of T-cell types). But it is clear that a necessary condition for distinction is that g_{act} can be chosen in such a way that, for physiologically realistic values of z_f,

(C1) $$\mathrm{P}(G(z_f) \geqslant g_{\mathrm{act}}) \gg \mathrm{P}(G(0) \geqslant g_{\mathrm{act}}).$$

Consequently, there is a region of intermediate values of N for which both α and β are small.

In order to prevent an autoimmune reaction, the probability $\mathrm{P}(G(0) \geqslant g_{\mathrm{act}})$ has to be tiny (roughly 10^{-7}). Since the normal approximation becomes too crude, this requires large deviation theory which is the subject of the next section.

5.2 Large deviations

For many families of random variables, *large deviation principles* (LDP's) are available to characterize their atypical behaviour. Here, we will be concerned with sums of random variables, i.e.,

$$S_n = \sum_{i=1}^{n} X_i,$$

where $(X_i)_{i \geqslant 1}$ is a sequence of independent (but *not* necessarily identically distributed) random variables (like those in Eq. (5.1)). An LDP characterizes the probability of a large deviation of S_n from its expectation; a *large deviation* is a deviation of order n (in contrast to a *normal deviation* of order $\sqrt{n}$, as covered by the central limit theorem). A basic result is Cramér's theorem, which says the following. For a sequence $(X_i)_{i \geqslant 1}$ of i.i.d. real-valued random variables whose moment-generating function $\phi(\vartheta) = \mathbb{E}(\exp(\vartheta X_1))$ is finite for all $\vartheta \in \mathbb{R}$, one has, for all $a > \mathbb{E}(X_1)$,

$$\lim_{n \to \infty} \frac{1}{n} \log \mathrm{P}(S_n \geqslant an) = -I(a), \tag{5.7}$$

where $I(a) = a\vartheta_a - \psi(\vartheta_a)$, $\psi(\vartheta) = \log \phi(\vartheta)$, and ϑ_a is the (unique) solution of $\psi'(\vartheta) = a$. That is, for large n, the probability that S_n is larger than an decays exponentially with n, with decay rate $I(a)$. The value ϑ_a is known as the *"tilting" parameter*. It is used for an exponential reweighting (or "tilting") of the distribution of the X_i (and hence of S_n) that inflates the right-hand tail of the probability distribution in such a way that the rare event $\{S_n \geqslant an\}$ turns into a typical one; this is a crucial step in the analysis. For a review of large deviation theory, see e.g. [24, 37]; Cramér's theorem and its proof are found in [37, Chap. I.3], for example.

Note, however, that the knowledge of the exponential decay rate $I(a)$ alone does not suffice to provide meaningful leading-order estimates of the probabilities of the rare event itself. This is because (5.7) is compatible with $\mathrm{P}(S_n \geqslant an) = f(n) \exp\left(-nI(a)(1 + o(1))\right)$ for any prefactor $f(n) = \mathcal{O}(n^\alpha)$, with arbitrary α. More accurate information is obtained from so-called *exact asymptotics*. For the situation at hand, this is given by a refinement of Cramér's theorem due to Bahadur and Rao (cf. [24], Chap. 3.7). Namely, under the assumptions of Cramér's theorem and the additional requirement that the distribution of X_1 be non-lattice (which is always fulfilled if X_1 has a density), one has

$$\mathrm{P}(S_n \geqslant an) = \frac{1}{\sqrt{2\pi n}\sigma \vartheta_a} e^{-nI(a)}(1 + o(1)) \text{ as } n \to \infty \tag{5.8}$$

for all a that satisfy $\mathbb{E}(X_1) < a < \sup_\vartheta \psi(\vartheta)$. Here, $I(a)$ and ϑ_a are as above, and $\sigma^2 = \psi''(\vartheta_a)$ is the variance of $\frac{1}{n}S_n$ after "tilting" with the exponential parameter ϑ_a. (The condition $a < \sup_\vartheta \psi(\vartheta)$ ensures that only those events $\{S_n \geqslant an\}$ are considered that are actually possible; the condition is void if X_1, and hence S_n/n, take values in all of $\mathbb{R}_{\geqslant 0}$.) What we need to tackle our stimulation rates (5.1) is the generalization of (5.8) to situations in which the $(X_i)_{i \geqslant 1}$ are *not* identically distributed. Fortunately, a very general result is available, which does not even require independence. This is the result of Chaganty and Sethuraman [19], which plays a crucial role in our analysis, and which we will now formulate.

Let $(S_n)_{n \in \mathbb{N}}$ be a sequence of $\mathbb{R}$-valued random variables, with moment generating functions $\phi_n(\vartheta) = \mathbb{E}\left(\exp(\vartheta S_n)\right)$, $\vartheta \in \mathbb{R}$. Suppose that there exists a $\vartheta^* \in (0, \infty)$ such that

$$\sup_{n \in \mathbb{N}} \; \sup_{\vartheta \in B_{\vartheta*}} \; \phi_n(\vartheta) < \infty \, , \tag{5.9}$$

where $B_{\vartheta*} = \{\vartheta \in \mathbb{C} \colon |\vartheta| < \vartheta^*\}$. Define

$$\psi_n(\vartheta) = \frac{1}{n} \log \phi_n(\vartheta) \, , \tag{5.10}$$

and let $(a_n)_{n \in \mathbb{N}}$ be a bounded sequence in $\mathbb{R}$ such that for each n the equation

$$a_n = \psi_n'(\vartheta) \tag{5.11}$$

has a solution $\vartheta_n \in (0, \vartheta^{**})$ for some $\vartheta^{**} \in (0, \vartheta^*)$. This solution is unique by strict convexity of ψ_n. Define

$$\begin{aligned} \sigma_n^2 &= \psi_n''(\vartheta_n) \, , \\ I_n(a_n) &= a_n \vartheta_n - \psi_n(\vartheta_n) \, . \end{aligned} \tag{5.12}$$

Theorem 12 (Chaganty-Sethuraman)**.** *If* $\inf_{n \in \mathbb{N}} \sigma_n^2 > 0$, $\lim_{n \to \infty} \vartheta_n \sqrt{n} = \infty$ *and*

$$\lim_{n \to \infty} \sqrt{n} \; \sup_{\delta_1 \leqslant |t| \leqslant \delta_2 \vartheta_n} \left| \frac{\phi_n(\vartheta_n + it)}{\phi_n(\vartheta_n)} \right| = 0 \quad \forall \, 0 < \delta_1 < \delta_2 < \infty \, , \tag{5.13}$$

then

$$\mathrm{P}\left(S_n \geqslant n a_n\right) = \frac{e^{-n I_n(a_n)}}{\vartheta_n \sigma_n \sqrt{2\pi n}} \left(1 + o(1)\right) \qquad \textit{as } n \to \infty \, . \tag{5.14}$$

Proof. See [19]. □

In analogy with the previous discussion, ϑ_n is the "tilting parameter" for the distribution of $\frac{1}{n} S_n$, σ_n^2 is the variance of the "tilted" $\frac{1}{n} S_n$, and $I_n(a_n)$ is the large deviation rate function.

The stated theorem is now applied to the situation of the generalized BRB model.

5.3   Activation curves

In order to investigate whether Condition (C1) can be fulfilled for physiologically realistic values of z_f, we consider the activation curves of $G(z_f)$ in (5.4) for different values of z_f.

5.3.1   Approximation

We begin by deriving an approximation based on Theorem 12. Consider a sequence of models defined by increasing numbers of constitutive and variable peptide types. Let

$$n = \begin{cases} n_c + n_v, & \text{if } z_f = 0, \\ n_c + n_v + 1, & \text{otherwise,} \end{cases}$$

and consider the limit $n \to \infty$ with $\lim_{n \to \infty} n_c/n_v = C_1 \in (0, \infty)$; note that the number of foreign peptides remains 1 throughout. Let S_n in Theorem 12 be

$$G_n(z_f) = \left(\sum_{j=1}^{n_c} q_n Z_j^{(c)} W_j \right) + \left(\sum_{j=n_c+1}^{n_c+n_v} q_n Z_j^{(v)} W_j \right) + z_f W_{n_c+n_v+1}$$

where

$$q_n = \frac{n_c \, m_c \, p + n_v \, m_v \, p - z_f}{n_c \, m_c \, p + n_v \, m_v \, p} \, ,$$

and let M_c, M_v and M be the moment generating functions of $Z_j^{(c)} W_j$, $Z_j^{(v)} W_j$ and W_j, respectively, i.e., for $\gamma \in \{c, v\}$,

$$M_\gamma(\vartheta) = \frac{1}{\bar{\tau}} \sum_{k=0}^{m_\gamma} \left(\int_0^\infty \exp\left(k\vartheta \, \frac{\exp(-t^*/\tau)}{\tau} - \frac{\tau}{\bar{\tau}} \right) \mathrm{d}\tau \right) \mathrm{Bin}_{m_\gamma, p}(k) \, , \tag{5.15}$$

and

$$M(\vartheta) = \frac{1}{\bar{\tau}} \int_0^\infty \exp\left(\vartheta \, \frac{\exp(-t^*/\tau)}{\tau} - \frac{\tau}{\bar{\tau}} \right) \mathrm{d}\tau \, . \tag{5.16}$$

Choose $a_n \equiv a$ and $g_{\mathrm{act}}(n) = an$. Let ϑ_n be the unique solution of

$$\begin{aligned}
a = \quad & \frac{n_c}{n} q_n \left[\frac{\mathrm{d}}{\mathrm{d}\vartheta} \log M_c(\vartheta) \right] \Big|_{\vartheta=q_n\vartheta_n} \\
& + \frac{n_v}{n} q_n \left[\frac{\mathrm{d}}{\mathrm{d}\vartheta} \log M_v(\vartheta) \right] \Big|_{\vartheta=q_n\vartheta_n} + \quad \frac{1}{n} z_f \left[\frac{\mathrm{d}}{\mathrm{d}\vartheta} \log M(\vartheta) \right] \Big|_{\vartheta=z_f\vartheta_n} \, .
\end{aligned} \tag{5.17}$$

We further define

$$\begin{aligned}
\sigma_n^2 = \quad & \frac{n_c}{n} q_n^2 \left[\frac{\mathrm{d}^2}{\mathrm{d}\vartheta^2} \log M_c(\vartheta) \right] \Big|_{\vartheta=q_n\vartheta_n} \\
& + \frac{n_v}{n} q_n^2 \left[\frac{\mathrm{d}^2}{\mathrm{d}\vartheta^2} \log M_v(\vartheta) \right] \Big|_{\vartheta=q_n\vartheta_n} + \frac{1}{n} z_f^2 \left[\frac{\mathrm{d}^2}{\mathrm{d}\vartheta^2} \log M(\vartheta) \right] \Big|_{\vartheta=z_f\vartheta_n}
\end{aligned} \tag{5.18}$$

and

$$I_n(a) = a\vartheta_n - \frac{n_c}{n} \log M_c(q_n\vartheta_n) - \frac{n_v}{n} \log M_v(q_n\vartheta_n) - \frac{1}{n} \log M(z_f\vartheta_n) \, . \tag{5.19}$$

Since we have only finitely many different types of random variables, all independent, it is straightforward to check

Lemma 6. *The conditions for Theorem* 12 *are satisfied.*

Proof. The moment generating function $\phi_n(\vartheta)$ is given by

$$\phi_n(\vartheta) = \begin{cases} (M_c(\vartheta))^{n_c} (M_v(\vartheta))^{n_v} \, , & \text{if } z_f = 0, \\ (M_c(q_n\vartheta))^{n_c} (M_v(q_n\vartheta))^{n_v} M(z_f\vartheta), & \text{otherwise.} \end{cases}$$

Let z_f be fixed. If a is chosen such that $g_{\mathrm{act}}(n) > \mathbb{E}(G_n(0))$ and $g_{\mathrm{act}}(n) > \mathbb{E}(G_n(z_f))$ for all n (in which case the strict inequalities are in fact uniform in n), then $\lim_{n \to \infty} \vartheta_n = C_2 \in (0, \infty)$. Consequently, $\lim_{n \to \infty} \vartheta_n \sqrt{n} = \infty$, and also $\inf_{n \in \mathbb{N}} \sigma_n^2 > 0$. It thus remains to

verify Condition (5.13). Let $F_c(x)$, $F_v(x)$ and $F(x)$ be the distribution functions of $Z_j^{(c)}W_j$, $Z_j^{(v)}W_j$ and W_j, respectively. Since

$$\nu_\gamma^{(n)}(t) = \frac{M_\gamma(q_n(\vartheta_n + it))}{M_\gamma(q_n\vartheta_n)} = \int_\mathbb{R} \exp(iq_n tx)\, \frac{\exp(q_n\vartheta_n x)}{M_\gamma(q_n\vartheta_n)}\, dF_\gamma(x), \qquad \gamma \in \{c, v\}\ ,$$

and

$$\nu^{(n)}(t) = \frac{M(z_f(\vartheta_n + it))}{M(z_f\vartheta_n)} = \int_\mathbb{R} \exp(iz_f tx)\, \frac{\exp(z_f\vartheta_n x)}{M(z_f\vartheta_n)}\, dF(x)$$

are characteristic functions of random variables that are not constant nor are lattice valued, and ϑ_n and q_n converge as $n \to \infty$, there exists an $\varepsilon > 0$ and an $n_0 < \infty$ such that, for all $t \neq 0$ and $n \geqslant n_0$, $|\nu_c^{(n)}(t)| \leqslant 1 - \varepsilon$, $|\nu_v^{(n)}(t)| \leqslant 1 - \varepsilon$ and $|\nu^{(n)}(t)| \leqslant 1 - \varepsilon$ (see Feller [27, Chapter XV.1, Lemma 4]). From this it follows that

$$\begin{aligned}
\left| \frac{\phi_n(\vartheta_n + it)}{\phi_n(\vartheta_n)} \right| &\\
&= \left| \frac{(M_c(q_n(\vartheta_n + it)))^{n_c} (M_v(q_n(\vartheta_n + it)))^{n_v} M(z_f(\vartheta_n + it))}{(M_c(q_n\vartheta_n))^{n_c} (M_v(q_n\vartheta_n))^{n_v} M(z_f\vartheta_n)} \right| \\
&= \left| \left(\nu_c^{(n)}(t)\right)^{n_c} \left(\nu_v^{(n)}(t)\right)^{n_v} \nu^{(n)}(t) \right| \\
&= o(1/\sqrt{n})
\end{aligned}$$

as $n \to \infty$ for all $t \neq 0$ (compare the argument leading to [27, Chapter XVI.6, Equation (6.6)]), which guarantees (5.13). $\qquad\square$

In view of Lemma 6, we may approximate the probability of T-cell activation as

$$P\left(G(z_f) \geqslant g_{\text{act}}\right) \approx \frac{e^{-nI_n(a)}}{\vartheta_n \sigma_n \sqrt{2\pi n}}\ , \tag{5.20}$$

where $G(z_f)$ is the stimulation rate of (5.4), $g_{\text{act}} = g_{\text{act}}(n) = an$, and we assume that n is large enough for a good approximation. (Note that the threshold g_{act} is not known; but we do know that reactions of T-cells are rare events. Especially, if there is no foreign peptide present, the probability of T-cell activation has to be smaller than 10^{-7} since there are roughly 10^7 up to 10^8 T-cells present in a day (which should not be activated), compare [2, 50]. The probabilities we are interested in are therefore so small that they do not lie in the range of the central limit theorem (compare Fig. 5.3 below). Rather g_{act} is such that large deviations results are applicable, as will also be confirmed by our simulations below.) The expression on the right-hand side of (5.20) must be evaluated numerically (we used Mathematica® [62]), since already the moment generating functions in (5.15) and (5.16) are unavailable analytically, and this carries over to ϑ_n, σ_n^2, and $I_n(a)$ in (5.17)-(5.19).

Remark. Rather than taking the limit in the way described above, we could as well consider a sequence of models with n_f different foreign peptides and let $n \to \infty$ such that n_c/n, n_v/n and n_f/n each tend to a constant; the approximation of our given finite system by (5.17)-(5.20) would remain unchanged.

The number of foreign peptides remains 1 in the limit considered. So, the influence of the foreign part fades away and one should be critical whether the approximation is adequate. Therefore we compare the approximation with simulations in the next subsection.

5.3.2   Comparison with simulations

Let us consider the activation curves for two extreme cases, namely, the self-background ($z_f = 0$), and a very large number of foreign peptides ($z_f = 2500$).
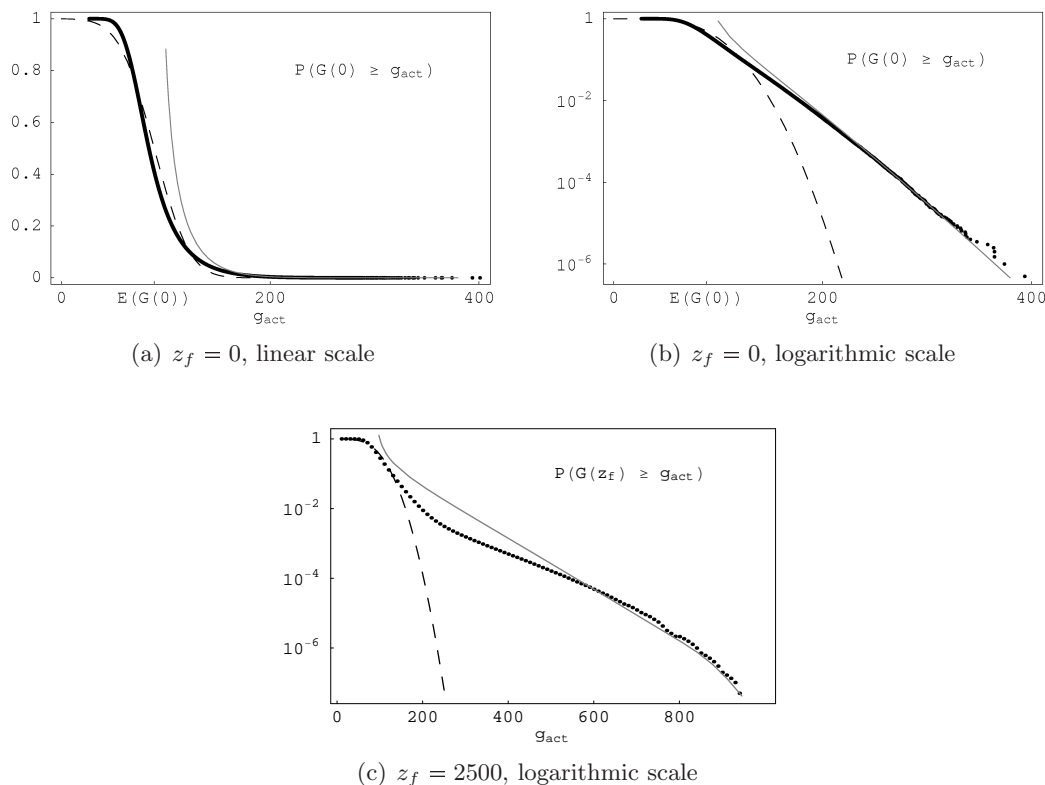

(a) $z_f = 0$, linear scale

(b) $z_f = 0$, logarithmic scale

(c) $z_f = 2500$, logarithmic scale

Figure 5.3: $P(G(z_f) \geqslant g_{\mathrm{act}})$ as a function of g_{act}, for the self background ($z_f = 0$), and a very large number of foreign peptides ($z_f = 2500$). The thick curve and the points, respectively, form the simulated activation curve resulting from two million [(a),(b)] and twenty million [(c)] sampling points. The dashed curve is the normal approximation, and the thin curve is the large deviation approximation (5.20). The simulation in (c) was kindly provided by F. Lipsmeier.

Fig. 5.3 shows the simulated curve in comparison to the normal approximation and the approximation in (5.20). As was to be expected, the normal approximation describes the central part well, whereas for the right tail (the relevant part of the probability distribution for the problem at hand) the large deviation approximation is appropriate. For $z_f = 0$, the latter describes the simulated activation curve in an excellent way; for $z_f = 2500$, it still gives correct approximations beyond $g_{\mathrm{act}} = 550$.

An improved approximation of the entire curve is obtained in BRB [11] (for the original model) by combining the normal and the large deviation approximations, applying them to the self-peptides only, and performing a convolution with the single foreign one. We prefer the direct approach (5.20) here, because it makes the large deviation aspect more transparent.

5.3.3 Approximated activation curves

As we have seen in the last subsection, the approximation in (5.20) is suitable for the calculation of the activation curves for various values of z_f. Fig. 5.4 shows the curves as a function of g_{act} for exponentially (a) and log-normally (b) distributed mean binding times. The results in (a) and (b) are qualitatively the same. Namely, we observe that the curves for $z_f = 250$ and $z_f = 500$ (both $\leqslant \mathbb{E}(Z_1^{(c)}) = 500$) do not differ visibly from the curve for the self-background; but, for $z_f > 1000$ and $g_{\text{act}} > 500$, Condition (C1) is fulfilled. Therefore, the model can indeed explain how T-cells are able to distinguish between foreign and self. Comparison with Fig. 3 of BRB [11] shows that the separation of the activation curves is indeed similar to that in the original model. In terms of the cartoon in Fig. 4.1, the threshold value g_{act} can be chosen so that T-cell 2 will be activated when it encounters APC 2 with three foreign peptides (the circles), while the other APCs without foreign peptides (the non-circles) will not activate any T-cell.

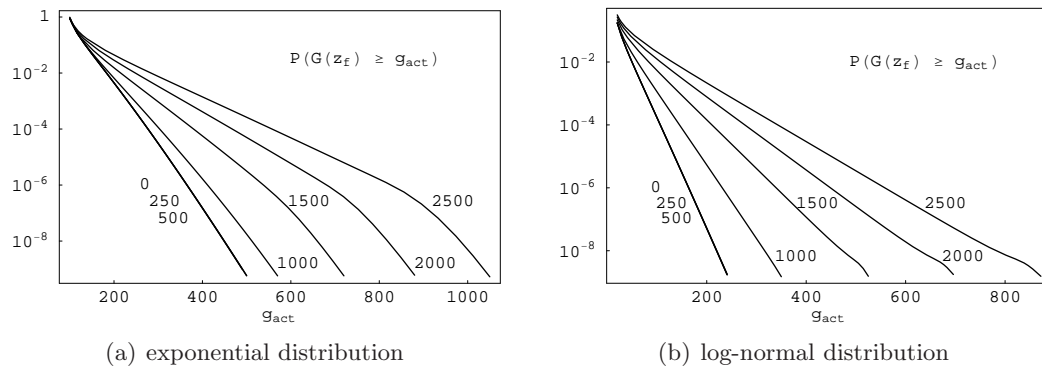(a) exponential distribution   (b) log-normal distribution

Figure 5.4: Activation curves for values of z_f ranging from 0 to 2500, calculated according to approximation (5.20) for two different distributions of the mean binding times. The horizontal axis is chosen to start at a value of g_{act} that yields a probability close to 1 in this approximation.

The intuitive reason behind the foreign-self distinction is an elevated number of presented foreign peptides in comparison with the copy numbers of individual types of self-peptides. Indeed, this increases the variability of G (which is reminiscent of the fact that for $n \geqslant 2$ i.i.d. random variables with positive variance, nY_1 has a larger variance than $\sum_{i=1}^{n} Y_i$). So far, the number of presented foreign peptides has to be fairly large: at least as large as the copy number of constitutive ones, which are, in turn, more abundant than the variable ones (one might actually reformulate the hypotheses pair (5.5) and (5.6) so as to test whether the foreign antigen is more abundant than the constitutive peptides or not). However, this restriction vanishes when we take the training phase of the young T-cells into account, as will be done in the next chapter.

Moreover, a second problem arises. For our analysis we used large deviation approximations. However, we do not have any error bounds. (In principle, error estimates (of Berry-Esséen type) can be obtained but in practice these are useless.) As we have seen in Fig. 5.3, the approximation fits in with the simulations in a large range. But there are parts where the distinction is overestimated. As one may see in Fig. 5.4, these parts are also relevant. This is the reason why exact results and error bounds, respectively, are desirable. Another reason is that the comparison of the results for different probability

distributions (as in Fig. 5.4 (a) and (b)) is difficult since one does not know how good the approximations are.

Therefore, we aim at exact results. But before we embark on these, let us again simplify the model.

5.4 Reduced model

The simplest case of (5.1) is the one where $Z_j = z$ is constant for all $j \in \{1, \ldots, n_s\}$. Then, the total stimulation rate with respect to a conjunction of a randomly chosen T-cell and a randomly chosen APC is given by

$$G(z_f) = \left(\sum_{j=1}^{n_s} q z W_j \right) + z_f W_{n_s+1} . \tag{5.21}$$

This random variable will be considered in the following. In order to derive results comparable to those of the last section we use the same parameter value for n_M as well as the intermediate values $n_s = 1000$ (i.e., $n_c < n_s < n_v$) and $z = 100$ (i.e., $z_v < z < z_c$). Moreover we maintain the ω-distribution for W_j, $1 \leqslant j \leqslant n_s + 1$.

We are interested in bounds for the activation curves. Since G is a sum we work out inequalities for the probability that a sum exceeds a threshold.

5.4.1 Inequalities for sums

The first upper bound goes back to the Markov inequality applied to the exponential of a sum, i.e., for all $\vartheta \geqslant 0$,

$$\mathrm{P}\left(X + Y \geqslant z \right) \leqslant \frac{\mathbb{E}\left(\mathrm{e}^{\vartheta(X+Y)} \right)}{\mathrm{e}^{\vartheta z}} .$$

This is also called "exponential Chebyshev" and results in the large deviation upper bound

$$\log \mathrm{P}\left(X + Y \geqslant z \right) \leqslant -I(z) \tag{5.22}$$

with

$$I(z) = \sup_{\vartheta \geqslant 0} \left(\vartheta z - \log \mathbb{E}\left(\mathrm{e}^{\vartheta(X+Y)} \right) \right)$$

(compare [24, Chap. 1.2]).

A second upper bound and a lower bound may be derived by truncation of the convolution

$$\mathrm{P}\left(X + Y \geqslant z \right) = \int_z^\infty \int_{-\infty}^\infty f_X(s) f_Y(t-s) \mathrm{d}s \mathrm{d}t$$

$$= \int_{-\infty}^c f_X(s) \, \mathrm{P}\left(Y \geqslant z-s \right) \mathrm{d}s + \int_c^\infty f_X(s) \, \mathrm{P}\left(Y \geqslant z-s \right) \mathrm{d}s .$$

The splitting into two integrals may be done for arbitrary values of c. If we bound the two terms from above or from below, the best bounds are obtained by taking the infimum or supremum over all c. Hence, we get the upper bound

$$\mathrm{P}\left(X + Y \geqslant z \right) \leqslant \inf_c \left(\mathrm{P}\left(X \leqslant c \right) \mathrm{P}\left(Y \geqslant z-c \right) + \mathrm{P}\left(X > c \right) \right)$$

and the lower bound

$$\mathrm{P}\left(X + Y \geqslant z\right) \geqslant \sup_c \left(\mathrm{P}\left(X \geqslant c\right) \mathrm{P}\left(Y \geqslant z - c\right)\right) \tag{5.23}$$

(compare the illustration in Fig. 5.5). These bounds only make sense if they capture the dominant terms in the convolution. They will be optimal if all mass is concentrated in the areas which are hatched or blank in both Fig. 5.5 (a) and (b).
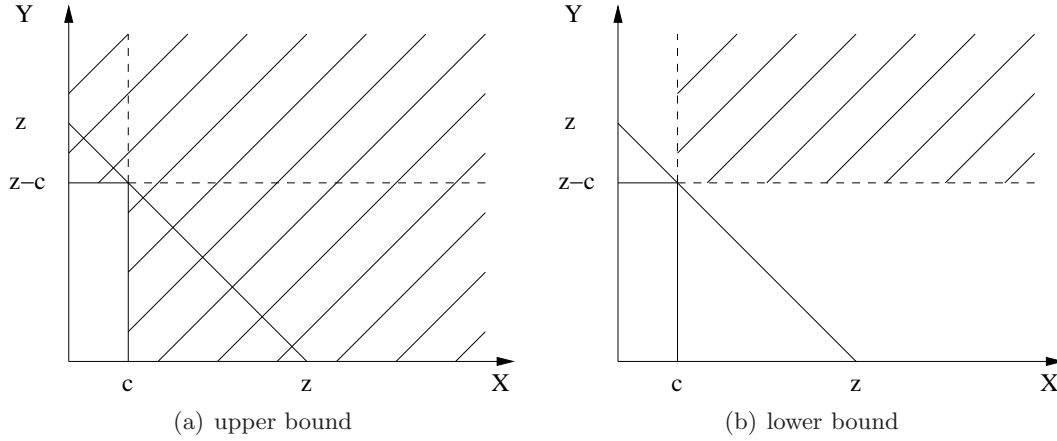

(a) upper bound   (b) lower bound

Figure 5.5: Illustration of the bounds resulting from cutting of the convolution

Remark. The supremum in (5.23) (for a distribution which possesses a density) is reached where the hazard function (the density divided by the *activation function* describing the activation curve) of X at $z - c$ equals the hazard function of Y at c. The reason is that

$$\left(P\left(X \geqslant c\right) P\left(Y \geqslant z - c\right)\right)' = f_Y(z - c)P\left(X \geqslant c\right) - f_X(c)P\left(Y \geqslant z - c\right) \ .$$

5.4.2 Lower bounds for the foreign-self distinction

In order to account for the possibility of a discrimination of foreign and self, the distinction between the activation curves for $z_f = 0$ and $z_f > 0$ has to be high enough. Therefore, we develop a lower bound for this distinction. This can be done by applying the bounds of the last subsection to G. Having a lower bound for the foreign activation curve and an upper bound for the background, the distinction between the activation curves is ensured to be greater or equal to the difference of the bounds (compare the illustration in Fig. 5.6).

We start with the calculation of a lower bound for the foreign activation curve. It is derived from (5.23) by choosing $c = \mathbb{E}(X)$. The logarithmic quantity is given by

$$\log \mathrm{P}\left(G(z_f) \geqslant g_{\mathrm{act}}\right) = \log \mathrm{P}\left(\sum_{j=1}^{n_s} qzW_j + z_f W_{n_s+1} \geqslant g_{\mathrm{act}}\right)$$

$$\geqslant \log \left[\sup_c \left(\mathrm{P}\left(\sum_{j=1}^{n_s} qzW_j \geqslant c\right) \mathrm{P}\left(z_f W_{n_s+1} \geqslant g_{\mathrm{act}} - c\right)\right)\right]$$

$$\geqslant \log p + \log \mathrm{P}\left(z_f W_{n_s+1} \geqslant g_{\mathrm{act}} - \mathbb{E}\left(\sum_{j=1}^{n_s} qzW_j\right)\right)$$
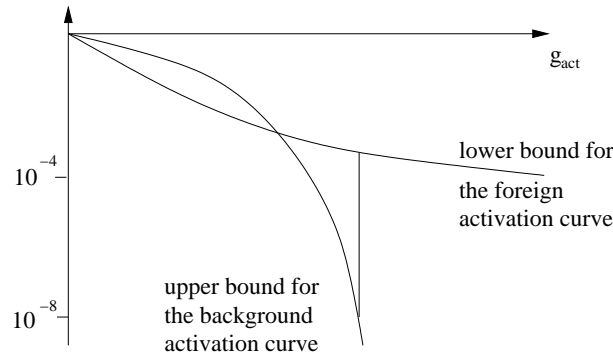
Figure 5.6: Illustration of the lower bound for the foreign-self distinction on a logarithmic scale

with

$$p = \frac{1}{2} - \frac{0.7975 \sum_{j=1}^{n_s} \mathbb{E}\left(|W_j - \mathbb{E}(W_j)|^3\right)}{\left(\sum_{j=1}^{n_s} \mathbb{E}\left((W_j - \mathbb{E}(W_j))^2\right)\right)^{3/2}}$$

due to the Berry-Esséen inequality (cf. [27], Chap. XVI).

In order to bound the background activation curve we use the large deviation upper bound (see (5.22)). The logarithmic probability is then given by (minus) the rate function

$$\log P\left(G(0) \geqslant g_{\text{act}}\right) \leqslant -I(g_{\text{act}}) = -\sup_{\vartheta \geqslant 0}\left(\vartheta g_{\text{act}} - \log \mathbb{E}\left(e^{\vartheta G(0)}\right)\right) \ .$$

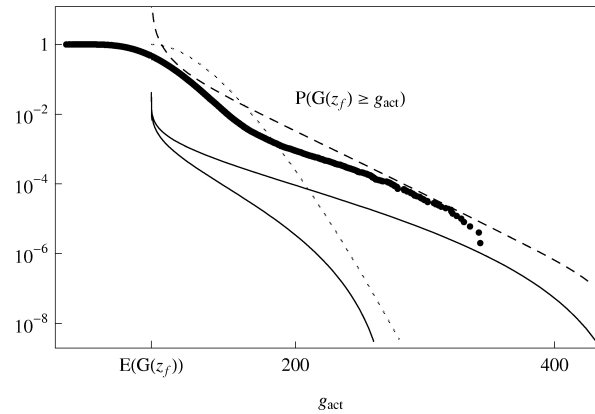The bounds are shown in Fig. 5.7. One can see that in the relevant range, where the

Figure 5.7: An upper bound of the background activation curve (dotted; $z_f = 0$), lower bounds for the foreign activation curves (thin; $z_f = 500$ for the left and $z_f = 1000$ for the right curve) as well as the simulation (thick and points; $z_f = 1000$) and the large deviation approximation (dashed) for the ω-distribution

probability of an immune response (i.e., $P(G(0) \geqslant g_{\text{act}})$) is very small (e.g. 10^{-8}), there is a distinction of several orders of magnitude for the parameter value $z_f = 1000$. For comparison, we have depicted the simulation result and the large deviation approximation,

too. This shows that the upper bound underestimates the real activation curve but it is good enough to explain the foreign-self distinction.

However, already for the parameter value $z_f = 500$ ($= 5z$) the foreign-self distinction cannot be reasonably bounded this way since the lower bound of the foreign activation curve lies below the upper bound of the background. The reason is the fact that the bounds become too crude in that case. As shown in Fig. 5.8 (a) the foreign-self distinction for $z_f = 500$ given by the large deviation approximation is much larger. The same is true for the simulated curves (see Fig. 5.8 (b)). However, the distinction becomes small even for $z_f = 300$.

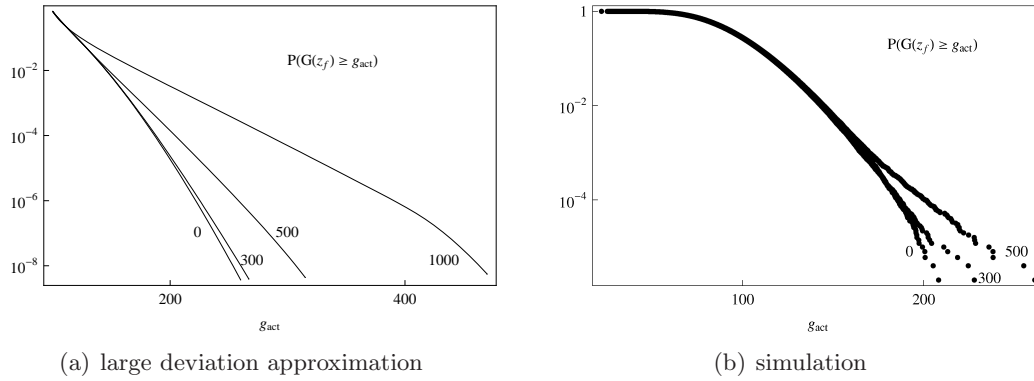(a) large deviation approximation   (b) simulation

Figure 5.8: Activation curves for values of z_f ranging from 0 to 1000, calculated according to the large deviation approximation for the reduced model and simulated, respectively

As already mentioned in Section 5.1, the ω-distribution may, as a first approximation, be described by a scaled Bernoulli distribution. We therefore further consider the alternative distribution $a\operatorname{Ber}(p)$ and let $\widetilde{W}_j$ i.i.d. $\sim a\operatorname{Ber}(p)$, $1 \leqslant j \leqslant n_s + 1$, take the role of W_j. Here, p is the relevant (free) parameter. a (scaling the axis) is chosen so that $a\,p = \mathbb{E}(W_1)$ for comparison with the distribution of W_1. We consider two choices: (a) $p = 8.89 \cdot 10^{-4}\mathrm{e}$ and $a = 1/\mathrm{e}$ as well as (b) $p = 8.89 \cdot 10^{-4}$ and $a = 1$. In the first case the maximal value is the same as that of W_j. The second case corresponds to a smaller value of p (an ad-hoc choice).

Our bounds together with the true activation curves (which may be exactly calculated in this case) and the large deviation approximation are depicted in Fig. 5.9.

As we may see in Fig. 5.9 (a), the result is similar to that in the case of the ω-distribution if we use the scaled Bernoulli distribution with $a = 1/\mathrm{e}$. However, as we may see in Fig. 5.9 (b), the lower bound for the foreign-self distinction in the relevant range becomes larger if we use a scaled Bernoulli distribution with larger maximal value ($a = 1$), i.e. smaller p.

In the scaled Bernoulli case, the lower bounds can be optimized by really taking the supremum in (5.23). It is given by

$$s_{z_f}(g_{\mathrm{act}}) := \max\left(p\,\mathrm{P}\left(\sum_{j=1}^{n_s} qzW_j \geqslant g_{\mathrm{act}} - z_f a \right), \mathrm{P}\left(\sum_{j=1}^{n_s} qzW_j \geqslant g_{\mathrm{act}} \right) \right). \qquad (5.24)$$

The true activation curves together with s_{z_f} are shown in Fig. 5.10. Obviously, s_{z_f} is a very good lower bound for the activation curves.
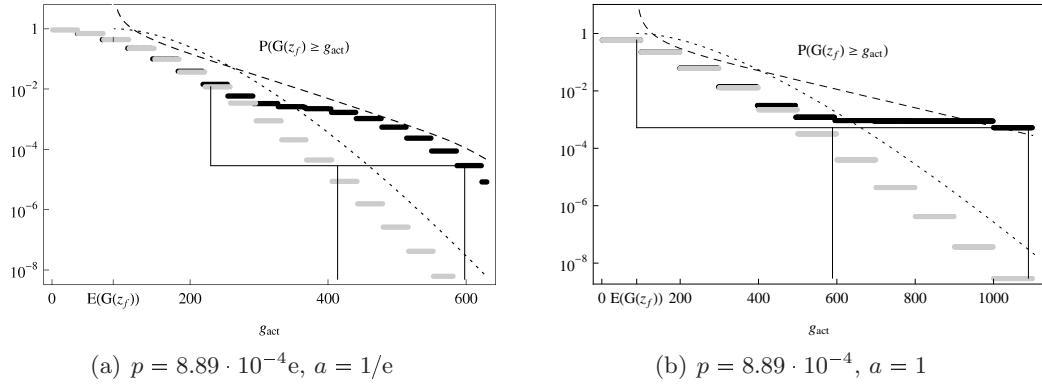
(a) $p = 8.89 \cdot 10^{-4}$e, $a = 1/$e

(b) $p = 8.89 \cdot 10^{-4}$, $a = 1$

Figure 5.9: The true background activation curve (gray; $z_f = 0$), its upper bound (dotted), lower bounds for the foreign activation curves (thin; $z_f = 500$ for the left and $z_f = 1000$ for the right curve) as well as the true foreign activation curve (black, thick; $z_f = 1000$) and the large deviation approximation (dashed) for scaled Bernoulli distributions with two different values of p

(a) $p = 8.89 \cdot 10^{-4}$e, $a = 1/$e
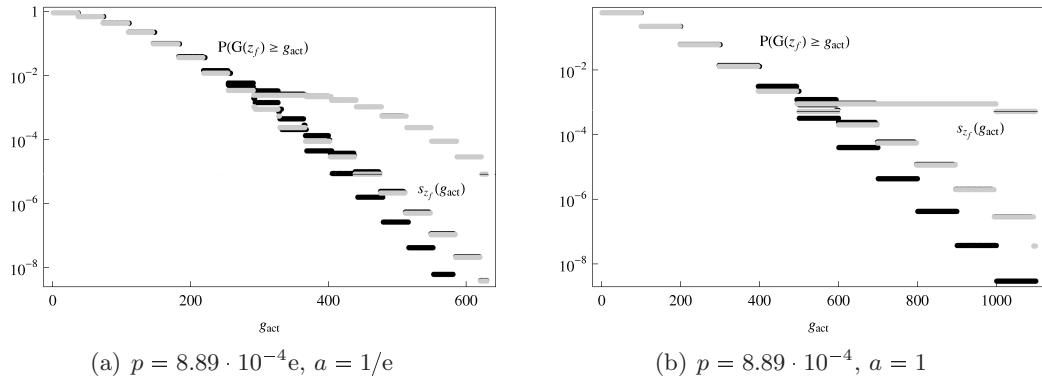
(b) $p = 8.89 \cdot 10^{-4}$, $a = 1$

Figure 5.10: The true activation curves (black) for $z_f = 0$, $z_f = 500$ and $z_f = 1000$ from left to right as well as s_{z_f} for $z_f = 500$ and $z_f = 1000$ (gray) for scaled Bernoulli distributions for two values of p (and a, respectively)

Altogether, we have to remark that fairly high copy numbers of the foreign peptides are necessary to ensure an adequate foreign-self distinction (in the Figures at least five times as much as self-peptides of a particular type). This is the reason why we take into account negative selection in the following.

Chapter 6

Inclusion of negative selection

Up to now, we have considered T-cell recognition neglecting the thymus, where negative selection takes place and induces the so-called *central tolerance* (i.e., tolerance toward self-peptides induced by negative selection). We have seen that the recognition process under assumption (A2) can work even without negative selection, but only under certain assumptions, namely fairly high copy numbers of the foreign peptide. These assumptions may be attenuated if we take into account the events in the thymus. This will be done in two different ways.

We start with the model proposed in [11] and analyze its effect on the BRB model and the generalized version. However, some problems arise. We will therefore put forward an alternative model.

The experimental literature (compare [23]) shows that it is not yet known how exactly the negative selection process works. In particular, the presentation of antigens by the thymical APCs may be modeled in different ways. On the one hand a thymical APC could present antigens of different tissues of the body; on the other hand it could present antigens of a particular tissue. In our new model we proceed on the latter assumption that the thymical APCs emulate the various locations (tissues) of the body; it is therefore called *emulation model*. The results are similar to those of the first model; but further insight is gained.

After that, we will come back to a model under assumption (A1).

6.1 Effect in the BRB model and the generalized version

For a long time, no active transport of antigens from the periphery into the thymus (except for circulation in the blood stream) has been described. Moreover, it has been assumed that there are only thymical antigens (i.e., constitutive and variable thymical peptides) present on the thymical APCs. Therefore, one proceeds on the assumption that the thymical APCs only present self-peptides, and it is assumed that all APCs (also the thymical ones) present the constitutive peptides together with a variable part which depends (amongst other conditions) on the location of the APC.

In order to model the process called *negative selection*, one postulates a second threshold g_{thy} with a similar role as g_{act}. As in the periphery, the T-cells encounter APCs (in this case thymical ones) in the thymus. If the stimulation rate of a young T-cell in its maturation phase in the thymus exceeds the threshold g_{thy}, the T-cell is induced to die.

For a caricature version of the negative selection process, let us assume that T-cell types present in the thymus exist in one copy each and encounter exactly one APC there.

The model then consists of two parts: first, the maturation phase is modeled to characterize the T-cell repertoire surviving negative selection; second, activation curves are calculated for this surviving repertoire. In the first step, we have to calculate the probability to survive negative selection conditional on the type of the T-cell. For a randomly chosen T-cell we have

$$\mathrm{P}(\text{survival}) = \mathrm{P}\left(\sum_{j=1}^{n_c} Z_j^{(c)} W_j + \sum_{j=n_c+1}^{n_c+n_v} Z_j^{(v)} W_j < g_{\text{thy}}\right) .$$

Now, the conceptual difference between constitutive and variable peptides has an effect, which is essential. As already mentioned, it is assumed that the constitutive types of peptides are the same on each APC, both in the thymus and in the periphery. Only these can be "learnt" as self by negative selection – the variable types, being a fresh sample for every APC, are entirely unpredictable. Therefore the constitutive stimulation rates characterize a T-cell type, and we have

$$\mathrm{P}(\text{survival of a certain T-cell}) = \mathrm{P}(\text{survival} \,|\, W_1, \ldots, W_{n_c}) .$$

In the case of fixed constitutive copy numbers z_c (as in the original BRB model), the constitutive part of the stimulation rate reads $G^{(c)} = \sum_{j=1}^{n_c} z_c W_j$, which is *constant* for a certain T-cell type. Therefore we have

$$\mathrm{P}(\text{survival} \,|\, W_1, \ldots, W_{n_c}) = \mathrm{P}(\text{survival} \,|\, G^{(c)}) .$$

This simplifies the second step, the calculation of the activation curves conditional on survival: only a single integration step is required. Numerically, it turns out that (C1) is already fulfilled for $z_f \leqslant 500$ ($= \mathbb{E}(Z_1^{(c)})$), see [11, 64]. Actually, the detection threshold for foreign antigens is reduced drastically (to about a third of the original value).

In the generalized version (where the copy numbers vary from APC to APC), the constitutive part $G^{(c)} = \sum_{j=1}^{n_c} Z_j^{(c)} W_j$ varies from encounter to encounter. Indeed, whereas the W_j, $1 \leqslant j \leqslant n_c$, are fixed for each T-cell, the copy numbers are tied to the APCs. Therefore $\sum_{j=1}^{n_c} W_j$ is not sufficient to determine $G^{(c)}$, and hence the survival probability; rather, the entire collection of the individual stimulation rates W_j for the constitutive types must be known to calculate the probability of the young T-cell to survive negative selection. The corresponding convolution required in the second step involves high-dimensional integrals, which appear to be computationally infeasible. In van den Berg and Molina-Paris [12] this difficulty is tackled by choosing $W_j \sim a\,\mathrm{Ber}(p)$ ($1 \leqslant j \leqslant n_c + n_v + 1$). In [65] and here we resort to simulations.

To this end, we assume that each mature T-cell encounters the same number (in our simulation 1) of APCs in the rest of the body. For $g_{\text{thy}} = 140$ (which for our choice of parameters corresponds to thymic deletion of about 5% of the young T-cells) the activation curves are shown in Fig. 6.1.

As in the case of fixed copy numbers, we observe an incipient separation of the activation curves for $z_f = 0$ and $z_f = 500$. All in all, the above shows that the reduced detection threshold for foreign antigens occurs in the case of random copy numbers, too. However, it seems that the separation of the activation curves is less pronounced here than in the
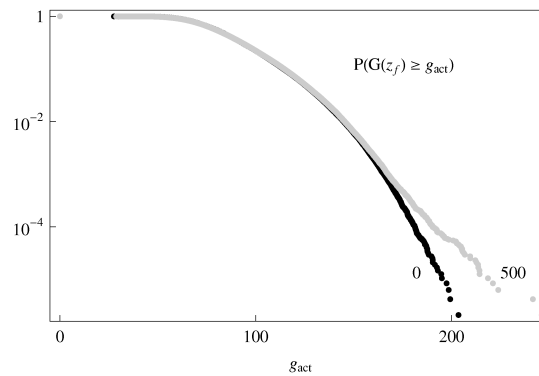
Figure 6.1: Simulated activation curves with $g_{\text{thy}} = 140$ for $z_f = 0$ (black curve) and $z_f = 500$ (gray curve)

original BRB model. This is plausible because the copy numbers of several constitutive peptides could be large (comparable to the copy number of the foreign peptide) and therefore the recognition does not work equally well.

As explained above, in the generalized version of the BRB model we had to resort to simulations since the emerging high-dimensional integrals were computationally infeasible. The desire for analytical results, in combination with novel insights into immunobiology (which will be presented in the next section), have been the reasons for designing a new model.

6.2   Emulation model

For a long time it was assumed that negative selection affects only the distribution of the constitutive peptides since they were thought to be present on all APCs, whereas the variable peptides were thought to vary dependent on the locations (tissues) that have been traveled by the APCs. This was the reason for the distinction between constitutive and variable peptides in the BRB model. Moreover, one thought that the variable peptides in the thymus were typical of the thymus.

However, it has been found recently that, in the thymus, *tissue-restricted antigens*[1] (TRAs) are *expressed* (i.e., produced) and presented, too (see [23, 43, 44, 48]). This finding extends the scope of central tolerance to virtually all tissues of the body.

6.2.1   Novel insights into immunobiology

The expression of TRAs is a physiological property of *medullary thymic epithelial cells*[2] (mTECs), which present the antigens on MHC I and II molecules [23, 46]. However, although mTECs can autonomously delete CD8 T-cells, crosspresentation by *dendritic cells*[3] (DCs) is required for the deletion of CD4 T-cells (see [29, 44]). Crosspresentation means that DCs have to absorb the peptides expressed by the mTECs and present them on their surface. The absorption of the antigens can be realized by different means. First

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[1] from anywhere of the body
[2] cells located in the so-called thymical medulla
[3] special APCs

of all, DCs can engulf apoptotic (dying) mTECs. Moreover, the antigens can be taken up from viable mTECs via secreted exosomes (membrane-enclosed vesicles) or a process referred to as *nibbling*. The latter means that DCs take membrane-enclosed blebs from the surface of mTECs. At last, antigens can be transferred through *gap junctions*[4].

Not much is known about the expression patterns of the various antigens. Gallegos and Bevan [30] observed that mTECs expressing low levels of MHC II together with a co-stimulatory molecule (CD80) express a narrow range of TRAs, representing one or a few tissues, while mTECs expressing high levels express the broadest range of TRAs. Moreover it has been found that the genes encoding the TRAs are often regulated in clusters (compare [22, 32, 44]) which are not necessarily cell type specific [23]. Altogether the expression is highly variable (see [57]). But at the same time a seemingly minuscule change of the amount of antigen expression can have a dramatic effect on tolerance [1, 44]. One possible way of antigen presentation is therefore that the various tissues of the periphery are emulated in the thymus.

Numerically, Kyewski et al. [44] state that a particular TRA is expressed in $1 - 3\%$ of all mTECs. Moreover, in the medulla, T-cells could potentially interact with 5000 APCs per hour [30, 44] and they stay in the medulla for about 5 days. Therefore, the T-cells encounter a great many APCs. Furthermore, expression of certain chemokines (signal proteins) by mTECs are likely to promote encounters (see [43]).

So far we have been concerned with the presentation of self-antigens in the thymus. We have seen that possibly all self-antigens could be represented in the thymus. However, the innocuous external antigens derived from commensal flora or food remain problematic if they are assumed not to be expressed by the thymical cells (as done in Section 6.1). But the following finding helps on. Bonasio et al. [16, 44] found that DCs with extrathymic origin, which collect antigens in the periphery, are recruited to the thymic medulla. Therefore, tolerance to the broad range of innocuous external antigens can be induced, too.

6.2.2 The model

The experimental findings explained in the last subsection allow us to consider a classification of the peptides on an APC that is different from the original BRB model and its generalization. Strictly speaking, the new model exceeds the former insofar as the variable part can be specified.

We have seen that not much is known about the antigen presentation in the thymus (the same holds for the antigen presentation in the periphery). As already mentioned, one possibility is that the thymical APCs represent (i.e., emulate) various locations (e.g., tissues) of the body; in addition to this "local part", the APCs in the periphery present a variable part including all imponderabilities as varying copy numbers and exchanged, additional or missing antigens.

We assume that each T-cell encounters at least one representative of every location in the thymus. This is again in line with the findings summarized in the last subsection where we saw that the T-cells encounter a great many APCs in the thymus. If the total stimulation rate during such an encounter exceeds the threshold g_{thy}, the T-cell is induced to die. Therefore, the local stimulation rates of the T-cells leaving the thymus lie below g_{thy}. The random variable with the modified (a posteriori) probability distribution (representing

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[4] connections between cells

the local stimulation rate in the periphery) is denoted by G_{thy} (for *thymically changed*). The stimulation rate during an encounter in the periphery then consists of the variable stimulation rate in addition to the thymically changed local stimulation rate and eventually the foreign part, i.e.,

$$G(z_f) = q(G_{\text{thy}} + G_{\text{var}}) + z_f W \, ,$$

with factor q as before and $W \sim W_1$.

The distribution of the variable part G_{var} is assumed to be a normal distribution with mean μ and variance σ^2. (The assumption is made due to the multitude of factors constituting the variable part.) As we will see, the variance of G_{var} is an important quantity. The goodness of the foreign-self distinction depends critically on this parameter. We choose $\mu = 0$ and $\sigma^2 = 10$.

Furthermore, we assume that the local component G_{loc} before negative selection is distributed according to the stimulation rate $G(0)$ given by (5.21):

$$G_{\text{loc}} = \sum_{j=1}^{n_s} z W_j \, . \tag{6.1}$$

The important fact that the local stimulation rate is cut off at the threshold g_{thy} has the consequence that the tail of the probability distribution is cut off. We may assume that it is cut off at the median. (This is an ad-hoc choice; its consequences are discussed below.) In this way we get the distribution of G_{thy}. The density is given by

$$f_{\text{thy}}(x) = \begin{cases} \frac{f_{\text{loc}}(x)}{F_{\text{loc}}(g_{\text{thy}})}, & x \leqslant g_{\text{thy}}, \\ 0, & \text{otherwise.} \end{cases}$$

In the following we analyze this distribution and the resulting activation curves for various distributions of the W_j, $1 \leqslant j \leqslant n_s + 1$. We start with the ω-distribution given by the function $w(\tau)$ with exponentially distributed τ (compare Section 5.1). (In the following, the resulting mean $\mathbb{E}(W_j) = 8.89 \cdot 10^{-4}$ is fixed for all distributions.)

We then proceed with two differently scaled Bernoulli distributions $a \operatorname{Ber}(p)$ with $a = 1/e$ and $a = 1$, respectively. As already mentioned, a scaled Bernoulli distribution shows some relevant features of the ω-distribution. In this context, it is a matter of discussion how a has to be chosen. In [12] $a = 1/e$ has been assumed; but in Fig. 5.2 it becomes clear that a smaller value of a would eventually fit better. However, decreasing p (i.e., increasing a) improves the foreign-self distinction, as we will see.

In the end, we also consider $W_j \sim \operatorname{Exp}\left(1/(8.89 \cdot 10^{-4})\right)$, $1 \leqslant j \leqslant n_s + 1$.

In the case of the ω-distribution for the W_j, $1 \leqslant j \leqslant n_s + 1$, the central part of the distribution of G_{loc} may be approximated by a one-sided truncated normal distribution. (The truncation on the left is the consequence of the fact that negative values cannot appear.) The density function of G_{loc} is therefore given by

$$f_{\text{loc}}(x) = \begin{cases} \dfrac{\frac{1}{z\sqrt{n_s \mathbb{V}(W_1)}} \varphi\left(\frac{x - n_M \mathbb{E}(W_1)}{z\sqrt{n_s \mathbb{V}(W_1)}}\right)}{1 - \Phi\left(\frac{0 - n_M \mathbb{E}(W_1)}{z\sqrt{n_s \mathbb{V}(W_1)}}\right)}, & x \geqslant 0, \\ 0, & \text{otherwise,} \end{cases}$$

with $\mathbb{E}(W_1) = 8.89 \cdot 10^{-4}$, $\mathbb{V}(W_1) = 4.28 \cdot 10^{-5}$ and φ the density of the standard normal distribution. Due to the truncation by negative selection we then get a two-sided truncated normal distribution for the thymically changed local part. Thus, the density function of G_{thy} is given by

$$
f_{\text{thy}}(x) = \begin{cases} \dfrac{\frac{1}{z\sqrt{n_s \mathbb{V}(W_1)}} \varphi\left(\frac{x - n_M \mathbb{E}(W_1)}{z\sqrt{n_s \mathbb{V}(W_1)}}\right)}{\Phi\left(\frac{g_{\text{thy}} - n_M \mathbb{E}(W_1)}{z\sqrt{n_s \mathbb{V}(W_1)}}\right) - \Phi\left(\frac{0 - n_M \mathbb{E}(W_1)}{z\sqrt{n_s \mathbb{V}(W_1)}}\right)}, & 0 \leqslant x \leqslant g_{\text{thy}}, \\ 0, & \text{otherwise.} \end{cases}
$$

In the case where $W_j \sim a\,\text{Ber}(p)$ $(1 \leqslant j \leqslant n_s + 1)$, the probability distribution before negative selection is a scaled binomial one $(za\,\text{Bin}(n_s, p)$ as a consequence of (6.1)). For $a = 1$, $p = 8.89 \cdot 10^{-4}$, truncation at the first median $(g_{\text{thy}} = z)$ results in a scaled Bernoulli distribution of the thymically changed local part, i.e., $G_{\text{thy}} \sim z\,\text{Ber}(0.47)$. However, for $a = 1/e$, $p = 8.89 \cdot 10^{-4}e$, the first median is $g_{\text{thy}} = 2z/e$, and there remain three atoms at 0, z/e and $2z/e$.

The activation curves of the thymical and the variable components with the ω-distribution and $a\,\text{Ber}(p)$ for the W_j are shown in Fig. 6.2 for the case where g_{thy} equals the median.
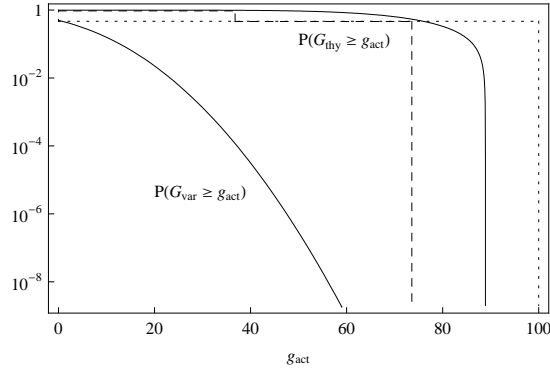

Figure 6.2: Activation curves of the variable component and the thymical component for the ω-distribution as well as $a\,\text{Ber}(p)$ for $a = 1$, $p = 8.89 \cdot 10^{-4}$ (dotted) and $a = 1/e$, $p = 8.89 \cdot 10^{-4}e$ (dashed)

The background activation curve is then given by convolution of the local and the variable part. First, we consider the case of the ω-distribution for the W_j, $1 \leqslant j \leqslant n_s + 1$. The background curve is the dashed curve in Fig. 6.3.

Moreover, lower bounds for the foreign activation curves for $2z \leqslant z_f \leqslant 10z$ are shown in Fig. 6.3. They are given by

$$
\begin{aligned}
\mathrm{P}\left(G(z_f) \geqslant g_{\text{act}}\right) &= \mathrm{P}\left(q(G_{\text{thy}} + G_{\text{var}}) + z_f W \geqslant g_{\text{act}}\right) \\
&\geqslant \mathrm{P}\left(q(G_{\text{thy}} + G_{\text{var}}) \geqslant q\mathbb{E}(G_{\text{thy}} + G_{\text{var}})\right) \times \qquad (6.2) \\
&\qquad \mathrm{P}\left(z_f W \geqslant g_{\text{act}} - q\mathbb{E}(G_{\text{thy}} + G_{\text{var}})\right)
\end{aligned}
$$

(due to (5.23)). As we may see, in addition to the highest copy number $(z_f = 1000)$ for which a foreign-self distinction could be explained by means of our bounds even in the absence of negative selection (compare Sect. 5.4), the distinction by means of our bounds now also succeeds for the next lower copy number $(z_f = 500)$. However, for the smallest
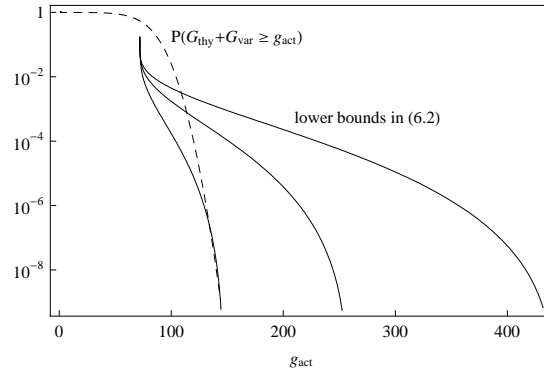
Figure 6.3: Background activation curve (dashed) and lower bounds for the foreign activation curves for $z_f = 200$, $z_f = 500$ and $z_f = 1000$ from left to right in the case of the ω-distribution

copy number ($z_f = 200$), the distinction is not ensured. But it possibly exists for the real curves (as for $z_f = 500$ without negative selection), see Subsection 5.4.2.

We now again consider $W_j \sim a\,\mathrm{Ber}(p)$, $1 \leqslant j \leqslant n_s + 1$, for $a = 1/e$ and $a = 1$, respectively.

(a) $a = 1/e$, $p = 8.89 \cdot 10^{-4}\mathrm{e}$
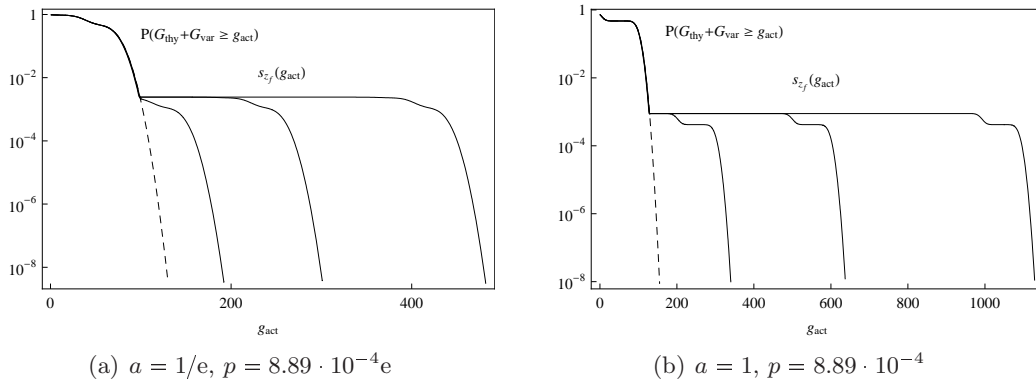
(b) $a = 1$, $p = 8.89 \cdot 10^{-4}$

Figure 6.4: Background activation curve (dashed) and lower supremum bounds for the foreign activation curves for $z_f = 200$, $z_f = 500$ and $z_f = 1000$ from the left-most to the right-most curve (recall that $z = 100$ throughout) for the choice $W_j \sim a\,\mathrm{Ber}(p)$, $1 \leqslant j \leqslant n_s + 1$, with various values of p (and a, respectively)

The background activation curves in both cases (shown in Fig. 6.4) look similar to that in the case of the ω-distribution.

The lower bounds for the foreign activation curves are given by the supremum in (5.23) and read

$$s_{z_f}(g_{\mathrm{act}}) := \max\left(p\,\mathrm{P}\left(q(G_{\mathrm{thy}} + G_{\mathrm{var}}) \geqslant g_{\mathrm{act}} - z_f a\right), \mathrm{P}\left(q(G_{\mathrm{thy}} + G_{\mathrm{var}}) \geqslant g_{\mathrm{act}}\right)\right) .$$

They are plotted for $z_f = 1000$, $z_f = 500$ and $z_f = 200$ in Fig. 6.4. As we may see, in addition to the two highest copy numbers for which a foreign-self distinction by means of our bounds could already be explained without negative selection (compare Sect. 5.4), the distinction now also succeeds for the lowest copy number ($z_f = 200$). Moreover it is already evident for $z_f = z$ and the foreign-self distinction in the relevant range is larger

than for the ω-distribution.

Thus, we have seen that for the ω-distribution of the individual stimulation rates a foreign-self distinction is only ensured for copy numbers larger than the copy number of the self-peptides. However, using the scaled Bernoulli distributions, a foreign-self distinction can already be explained for $z_f = z$ (see Fig. 6.4). Note that for smaller p the distinction is slightly improved since the variance of $z_f W_{n_s+1}$ is increased while the variance of the variable part remains unchanged.

Altogether, we arrive at the conclusion that for a scaled Bernoulli distribution and the ω-distribution of the W_j, $1 \leqslant j \leqslant n_s + 1$, the foreign-self distinction can be explained. For comparison we have done the calculations for an exponential distribution with the same mean, too (see Fig. 6.5). Obviously, the foreign-self distinction does not exist since the true activation curves for $z_f = 200$, $z_f = 500$ and $z_f = 1000$ do not differ visibly from the background activation curve and therefore, needless to say, the distinction cannot be explained by means of our lower bounds in this case.
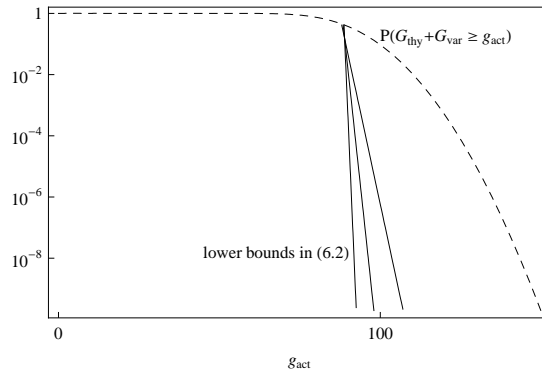

Figure 6.5: Background activation curve (dashed) and lower bounds for the foreign activation curves for $z_f = 200$, $z_f = 500$ and $z_f = 1000$ from left to right in the case of an exponential distribution (the true foreign activation curves do not differ visibly from the background)

Up to now we have analyzed two models of negative selection proceeding on assumption (A2). In the process, we proceed to some extent on the assumption of a scaled Bernoulli distribution. In this case we can establish a link to a model under assumption (A1). It is called *individual model* since it relies on individual pMHCs instead of the sum of the individual stimulation rates.

6.3   Individual model

A scaled Bernoulli distribution for the individual stimulation rates stands for an all-or-none law. Either a certain pMHC (of type j) stimulates with a fixed rate (i.e., $W_j = a$) or it does not (i.e., $W_j = 0$). This may be interpreted in the following way: A pMHC is either suitable for the TCR or it is not.

Recall that (A1) states that the activation of a T-cell depends on a single (or few) pMHC(s). This may be modeled in the following way: If there is at least one (or few) pMHC(s) suitable for the TCR, the T-cell will be activated.

Let p_{rec} be the *recognition probability* (i.e., the probability that a certain pMHC is suitable for a particular TCR). The probability of T-cell activation is then given by

$$1 - (1 - p_{rec})^{n_s}$$

since $(1 - p_{rec})^{n_s}$ is the probability that no pMHC in the randomly chosen immunological synapse is suitable for the TCR. (The recognition probability in the case when activation depends on a few pMHCs can be calculated in an analogous way.)

As in the models under assumption (A2) we suppose that elimination in the thymus (in the context of the negative selection process) occurs in the same way as activation in the periphery. Thus, in the individual model a T-cell is eliminated if it encounters a thymical APC carrying a suitable pMHC. Therefore, the pMHCs presented in the thymus are unsuitable for the T-cells in the periphery, i.e., the background probability is 0. The probability of T-cell activation in the periphery, where one foreign peptide is present, is then given by p_{rec}.

Remark. The individual model has already been discussed in [64] on the basis of works by Borghans, de Boer et al. [17, 18]. There, it has been advised of the weak point that all self-peptides would have to be presented in the thymus. At that time, the novel insights into immunobiology stated in Subsection 6.2.1 were not yet available. Therefore it was assumed that the TRAs were not presented in the thymus. However, now we know that they are still present. Hence the weak point does not exist anymore.

In the emulation model with $W_j \sim a \operatorname{Ber}(p)$, $1 \leqslant j \leqslant n_s + 1$, truncation of the Binomial distribution results in a scaled Bernoulli distribution (or a distribution with three atoms). This means sorting out of T-cells if there is more than one (or two) type(s) of stimulating peptides present (at a certain location). Then, it is clear that the foreign-self distinction is guaranteed if the variance of the variable part is small enough and a stimulating foreign peptide is present in the periphery.

If the threshold g_{thy} has been chosen smaller than za, the choice $W_j \sim a \operatorname{Ber}(p)$, $1 \leqslant j \leqslant n_s + 1$, in the emulation model would have been equivalent to the individual model.

Therefore, in the end, our model under assumption (A2) together with the scaled Bernoulli distribution equals a model under assumption (A1). The reason is that in the Bernoulli case a pMHC either stimulates or it is irrelevant. But the question remains whether any T-cell survives negative selection in this case. This is not discussed in the biological literature but we will shortly analyze this problem in the following.

6.4   Problem

We have to distinguish between two survival probabilities. Let p_{surv} be the probability of a T-cell to survive an encounter with a thymical APC and P_{surv} the probability to survive negative selection, i.e., all the encounters with APCs in the thymus. If we assume independence of the survivals of encounters with different APCs, the relation between the two survival probabilities is given by

$$P_{surv} := (p_{surv})^{n_{enc}} \ ,$$

where n_{enc} is the number of encounters. It is clear that for small p_{surv} and large n_{enc} the probability P_{surv} is very small, i.e., the fraction of T-cells which survives negative selection is tiny.

In particular, this problem arises in every emulation model with relatively small p_{surv} (in our case $p_{\mathrm{surv}} := \mathrm{P}(G_{\mathrm{loc}} \leqslant g_{\mathrm{thy}}) = 0.5$ due to the cut-off at the median) since n_{enc} is high due to the emulation of the various tissues. We assumed that the thymical APCs are exact images of the various tissues. If we additionally assume that each T-cell encounters all these representatives, n_{enc} equals the number of different tissues. A reasonable value could be 200 as the approximate number of different cell types (compare [52]). Then, $\mathrm{P}_{\mathrm{surv}}$ would really be tiny.

Remark. Potentially, n_{enc} could be assumed to be smaller (e.g., 4 as the number of major types of tissues[5], see [59]) in order to ensure that adequately many T-cells survive the thymus. However, then the variance of the variable part has probably to be enlarged.

Since the individual model (with $p_{\mathrm{surv}} = (1 - p_{\mathrm{rec}})^{n_s}$) is a special case of the emulation model (with scaled Bernoulli distribution and appropriate cut-off; compare Section 6.3), the problem arises there, too. In this case it is obvious that the independence assumption (see above) is bad. The reason is that the various APCs representing the different tissues do not carry completely different peptides. Therefore,

$$\mathrm{P}_{\mathrm{surv}} = (1 - p_{\mathrm{rec}})^{n_s \cdot n_{\mathrm{enc}}}$$

does not hold.

The way out for relatively small p_{surv} together with large n_{enc} is the introduction of dependencies. This line of thought is confirmed by experimental statements. Borghans and De Boer [17] estimate that there are 10^5 different self-antigens present in a mouse. Therefore, a large overlap of the presented antigens on the various APCs is inevitable. Thus, dependencies have to occur.

6.5   Résumé

We have analyzed various models for T-cell recognition under different assumptions about when a T-cell may become activated. Recall that (A1) states that activation depends on a single (or few) pMHC(s). In contrast, (A2) states that activation depends on all pMHCs in an immunological synapse.

In Section 6.3 we have shown that a model under assumption (A1) is able to explain the foreign-self distinction (if one takes into account negative selection). However, this model relies on a scaled Bernoulli distribution of the stimulation of the single pMHCs, but this all-or-none law is biologically unrealistic. The reason is the following:

A T-cell is unable to discriminate between different pMHCs at the level of individual stimulation rates. The stimulation rates may only be considered as a sum. Therefore, in a model under assumption (A1) it has to be guaranteed that the sum reveals something about the individual pMHCs. This is guaranteed only if the stimulation rates follow an all-or-none law. (Due to the resulting binomial distribution, the number of stimulating pMHCs is revealed.) This means that a pMHC (if present in the immunological synapse) is either suitable for the TCR ($W_j = w_{\max} \geqslant g_{\mathrm{act}}$) and therefore activates the particular T-cell or it is unsuitable ($W_j = 0$) and therefore does not activate the T-cell on its own. In the case when activation depends on a few pMHCs, the value of g_{act} has to be altered

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[5] epithelial, muscular, connective and nervous

(e.g., $w_{\max} \leqslant g_{\mathrm{act}} \leqslant 2\,w_{\max}$). However, it is unclear how such an all-or-none law may be realized biologically. As we have seen at the beginning of Chapter 5, stimulation occurs in a probabilistic way.

Therefore, the analyzed models under assumption (A2) are biologically more realistic. As a start, they were considered without negative selection (compare Chapter 5).

For the analysis of the models we have stated a large deviation result due to Chaganty and Sethuraman and applied it. The results are compared with simulations. Moreover, appropriate bounds are developed.

We have seen that recognition under assumption (A2) even works in the absence of negative selection. However, this must be compensated by other assumptions (like a high abundance of the invader).

Afterwards (compare Section 6.1 and 6.2), negative selection was included. We have shown that the foreign-self distinction in this case even works for lower numbers of the invader. However, the invader has to be present in an adequate amount.

Altogether, for all considered models, the ability to explain a reliable recognition was shown.

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