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Monte Carlo Simulations of the Equilibrium Properties of Semi-stiff Polymer Chains

*Efficient Sampling from Compact
to Extended Structures*

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Abstract

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Polymers is a class of molecules which can have many different structures due to a large number of degrees of freedom. Many biopolymers, e.g. DNA, but also synthetic macromolecules have special structural features due to their backbone stiffness. Since such structural properties are important for e.g. the biological function, a lot of effort has been put into the investigation of the configurational properties of semi-stiff molecules.

A theoretical treatment of these systems is often accompanied by computer simulations. The main idea is to compare theoretically derived models with experimental results for real polymers. Using Monte Carlo simulations, I have investigated how this computational technique can build a bridge between theoretical models and experimentally observed phenomena. The effort was mainly directed to develop sampling techniques, for efficiently exploring the configurational space of semi-stiff chains in a wide range of structures. The work was concentrated on compact conformations, since they, as is well known from previous studies, are difficult to sample using conventional methods.

In my studies I have shown that the simple and, at a first glance, time consuming method of bead-by-bead regrow as a way of changing the configuration of a semi-stiff chain gave very promising and encouraging results when combined with modern simulation techniques, like Entropic Sampling with the Wang-Landau algorithm. The resulting simulation package was also suitable for parallelization which resulted in a further speed-up of the calculations.

In addition to the more elaborate sampling methods, I also investigated external conditions to induce compaction of a semi-stiff polymer. In the case of a polyampholyte the condensing agent could be a multivalent salt, creating effective attraction between the loops of the chain, while for neutral polymers, an external field and the geometry of the confining volume can induce a compaction.

Keywords: polymers, equilibrium properties, statistical mechanics, computer simulation, Monte Carlo, Wang-Landau, compact structures, parallel computations

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List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

- I Siretskiy A., Khan M.O. (2010) Number fluctuations of the condensing agent affects the coil-toroid coexistence for semi-stiff polyelectrolytes, *Journal of Physics: Condensed Matter*, 22(414103):1-6
- II Czapla L., Siretskiy A., Grime J., Khan M.O., (2010), Free energy Monte Carlo simulations on a distributed network, Para 2010 conference, LNCS series, Springer, 2011
- III Siretskiy A., Elvingson C., Vorontsov-Velyaminov P., Khan M.O. (2011) A new method for sampling compact configurations for semi-stiff polymers, *Phys. Rev. E.* , submitted
- IV Siretskiy A., Elvingson C., Khan M.O. (2011) Determination of the equilibrium charge distribution for polyampholytes of different compactness in a single computer experiment, *Journal of Physics: Condensed Matter*, submitted
- V Siretskiy A., Elvingson C. (2011) Polymer shape transition by nonuniform confinement, *Journal of Physics: Condensed Matter*, submitted

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List of Abbreviations

AFM	Atomic Force Microscopy
CBMC	Configurational-Bias Monte Carlo
DNA	Deoxyribonucleic Acid
ES	Entropic Sampling
FENE	Finitely Extensible Nonlinear Elastic
LJ	Lennard-Jones
MC	Monte Carlo
MD	Molecular Dynamics
MMC	Metropolis Monte Carlo
PA	Polyampholyte
PBC	Periodic Boundary Conditions
PTFE	Poly(tetrafluoroethylene)
RMS	Root-Mean-Square
RR	Rosenbluth-Rosenbluth
UHMWPE	Ultra-High Molecular Weight Poly(ethylene)
WL	Wang-Landau

1. Introduction

Let us consider the fact, that the Earth orbits round the Sun. This phenomenon can be described in many different ways, depending on how detailed the description is, which in turn depends on the audience. The knowledge, once being unit in the time of Ancient Athens, is currently extremely specialized. Today, even scientists are not able to be specialists in *every* area of modern physics or chemistry, which was the case (to a large degree) in the time of Newton and Kepler. Modern scientists can just hope to be a specialist in a *narrow* area and have a *basic* knowledge about the Science of Nature, which the Greeks called 'Physics'. Indeed, physics¹ is today separated into e.g. mechanics, thermodynamics, optics, electricity, statistical mechanics, quantum mechanics, and nuclear physics. Further, each of these disciplines is separated into subareas, like mechanics is separated into classical and relativistic mechanics and electricity consists of electrostatics and electrodynamics. It takes about five years² just to meet, and hopefully understand, very general and the most well established laws and principles. Taking into account that *development* of new knowledge is always on the edge of the confirmed knowledge, the result is that even specialists in neighbouring areas can hardly understand each other on the level accessible for each specialist in his or her own area.

Returning to the Earth, which hopefully revolves round the Sun. To convince a listener without scientific education, one can try to use the idea that the Sun is much bigger and heavier than the Earth, then one can imagine a kind of carousel, where the Sun is placed in one seat and the Earth is in an opposite seat and that the center of rotation will be much closer to the Sun than to the Earth. The Sun will then move less than the Earth. For a listener with scientific background one can instead mention the stellar parallax, Kepler's laws and Newton's law of universal gravitation.

Following the ideas above, the content of this text will be given in a reasonably relaxed and general manner with the hope, that it will be possible to follow without being a specialist in computer simulations of semiflexible polymers by stochastic methods. For a reader with a special interest there are papers at the end of this thesis, where one can enjoy the plentitude of special notations and mathematical constructions.

The text below can be separated into two parts. Firstly we will describe some basics, necessary for a general understanding of the second part, which

¹'Science is divided into two categories, physics and stamp-collecting'. Lord Rutherford.

²The time to obtain a Master of Science degree.

is dedicated to describing the projects I have been working with during the PhD study period.

The main point of the text is to meet the reader and to put forward the ideas about the methods of investigation of compact structures of semi-stiff polymers using computer experiments. The focus will be on the methods for generating compact structures, sampling between different conformations and evaluating the configurational properties for a system in equilibrium.

2. Polymers – properties and models

Wikipedia says¹, that 'A polymer is a large molecule (macromolecule) composed of repeating structural units. These subunits are typically connected by covalent chemical bonds.' Such a definition, which is essentially what can be found also in more specialized books[1, 2] shows that there is at least some ambiguity about the size range, and perhaps also about the structure of polymers: the contour length of human DNA is about 1m[2], but the two methyl units in ethane C₂H₆ representing a contour length of about $2\text{Å} = 2 \times 10^{-10}\text{ m}$ is not regarded as a polymer. The concept of repeating structural units can also be discussed since the A,T,G,C units of DNA are not distributed in a regular fashion, but represent the 4-letter alphabet, coding the molecule of life[3]. Also the process of vulcanization does not really mean, that a whole bicycle tyre is regarded as a single polymer molecule.

No less remarkable to notice, however, is that DNA, 1 m long, is packed inside the nucleus of a cell of typical size $100\ \mu\text{m}$ [4]. The covalent chemical bond of most polymers (348 kJ/mole for a $[-\text{C} - \text{C}-]$ bond) is strong enough[5] for the molecules to be able to be used in a wide range of temperatures from -200°C to $200 - 300^\circ\text{C}$ [6]. Polymers can form materials like ultra-high molecular weight polyethylene(UHMWPE), which is '15 times more resistant to abrasion than carbon steel' and Kevlar, which 'is 5 times stronger than steel on an equal weight basis'². UHMWPE is the base of all modern skies and snowboards[7], while the Kevlar fabric is a material for bulletproof vests and race yacht sails[8, 9]. Materials like GoreTex[6] and eVent[10] used in everyday life in the form of jackets, gloves and shoes are made of polytetrafluoroethylene(PTFE), which is strongly hydrophobic[11].

To be able to predict or synthesize a polymeric material with some desired properties one has to have some idea, as to why different polymers will have specific properties. Such a discussion will inevitably lead to the necessity of finding a theory of some sort. A theory should start from a number of assumptions, facts and ideas and be able to predict a result which can be tested in a laboratory experiment. Any theory can describe real objects to a certain degree. In other words, any theory is a simplification of the real object (ideal gas, monochromatic wave, absolutely rigid body etc.). In polymer physics, scientists often leave the quantum mechanical description of individual atoms. The

¹Readers more comfortable with 'classical' references taken from the shelf, compared to references on internet, can find an equivalent definition in e.g. Encyclopaedia Britannica.

²... Wikipedia says...

chemical bond is thus not described as an overlapping of electronic orbitals, but by sticks which are of fixed length or obeying Hook's law. The angle between bonds is not explicitly given by the electronic structure, but determined by some simple analytical relation.

Following this idea of model building we begin with the simplest polymer model – the *freely-jointed model*, also sometimes referred to as the *random flight model* or *random walk model*.

2.1 Freely-jointed model

In this model the polymer consists of $N + 1$ beads, connected by N bonds of constant length l , Figure 2.1. The beads have no size and can be treated as mathematical points. There is no correlation between sequential bonds, so the direction of the next bond does not depend on the orientation of the previous one[2].

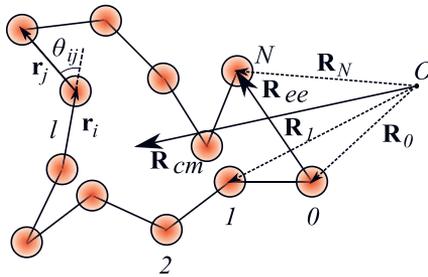


Figure 2.1: An example of a freely-jointed chain, with $N + 1$ beads, having bond length l , and $\theta_{ij} = \widehat{\mathbf{r}_i, \mathbf{r}_j}$ is the angle between bond vectors \mathbf{r}_i and \mathbf{r}_j . The end-to-end vector is \mathbf{R}_{ee} , while $\mathbf{R}_0, \mathbf{R}_1, \dots, \mathbf{R}_N$ are the position vectors of the beads. The center of mass vector is \mathbf{R}_{cm} .

To characterize the size and shape of a chain, one can use the *root-mean-square*(RMS) end-to-end distance, $\sqrt{\langle R_{ee}^2 \rangle}$, RMS radius of gyration, $\sqrt{\langle R_g^2 \rangle}$ and asphericity, describing how much the shape deviates from a sphere. It is easy to show[2], that for the freely-jointed model the square end-to-end distance becomes:

$$\langle R_{ee}^2 \rangle = \sum_{j=1}^N \sum_{i=1}^N \langle \mathbf{r}_i \cdot \mathbf{r}_j \rangle = l^2 \sum_{j=1}^N \sum_{i=1}^N \langle \cos \theta_{ij} \rangle = Nl^2, \quad (2.1)$$

where \mathbf{r}_i is a bond vector from bead $i - 1$ to i , θ_{ij} is the angle between bond vectors \mathbf{r}_i and \mathbf{r}_j , and $l = |\mathbf{r}_i|$ is the constant bond length. The RMS end-to-end

distance thus becomes:

$$\sqrt{\langle R_{ee}^2 \rangle} = l\sqrt{N}. \quad (2.2)$$

Note that we use $\sqrt{\langle R_{ee}^2 \rangle}$ instead of $\langle \mathbf{R}_{ee} \rangle$, since there is no *preferred* orientation in the absence of an external field. The probability for the end-to-end vector to be in the interval $[-a : -a \pm \delta a]$ is equal to be in $[a : a \pm \delta a]$, so the average *vector* is zero, while the average *length* of the vector is not zero, and is given by $\sqrt{\langle R_{ee}^2 \rangle}$.

The square radius of gyration is defined as[2]:

$$R_g^2 = \frac{1}{N+1} \sum_{i=0}^N (\mathbf{R}_i - \mathbf{R}_{cm})^2, \quad (2.3)$$

where \mathbf{R}_i is the position vector of bead i and \mathbf{R}_{cm} is the position of the center of mass of the polymer. The RMS radius of gyration for this model can be written[2]:

$$\sqrt{\langle R_g^2 \rangle} = l \sqrt{\frac{N(N+2)}{6(N+1)}}. \quad (2.4)$$

The model of a freely-jointed chain can be used when a polymer is divided into parts, which can be considered independent. These pieces are called *Kuhn* monomers, with a length b . For example, for polyethylene $b \approx 1.4 \text{ nm}$ [2] and for double-helical DNA $b \approx 100 \text{ nm}$ [2] while the Kuhn length for an actin filament is about $16 \mu\text{m}$ [12].

This means, that using the freely-jointed model one can not with enough accuracy investigate phenomena which occur on a scale smaller than the Kuhn length for a given polymer. For example, if one would like to model the shape of an actin filament on a length scale of 100 nm it is not feasible to do this in the frames of the freely-jointed model, since it gives a statistically correct description of actin on a scale larger than $50 - 100 \mu\text{m}$. To be able to descend to a more detailed level, one has to use more complicated models. A more representative picture in this case can be given, for example, by the *freely-rotating model*.

2.2 Freely-rotating model

This model assumes that the bonds lengths, l , and bond angles, θ , are fixed, but all torsion angles, ϕ , are equiprobable and independent[2], as shown in Figure 2.2.

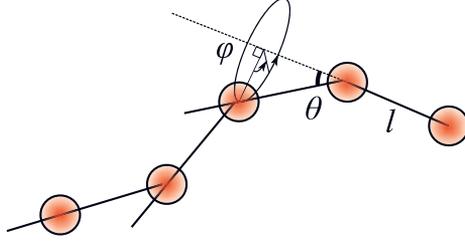


Figure 2.2: An example of a freely-rotating chain with bond angle θ , bond length l and the torsion angle φ at a random value.

The RMS end-to-end distance and RMS radius of gyration can be calculated analytically[13]. The RMS end-to-end distance will be:

$$\sqrt{\langle R_{ee}^2 \rangle} = lN^{1/2} \left(\frac{1 + \alpha}{1 - \alpha} + \frac{2\alpha(\alpha^N - 1)}{N(\alpha - 1)^2} \right)^{1/2}, \quad (2.5)$$

where $\alpha = \cos \theta$, and N is the number of bonds. The RMS radius of gyration becomes[13]:

$$\sqrt{\langle R_g^2 \rangle} = l\sqrt{N} \left[\frac{(1 + \alpha) N + 2}{6(1 - \alpha) N + 1} + \frac{2\alpha^3(\alpha^N - 1)}{N(N + 1)^2(\alpha - 1)^4} - \frac{2\alpha^2}{(N + 1)^2(\alpha - 1)^3} - \frac{\alpha}{(N + 1)(\alpha - 1)^2} \right]^{1/2}. \quad (2.6)$$

Since the bond angle, θ , is fixed, the *correlation between bonds* in this model, expressed in the terms of the inner product becomes:

$$\langle \mathbf{r}_i \cdot \mathbf{r}_j \rangle = l^2(\cos \theta)^{|i-j|}, \quad (2.7)$$

which is different from the freely-jointed model, where there was no correlation between different bond vectors. Moreover in the freely-rotating model one can steer and adjust the correlation by varying the angle between sequential bonds, θ , as one can see from (eq. 2.7). It means, that a segment of a real polymer which was a rigid Kuhn segment in the *freely-jointed model* can fluctuate and bend in the *freely-rotating model*, allowing us to investigate properties on smaller length scales. This difference leads e.g. to a qualitative difference in the extension under an external force[2].

2.3 Worm-like chain model

A worm-like chain model (also known as Kratky-Porod model[14]) is a special case of a freely-rotating model taking the limit $\theta \rightarrow 0$ and $l \rightarrow 0$, while the contour length $l \times N = L$ and the Kuhn length b are preserved[2]. This model is most suitable for describing properties of semi-stiff and stiff polymers, like double stranded DNA or actin. An analytical theory of the worm-like model can be derived[15], and the RMS end-to-end distance becomes[2]:

$$\sqrt{\langle R_{ee}^2 \rangle} = bL - b^2/2 \left(1 - e^{-2L/b}\right), \quad (2.8)$$

where the Kuhn length is $b = 4l/\theta^2$. For this kind of model it is common to introduce a *persistence length*, l_p , which is closely related to the Kuhn length, $l_p = b/2$ for the *worm-like model*.

An important point is that if one would like to investigate the properties of a polymer on a scale larger than the Kuhn length one can use the freely-jointed model, while for phenomena occurring on the scale of a Kuhn length these can be treated using the worm-like chain model.

There are also other models for describing polymers, introducing different features. For example the *hindered rotation model* assumes that the torsional angles are not equiprobable, as is assumed in the freely-rotating model, but distributed according to some hindering function[2]. The *rotational isomeric state model* does not use a continuous hindering function, but is defined in discrete points, resulting e.g. in *trans* and *gauche* states[2].

3. Theory and theoretical experiments

As for any objects in our world we can conduct experiments to investigate the properties of polymers. Using the word 'investigate' one should understand the process of establishing a connection between the properties of the polymer and the conditions of an experiment where these properties are measured. A sentence like: 'the weight of this stone is 10 Newton' can not be interpreted unambiguously, since the weight of the same stone on Earth and on Mars will be different. On the other hand, a sentence like: 'the mass of this stone is 10 kilos' provides a good connection between the physical characteristics of the stone and the number, describing the measurement of this property. Care should also be taken to perform the measurement in a way which makes it possible to reproduce the results.

3.1 Laboratory methods

Laboratory methods allow one to investigate many properties under different conditions. The conformational properties of polymers are usually measured using different techniques, such as small angle scattering to determine the average radius of gyration, $\langle R_g \rangle$ [2], atomic force microscopy to measure how a force, applied to the end of the polymer, depends on the distance between the ends, R_{ee} [16], and osmotic pressure measurements can be used to obtain the molecular mass of a polymer[2]. The results can confirm and support theoretical models used to describe a polymer (or the contrary). In the case of macromolecules i.e. large molecules consisting of hundreds to millions of monomers, the number of possible conformations is huge and what we can measure are averages of a few (hopefully representative) properties, describing e.g. the size and shape of the polymers. Any theoretical approach starting from even a rather simplified model must rely on a way of determining averages from very many degrees of freedom. In other words a theoretical approach should be based on statistical mechanics.

3.2 Statistical mechanics

Statistical mechanics describes the behaviour of systems with many particles. To that end, the theory deals with averages over different distributions, i.e.

quantities for which we can determine an average with some measurable and hopefully small deviation. The necessity to use an alternative to an analytical approach is clear from the fact, that even classical systems with more than two interacting bodies are not solvable exactly (the three body problem), so the task to describe the behaviour of a system of thousands of interacting particles on the microscopic level is hopeless. 'For example, from thermodynamics we know that experimental values of the two heat capacities C_p and C_V for a given system must be interrelated by an exact and well known equation, but thermodynamics is unable to furnish any explanation of why particular experimental values of either C_p or C_V , taken separately, should be observed' [17]. The picture becomes even more complicated if we take into account that the interaction between particles in reality is not pairwise. It means, that the interaction between particle A and particle B depends not only on the properties of each particle individually and their mutual orientation, but also on the presence (or absence) of other particles in the vicinity of A and B [18].

Nevertheless, in many situations the interaction between particles can to a good approximation be considered pairwise, so the interaction between A and B does not *explicitly* depend on the exact location of C . Notice that the polymer models described above (the freely-jointed, the freely-rotating and even the worm-like chain) *do not* describe polymers on the *atomic* level, so the assumption of pairwise interactions can still be a reasonable approximation.

Such an assumption simplifies the calculations significantly. From now on and throughout we will consider all interactions as pairwise, as well as all the models and their description will be given in the frames of classical mechanics.

The ideas and apparatus of statistical mechanics can be rather demanding, so we will approach them involving well known physics. Let us consider a system with N particles and the interaction between them depends only on the distance between their centers of mass. These particles are put inside a confining shell. For the sake of simplicity we consider the shell in the form of a cube of volume V , so a system can not exchange neither energy nor substance with its exterior. Such kind of system is called an *isolated* system [17] and is denoted by (N, V, E) showing that the amount of matter N , the volume V and the total energy E of the system are constant.

From Newton's second Law it follows that, if one knows the initial positions and momenta of all the particles, one would be able to predict all future of the system [19]. In scientific language one can say that the behaviour of a classical many-particle system is completely determined, knowing the initial (and boundary) conditions. The necessity of the initial positions and momenta arises from the fact, that the second Law is a second order differential equation, requiring two initial conditions for each particle. Following classical mechanics, we must also describe how the particles will interact with the confining volume (the boundary conditions). In most cases it is enough to consider a momentum conservation law for every particle. Since we have the

total energy conserved, because the system is isolated, initial velocities \mathbf{v}_0 can be determined and the initial positions \mathbf{r}_0 can be chosen to keep the energy constant.

Due to the deterministic behaviour of the classical system it is (in principle) possible to track every individual particle and determine all its past and future. Such a way of treating a system is used in Molecular Dynamics(MD) simulations[20]. There are a lot of commercial and free packages with MD for different purposes[21], but with the same principle – one will obtain the time dependence of the properties of interest and their change with the *wall clock* time.

The price one has to pay for a such detailed description of the system is the short time step. For a single time step one usually has to choose $\Delta t = 1 \text{ fs} = 10^{-15} \text{ s}$ [20] and the computer has to solve the system of equations of motion, so if the process in real life takes 1 second, it might take half a year of calculation on a present day computer with 1000 CPUs[22]. Sometimes scientists have no choice but to use MD, if the task is to calculate diffusion coefficients, relaxation times or other dynamical properties[20, 21, 23]. Sometimes, however, the task is to understand what will happen with the system when all macroscopic changes in the system are over: all the particles mixed with each other, the pressure exerted on the wall and the average speed of a particle converged and does not depend on the wall clock time. In scientific language one would say, that the system has reached *thermodynamic equilibrium*[17, 21, 24].

Thus MD, in general, has a broad application area, since it can give us both *dynamical* and *equilibrium* properties (if one is ready to wait long enough). Imagine one has a system *isolated* from the outer world, thus with

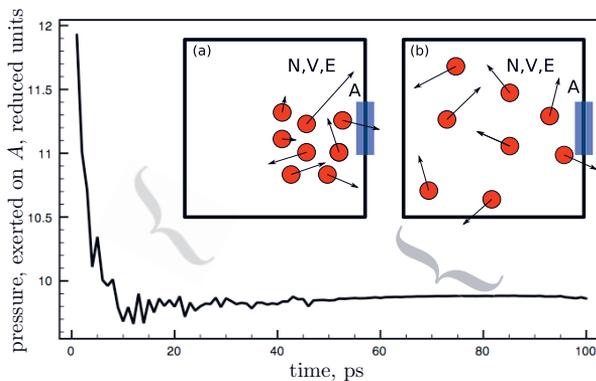


Figure 3.1: Sketch of an imaginary system (N, V, E) showing the pressure exerted on the unit surface A as a function of a wall-clock time. The insets (a) and (b) show the system before and after equilibration.

constant (N, V, E) . Let us choose a unit surface A arbitrarily on the wall of the confining volume V . The property under investigation will be the pressure exerted on A . To get a feeling for the difference between the *dynamical* and *equilibrium* properties, one can follow the *wall clock time* dependence of the pressure as shown in Figure 3.1. The timescale where pressure can be evaluated using MD is shown by the bracket pointing from the initial state of the system, inset (a). The bracket from inset (b) points to the part of the pressure vs. time curve, where pressure does not depend on wall clock time. In this case the *equilibrium* pressure can be evaluated via the *statistical mechanics ensemble* apparatus. Since the pressure *does not* depend on wall clock time, one ignores the exact dynamical processes in the system and concentrates on the effort to investigate the equilibrium properties.

3.3 Statistical ensembles

Initially the ensemble concept was proposed by Gibbs in the 19th century[17, 25] for the purpose of connecting *time* and *ensemble* averages of a given property. An ensemble is simply a huge amount of systems each of them being a replica (on the *macro* level) of the system under investigation. Replicas can be different on the *micro* level, for example, positions of the particles can be different in different replicas, but the macro parameters, like the average pressure, volume, or average energy are the same[17]. Returning to Figure 3.1, replicas can be visualised as a huge set of pictures, like in the inset (b), though with different instant configurations.

To be able to extract information from the replicas one has to develop some rules or definitions. The two postulates of statistical mechanics are[17]:

1. *the ergodic principle*
2. *the postulate of equiprobability of microstates of an isolated system.*

The mathematical apparatus needed to extract equilibrium properties in different ensembles can be built up using these postulates.

Since the *macroscopic parameters* characterising a system (volume, average pressure, average energy, temperature) are not all independent, it is possible to divide them into groups, where each group contains a minimal set of parameters, enough to uniquely describe a system on the *macro* level. It is important to note that the ensemble concept does not allow a description of the system on the *micro* level, for it would demand $6N$ variables for N particles instead of 3 used in the ensemble concept. These classes constitute different ensembles: Canonical (N, V, T) , isothermic-isobaric (N, p, T) , microcanonical (N, V, E) and so on. Different ensembles are suitable for calculating different *equilibrium* properties. If one would like to investigate e.g. a phase transition, probably the (N, p, T) ensemble would be more suitable, than the (N, V, T) ensemble, due to the physical system it reflects. What is important, however, is that the same property calculated in different ensem-

bles has to be the same. The average configurational energy, calculated in the (N, V, T) ensemble is equal to the average configurational energy calculated in the (N, p, T) ensemble etc.[17, 21, 24]. It is also worth mentioning, that using modern simulation techniques and algorithms almost any property can be obtained in the frame of the (N, V, T) ensemble, which is the most widely spread ensemble in use. We will thus concentrate on the Canonical ensemble.

3.4 Some mathematical tools of statistical mechanics

We must now determine what type of averages to use when calculating the properties of specific system. Consider a set of 7 numbers

$$a = \{1, 2, 5, 3, 2, 4, 5\}. \quad (3.1)$$

To calculate the average of this set, $\langle a \rangle$, one could propose:

$$\langle a \rangle = \frac{1 + 2 + 5 + 3 + 2 + 4 + 5}{7}, \quad (3.2)$$

what is the correct arithmetic mean.

One can notice, that some numbers in the sequence (eq. 3.1) are equal. It allows us to use an alternative form rewriting the same average (eq. 3.2):

$$\langle a \rangle = \frac{1 \times 1 + 2 \times 2 + 3 \times 1 + 4 \times 1 + 5 \times 2}{7} = \frac{\sum_{j=1}^5 a_j \Omega(j)}{7}, \quad (3.3)$$

where $\Omega(1) = 1, \Omega(2) = 2, \Omega(3) = 1, \Omega(4) = 1, \Omega(5) = 2$ are the frequencies of the different number *types* in the sequence.

Let us rewrite (eq. 3.2) once more:

$$\langle a \rangle = \sum_{j=1}^5 a_j p(j), \quad (3.4)$$

where

$$p(j) = \Omega(j)/7 \quad (3.5)$$

is the *probability* of the number *type* j in the sequence (eq. 3.1).

In other words, if one would like to calculate the average of a certain property over a certain set of values, one can use a formula, like (eq. 3.4), provided the probability for number type is known, (eq. 3.5).

In the Canonical (N, V, T) ensemble the probability, p_i , for system to be in the microstate i with energy $E_i = E_{i,kinetic} + E_{i,potential}$, is given by[17]:

$$P_i = \frac{e^{-E_i/k_B T}}{\sum_{\{i\}} e^{-E_i/k_B T}}, \quad (3.6)$$

where $\{i\}$ is the set of all possible microstates¹, k_B is the Boltzmann constant, T is the absolute temperature and E_i is the energy of the microstate i . One can notice the similarity between (eq. 3.5) and (eq. 3.6). The Canonical ensemble average is then:

$$\langle a \rangle = \sum_{\{i\}} a_i \frac{e^{-E_i/k_B T}}{\sum_{\{i\}} e^{-E_i/k_B T}} = \frac{\sum_{\{i\}} a_i e^{-E_i/k_B T}}{\sum_{\{i\}} e^{-E_i/k_B T}}, \quad (3.7)$$

where the similarity between (eq. 3.4) and (eq. 3.7) is obvious.

As one can see, there is nothing terribly complicated in the ensembles and ensemble averages. Often one can read in the literature[17, 20, 21, 24, 26], that all thermodynamics of a system is hidden in its partition function or if one would know the partition function of a system one would be able to calculate any macro-property of interest. Let us try to clarify this a little. The denominator in (eq. 3.7) is called the Canonical partition function, defined by[17]:

$$Q(N, V, T) = \sum_{\{i\}} e^{-E_i/k_B T}. \quad (3.8)$$

The sum is taken over all possible microstates of the system, so the information for each microstate i with energy E_i is taken into consideration. It means, that the probability of being in the microstate i for all microstates $\{i\}$ is known and the canonical average of any macro property of interest, $\langle a \rangle$, can be evaluated using (eq. 3.7). Another approach to extract thermodynamic properties is to take various partial derivatives of $Q(N, V, T)$. For example, the *ensemble average* energy is $\langle E \rangle = - \left(\frac{\partial \ln Q}{\partial \beta} \right)_{V, N}$, the *ensemble average* pressure is $\langle p \rangle = \frac{1}{\beta} \left(\frac{\partial \ln Q}{\partial V} \right)_{T, N}$, and the chemical potential is $\mu = -\frac{1}{\beta} \left(\frac{\partial \ln Q}{\partial N} \right)_{T, V}$ [17, 20, 21, 24, 26], where $\beta = 1/k_B T$.

In principle, (eq. 3.7) is a key to evaluate equilibrium properties. Nevertheless calculations using (eq. 3.7) can be done in very rare cases, for example for the ideal gas, where $E_i = E_{i,kinetic}$ and (eq. 3.7) can be evaluated *analytically*[21]. The reason is that even a system of 100-200 particles has an enormous amount of microstates, so the set $\{i\}$ consists of billions of elements, and most of these have a vanishingly small contribution to the average in (eq. 3.7).

Nevertheless, some simplifications can be done at this stage. Due to that the kinetic energy can be written $E_{i,kinetic} = \sum_{j=1}^N m_j \mathbf{v}_j^2 / 2$, (m_j and \mathbf{v}_j are the mass

¹in the previous example the number of all possible states was equal to 7

and velocity of particle j) it is possible to separate the kinetic and potential energy contributions to the total energy by using the *equipartition of energy* theorem[27, 28]. Then (eq. 3.8) becomes:

$$Q(N, V, T) = \frac{1}{N! \Lambda^{3N}} \sum_{\{i\}} e^{-\beta E_{i,potential}}, \quad (3.9)$$

where $\Lambda = h/(2\pi mk_B T)^{1/2}$ is the de Broglie wavelength, particle masses are taken to be the same, m , and h is the Planck's constant. The magic here is that such kind of separation is *always* possible, regardless of the interaction between the particles. The kinetic contribution is always possible to calculate separately and *exactly*!

Using this separation of the kinetic and potential energy contributions we can rewrite the canonical averages for a property a (not depending on the velocity) as :

$$\langle a \rangle = \frac{\sum_{\{i\}} a_i e^{-\beta E_{i,potential}}}{\sum_{\{i\}} e^{-\beta E_{i,potential}}}. \quad (3.10)$$

The denominator in (eq. 3.10) is called a configurational sum:

$$Z(N, V, T) = \sum_{\{i\}} e^{-\beta E_{i,potential}}. \quad (3.11)$$

This, however, hardly helps us to evaluate Canonical averages, since in (eq. 3.10) we still have to sample through the same amount of microstates $\{i\}$ as in (eq. 3.7).

The possible solution can be to determine and take into account mainly such microstates, which would give the *largest* contribution to (eq. 3.10).

3.5 The Monte Carlo method

The equilibrium properties of the *closed* system, (N, V, T) , can be obtained as shown in (eq. 3.10). Using the notations of (eq. 3.11) we can write:

$$\langle a \rangle = \frac{\sum_{\{i\}} a_i e^{-\beta E_{i,potential}}}{Z(N, V, T)}. \quad (3.12)$$

This equation in principle allows us to calculate average properties at the given temperature in the Canonical ensemble, if one is able to sample all possible microstates $\{i\}$ and for every microstate calculate the potential energy, $E_{i,potential}$, of the system. Unfortunately such a procedure is hopeless to use directly, since the number of microstates is enormous even for a small system of $N = 100$ particles. Let us try to estimate the number of microstates

for $N = 100$ in one-dimensional space. Let us assume that particle '1' can occupy one of 10 positions along the segment $[1 : 10]$. Since each of the $N = 100$ particles is independent, every particle has 10 possibilities to be placed on the segment. It means that the resulting number of microstates of these N particles in one-dimensional space is proportional to 10^{100} , which is much larger than the Avogadro's number $N_A = 6.02 \times 10^{23}$. For a computer with CPU clock frequency of 1GHz it will take $10^{100}/10^9 \approx 10^{90}$ seconds to enumerate all of them, what is much longer than the Earth has existed ($\approx 10^{17}$ seconds). The only chance for us to tackle the problem is to sample *not all* possible microstates, but just these which give the largest contribution to the average (eq. 3.12). This selection mechanism is called *importance sampling*[20, 24, 26], stressing that not all, but only the most important microstates *for the given macro-parameters* (N, V, T) are taken into account. The first time this type of computer calculations using importance sampling were conducted was in 1953 by Metropolis et.al.[29]. Similar types of computer simulations are used in almost any area of science today, and the idea has hardly changed and is referred to as the Metropolis Monte Carlo method(MMC). The term 'Monte Carlo' is used because the algorithm introduced by Metropolis relies heavily on *random numbers*, which quite often mean 'Win' or 'Loose' in the gambling places.

The great success of the *importance sampling* technique is clouded by the fact, that since we do not consider all points in the configurational sum (eq. 3.11) (or not sample all microstates), we are *not* able to evaluate the configurational sum, but we can still, however, evaluate the averages (eq. 3.12)[20, 24].

The importance sampling technique allows us to select the most important states of the system under given conditions. These states are forming a so-called *Markov chain*[30] and the transition from one member of the chain to another is given, for example, by[20, 21, 24, 29]:

$$acc(o \rightarrow n) = \min[1, e^{-\beta\Delta E}], \quad (3.13)$$

where $acc(o \rightarrow n)$ stands for the transition probability from the old state 'o' to the new one 'n' and $\Delta E = E_n - E_o$ is the configurational energy change corresponding to the transition from the old to the new state.

It is worth to mention, however, that the Metropolis solution, (eq. 3.13), is not the only possibility. Detailed balance will be preserved if one would choose

$$acc(o \rightarrow n) = \frac{e^{-\beta E_n}}{e^{-\beta E_o} + e^{-\beta E_n}}, \quad (3.14)$$

which is symmetric about E_o and E_n [24].

Actually, (eq. 3.13) is responsible for selecting points (sampling the distribution) according to (eq. 3.6). This is the mathematical meaning of (eq. 3.13). Let us now consider (eq. 3.13) from the another point of view.

One can see that $\Delta E < 0 \rightarrow e^{-\beta\Delta E} > 1$ and the transition is accepted. If the energy in the new state is lower than the energy in the old one, we thus accept the transition to a new configuration. When instead $\Delta E > 0 \rightarrow e^{-\beta\Delta E} < 1$, so $acc(o \rightarrow n) = e^{-\beta\Delta E} < 1$. Thus if the energy in a new state is greater than in an old state, then the probability to move from 'o' to 'n' is less than 1, but greater than 0 and *exponentially* depends on temperature. It displays the fact that to sample the most important states of the system it is not *only* the energy, which is important, but also the temperature. One can show that a more stable state (more probable state) of the system is not necessarily a state with a lower energy, but a state with a lower *free energy* (Helmholtz free energy for our choice of ensemble)[20, 21, 24, 26, 31]:

$$F = E - TS, \quad (3.15)$$

where S is the entropy, showing the importance of the temperature for a system with given parameters. In statistical thermodynamics, Helmholtz free energy is defined as[20, 21, 24, 25, 26]:

$$F = -k_B T \ln Q(N, V, T). \quad (3.16)$$

Equations (3.15 and 3.16) mean the same thing. One can show that (eq. 3.16) transforms to the form of (eq. 3.15) when considering a *macroscopic* system[17].

3.6 Entropic Sampling and the Wang-Landau algorithm

Let us consider a system which undergoes a phase transition. The phase transition can be observed by looking at, for example, the energy distribution, $p(E) = \Omega(E) \exp(-\beta E)$, where $\Omega(E)$ is the energy density of states, Figure 3.2. If, at the given temperature, the $p(E)$ curve shows two maxima, it means that two phases are present. A minimum between the maxima is a bottleneck in the configurational space, making the conventional Metropolis algorithm, (eq. 3.13), inefficient: one can sample the configurations in the vicinity of *one* of the maxima, but not in the area including *both* of them.

The idea of the Entropic Sampling(ES) method[32] is to obtain the entropy of the system, $S(E)$, having *proposed* a rough estimate *before* the actual simulation starts. A rather good initial guess makes it possible to *overcome* the bottleneck during the Monte Carlo simulation and to calculate properties

for both phases. If the initial guess was not successful enough a new estimate will be needed.

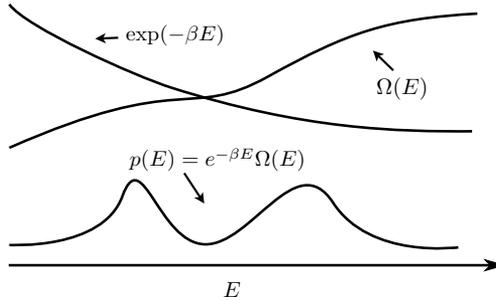


Figure 3.2: A sketch explaining the origin of the 'difficult' energy landscape for a system under a phase transition. The product of the canonical Boltzmann factor $\exp(-\beta E)$ and the energy density of states $\Omega(E)$ results in the double maxima curve of the energy distribution function $p(E)$. The left and right maxima correspond to two different phases of the system.

The ES method can be significantly improved by involving the Wang-Landau(WL) algorithm[33] which takes care of the initial guess and calculates the estimate *automatically* during the simulation. Briefly the WL procedure can be summarized as follows: the configurational space is projected onto the configurational energy E , as a reaction coordinate. The range of change for E is divided into a number of intervals. Two counters are used: one for estimation of $\Omega(E)$ and another, $H(E)$, for counting the visits in the intervals. Initially both of them are set to zero. When the simulation starts we sample the configuration space and visit the energy intervals according to the transition probability:

$$\text{acc}(o \rightarrow n) = \min \left[1, \frac{\Omega(E_o)}{\Omega(E_n)} \right], \quad (3.17)$$

where 'o' and 'n' denote the old interval and the new interval respectively. Every time a certain interval, i , is visited we update the counters $\Omega(E_i) = \Omega(E_i)f$ and $H(E_i) = H(E_i) + 1$, where f is a modification factor, initially set, for example, to $f = e^1 \approx 2.7182\dots$. Formula (eq. 3.17) results in a flat histogram of visits, $H(E)$. When $H(E)$ is flat we reset $H(E)$ to zero and reduce the modification factor $f = \sqrt{f}$ and continue the simulation. The simulation is terminated, when f becomes less than some predefined number e.g. $f_{final} \approx \exp(10^{-5})$.

An advantage of the WL algorithm is that it can be used to sample configurational space projecting it on different reaction coordinates[34]. In paper I we used the radius of gyration R_g as a reaction coordinate.

3.7 Boundary conditions

In a laboratory, people in white coats usually deal with macroscopic systems i.e. with a number of particles comparable with the Avogadro's number, $N_A \approx 10^{23}$. It is said 'usually' because modern techniques, like atomic force microscopy (AFM) allow one to deal with a single polymer molecule, which could have up to 10^9 atoms. Numerical methods, like MD or MMC are unable to digest macroscopic systems due to lack of computational power. At present the largest systems MD can deal with is about 10^6 particles[35], while for the MMC this number is much more modest, 10^4 particles. Such a big difference in the manageable system size is due to the specifics of the methods: for MD we can vary the real experiment time, up to microseconds[36], to be able to finish the computation in a reasonable *wall clock* time, while for the MMC one is doomed to sample configurations until reliable statistics is accumulated.

As we know from experiments, the properties of a system of 10 particles and of 10^3 of the same particles are different. For example, the electrostatic energy of one monovalent cation '+1' in contact with another monovalent anion '-1' is -1.0 in reduced units, while for the infinite crystal of the same '+1' and '-1', like a crystal of NaCl, the energy is $-1.748\dots$, which is known as the Madelung constant[37].

To minimise the deviations based on the small system size, periodic boundary conditions (PBC) in various dimensions are used, especially for the long-ranged interactions, like the Coulomb potential. One chooses the *main simulation cell* with 100-1000 particles, and the remaining space is filled with *exact replicas of the main cell*. As a result we have an illusion of a large macroscopic system, while the computational demands are of the same order, as without PBC. This trick can be done in different dimensions, $\mathbb{R}^1 - \mathbb{R}^3$. The only thing one has to take care of is:

- the size of the main cell has to be larger than some number, related to the structure of the radial distribution function[24]
- the shape of the main cell should satisfy the *tesselation* condition for a given dimensionality (fill the space without gaps and holes), so the main cell in the shape of a cube is allowed, while in the shape of a tetrahedron it will not satisfy the tesselation condition[38].

It is worth mentioning the difference in meaning between the *replicas* with PBC and the *replicas* in the statistical ensemble definition. Replicas in PBC are *exact* replicas of the particular configuration in the main simulation cell, and the displacement of one particle in the main cell leads to the displacement of *all* its images in the replicas as shown in Figure 3.3. Replicas in the statistical ensemble definition are *equivalent* among themselves on the *macro* level e.g., $(T, \langle p \rangle)$ are the same), while on the *micro* level all the replicas can be different (different instant configurations), and there is no favoured main cell.

Finally there are cases, when no PBC conditions are used at all[39, 40]. These cases could correspond to real systems investigated with AFM, when

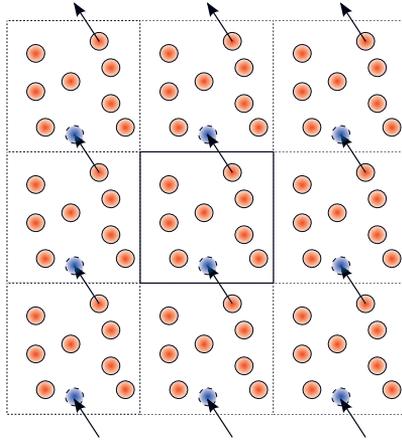


Figure 3.3: Sketch of a two dimensional system with periodic boundary conditions. The main cell is the solid square in the center. The closest replicas are shown as dashed squares. A displacement of one particle is shown by the arrow. The trial position is marked with the dashed circle. The total number of particles inside the main cell is preserved.

an experimentalist works with a single molecule. In computer simulations it is referred to as a *small system*, suitable for studying single molecules or stand alone clusters. In this case PBC are not used and quite often the main cell has a sphere-like shape with hard walls, so no particle can leave or enter the cell[24]. Another possibility to avoid the PBC is to work in non-Euclidean closed space e.g. in the \mathbb{S}^3 space[41].

4. Compaction of Polymers

We have now learnt, that the configurational properties of our system can be evaluated using the apparatus of statistical mechanics, and techniques derived from this, e.g. Metropolis Monte Carlo, while contribution from the kinetic degrees of freedom can be evaluated analytically. It was also said that polymers are molecules consisting of repeating units called monomers, which are chemically connected with each other. The configuration of a polymer chain can be rather varying, and it can form e.g. coils, mushrooms, and globules[2]. In this section we will concern ourselves with non-flexible polymers, i.e. those having a *persistence length* greater than zero, which means the presence of *correlations* between the monomers as in, for example, DNA[2]. These kinds of polymers are known for their ability to form toroidal-like structures, as has been seen both in laboratory experiments[42, 43, 44] and also in computer simulations[45, 46, 47]. There are several ways to achieve such compact conformations.

In the following sections we will briefly describe, as we believe, the most important results from the projects presented in this thesis given in papers I-V dealing with the compaction of semi-stiff polymers. The interested reader is welcome to get a deeper insight from the papers presented in the appendices.

4.1 The effect of condensing agents

One way to induce a compaction of a semi-stiff polymer is to add some substance to the polymer solution, which will act as a compacting agent, glueing loops of the polymer together[48, 49].

We consider a semi-stiff polymer chain in the frames of the MMC method in the Grand Canonical ensemble (an open system), each bead carrying a unit negative charge. We then add a neutralizing amount of unit positive charges. We further add a tetravalent salt which is used as a compacting agent. In the solution the added salt dissociates into four monovalent negative charges and one tetravalent cation. These tetravalent positive charges are attracted by the negative charge of the chain's backbone and can induce an effective attraction between the coils of the polymer.

The choice of ensemble was governed by the idea to be able to vary the number of tetravalent cations. For a small amount of tetravalent salt or for cations with a valency less than three, earlier simulations and experiments

have shown that even if compaction is possible, the compact structure will be unstable[45, 50]. By varying the number of tetravalent ions, we were able to find a critical concentration for the tetravalent salt in our model which would trigger the compaction. By slightly increasing the amount of tetravalent salt, the polymer collapsed from an extended (stable) configuration to a compact (stable) toroidal-like structure. By slightly decreasing the concentration – it unfolds again to the stable extended structure.

In this work, a freely-jointed model with a bending stiffness was used, and the chain was inscribed into a rigid sphere larger than the polymer contour length. The first bead of the chain is fixed in the center of the sphere. Coulomb interactions between charges and excluded volume interactions between chain beads, free ions and with the wall of the sphere were considered.

The energy of the system thus becomes:

$$U_{tot} = U_{HC} + U_{el} + U_{bend}. \quad (4.1)$$

In this work dimensionless units are used. As a natural unit of length the bead size a is chosen. All the distances are expressed as $r^* = r/a$. The natural units for energy, ω , can be obtained from:

$$U_{el} = \frac{1}{4\pi\epsilon_0} \frac{q_1 q_2}{\epsilon_r r} = \left(\frac{e^2}{4\pi\epsilon_0 \epsilon_r a} \right) \frac{Z_1 Z_2}{r^*} = \omega U_{el}^*, \quad (4.2)$$

$$U_{el}^* = \frac{Z_1 Z_2}{r^*}, \quad (4.3)$$

where ϵ_0 is permittivity of vacuum, e is the elementary charge, ϵ_r is the dielectric constant of the solvent, Z_1, Z_2 are the valencies of the charges and r^* is the reduced distance between the centers of the beads.

We have also used a hard core excluded volume energy:

$$U_{HC}^* = \begin{cases} \infty & r^* < 1.0 \\ 0 & r^* \geq 1.0. \end{cases} \quad (4.4)$$

The polymer is modeled as a sequence of beads, connected by rigid bonds of constant length $b^* = 1.5$ with an intrinsic stiffness potential:

$$U_{bend}^* = \kappa \sum_{i=1}^{N-1} (1 - \cos \theta_i), \quad (4.5)$$

where θ_i is the angle between two sequential bond vectors \mathbf{r}_i and \mathbf{r}_{i+1} and κ is a dimensionless bending constant. The bond length is the distance between two neighbouring centers of beads.

The total energy of a system in reduced units U_{tot}^* can be expressed as:

$$U_{tot} = U_{HC} + U_{el} + U_{bend} = \omega(U_{HC}^* + U_{el}^* + U_{bend}^*) = \omega U_{tot}^*. \quad (4.6)$$

The dimensionless inverse temperature, $\beta^* = 1/T^* = \omega/k_B T$, can be found from the relation:

$$\beta U_{tot} = \beta^* U_{tot}^*.$$

A pure MMC simulation is not a good choice for systems with multiple minima in the free energy profile[32, 51]. The Metropolis simulation scheme will sample configurations from a minimum of the free energy, but that minimum can be a *local* minimum. The MMC usually does not allow the system to descend from a local to the global minimum. There are a number of techniques to improve the sampling scheme to be able to sample a broader area in the free energy landscape, for example, histogram methods, expanded ensemble, entropic sampling methods[32, 51]. The latter is based on the idea that it is possible to *project* a configurational space onto a so called *reaction coordinate*. For example, we have a system of 6 objects:

- red triangle
- green triangle
- red circle
- green circle
- red square
- green square.

The total number of elements in the set is 6, but we can *group* them according to different criteria: one type of grouping can be defined by the shape (3 groups), another by the colour (2 groups). In the former case we can say that we have 3 groups and each has 2 members. In the latter case we have 2 groups with 3 members in each. In both cases we consider all 6 elements, but the *selection* criteria is different. In the first case the reaction coordinate will be the 'shape', while in the second it is the 'colour'.

In the case of polymers, it is possible to project the configurational space onto the radius of gyration, R_g , as a reaction coordinate. So, by sampling all possible radii of gyration *and* calculating the frequency with which a certain radius of gyration will occur, $\Omega(R_g)$, it is possible to explore the configurational space of the polymer. Sometimes, however, it is not the radius of gyration density of states, $\Omega(R_g)$, which is of interest, but a related property, namely the radius of gyration distribution function, $p(R_g, \beta)$, showing how probable it is to observe a conformation with a certain R_g at the given temperature. The latter quantity can be obtained in two ways, knowing $\Omega(R_g)$:

$$p(R_g) = e^{-\beta \langle E(R_g) \rangle} \Omega(R_g), \quad (4.7)$$

where $\langle E(R_g) \rangle$ is the average energy for the given R_g , or during a MC simulation with the sampling scheme:

$$acc(o \rightarrow n) = \min \left[1, e^{-\beta \Delta E} \frac{p(R_g(o))}{p(R_g(n))} \right], \quad (4.8)$$

describing a transition probability from the old state, 'o', to the new, 'n', and where $p(R_g)$ is *dynamically updated during the simulation* according to the Wang-Landau algorithm[33].

The entropic sampling method within the WL algorithm is one of the most suitable choices to sample the configurations of a polymer chain in a *wide* range of compactions, much wider than can be achieved in the frames of the conventional MMC. Another advantage of the WL algorithm is that it allows one to write a parallel code for clusters of computers, resulting in significant speed-ups and significant reduction of simulation time (see paper II).

The results of paper I can be summarized as:

1. there is a critical concentration of the condensing agent, as seen from $p(R_g)$ in Figure 4.1, showing that the most probable configuration of the chain is either compact (small R_g) or prolonged (large R_g)
2. semi-stiff polymers are collapsing according to the 'all-or-nothing' mechanism, so in our simulations no structures of *intermediate* compaction were observed as a *stable* conformation, (Figure 4.1)
3. the tetravalent cations are *always* located in the vicinity of the negatively charged backbone of the chain, (Figure 4.2)
4. monovalent ions of both positive and negative charge are not confined to the charged polymer, but almost uniformly distributed in the volume of the simulation cell, (Figure 4.2).

4.2 Sampling compact configurations

Sometimes the result of a number of small steps is not equal to the result of one big step. For example, it is more likely to be able to climb up a slippery slope having an initial acceleration on the horizontal surface, rather than trying to take small steps to conquer the top in a quasistatic manner.

The same can be applied to polymers, when one would like to sample very compact structures. The most common techniques of changing the chain geometry, like pivot moves (one of the ends of random length is rotated a random angle), crank shaft moves (a piece of the chain between two randomly selected beads is rotated a random angle), or slithering snake moves (a part of random length is transferred parallel from one end of the chain to the other) are inefficient to sample very compact structures[48, 52].

One can easily understand this by conducting a thought experiment. Let us start with a chain of N beads, using the *freely-rotating* model as the most suit-

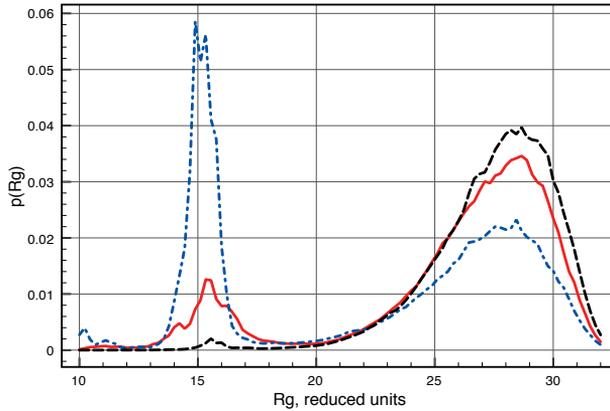


Figure 4.1: The radius of gyration distribution, $p(R_g)$, for different amounts of tetravalent ions from simulations in the Grand Canonical ensemble. Parameter B is proportional to the amount of the tetravalent salt. Dot dashed curve for $B = 8.0$, solid curve for $B = 7.0$, dashed curve for $B = 6.0$. The system is: $N = 80$, $b = 1.5$, $\kappa = 20.0$. The figure is taken from paper I.

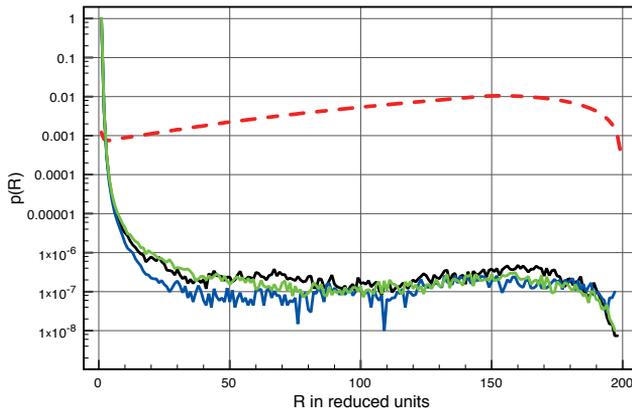


Figure 4.2: Distributions of different counterions vs. distance from the closest bead during a Grand Canonical MC simulation. The parameter B is proportional to the amount of the tetravalent salt. Tetravalent counterions (solid curves) are mostly located in the vicinity of the chain and monovalent counterions (dashed curve shown only for $B = 7.0$) are almost indifferent to the chain's location and can be found throughout the volume of the simulation cell. For the tetravalent counterions, results are shown for three different B : $B = 6.0$, $B = 7.0$, $B = 8.0$. The system is $N = 80$, $b = 1.5$, $\kappa = 20.0$ for these simulations. The figure is taken from paper I.

able to generate possible compact structures for semi-stiff chains. To be able

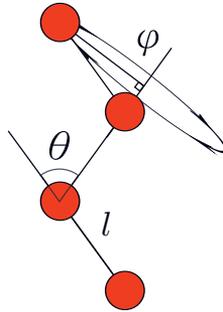


Figure 4.3: A segment of a freely-rotating chain. The angle (θ) and the bond length (l) are parameters of the model. The torsional angle (φ) provides a torsion stiffness.

to construct e.g., a toroid we should select one monomer at a time and rotate *each* of them a certain angle, Figure 4.3. A pivot move technique[53] assumes that one *randomly* selects a monomer, $i \in [2, N - 1]$, and the tail $\in \{\mathbf{r}_{i+1} : \mathbf{r}_N\}$ of the chain which is rotated as a rigid object a random angle φ , see Figure 4.4(a). One can see that it is *extremely* improbable, that a random angle in combination with selecting a random bead will result in a compact structure, compared to a statistical coil.

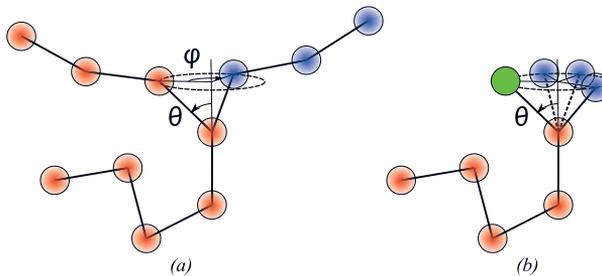


Figure 4.4: A segment of a freely-rotating chain. (a) Pivot move about a randomly selected bead i for a random angle φ . The tail of the chain is rotated as a rigid body, and (b) bead-by-bead regrow. Several (four here) possible orientations of the next monomer are on the surface of the cone. To generate a compact structure a position marked with solid green is the most probable to be selected as a trial position.

To generate compact structures we have instead used the following procedure: grow the chain bead by bead and select the orientation of *every* bead using a *configurational bias*, so configurations of *different compactness would have different probability to be generated*, according to some rule, illustrated in Figure 4.4(b). The closest idea is the Rosenbluth-Rosenbluth(RR) sam-

pling, initially proposed in 1955[54] to sample compact configurations of lattice polymers. Later it was modified and corrected by Frenkel for a continuous model[20]. Combining the RR sampling with the Entropic Sampling(ES) technique for lattice models has also been done by de Pablo[55]. In paper III we derive, test and apply a scheme for RR sampling combined with ES for a continuum model of the freely-rotating chain with a torsional stiffness. In the case of a configurational bias involved in the MC simulation, the latter is referred to as Configurational-Bias Monte Carlo(CBMC).

To convince the reader we present in Figure 4.5 a graph showing how the chain will sample the configurational space during the MMC simulation in frames of ES with the WL algorithm. The only difference between Figure 4.5(a) and Figure 4.5(b) is the algorithm used for modifying the geometry: (a) by pivot moves or (b) using bead-by-bead regrow. Figure 4.5 shows how configurations of a given compactness (represented by R_g intervals) are visited during the simulation. One can see that using pivot moves one can not sample very compact configurations (small R_g interval numbers) at all, (Figure 4.5(a)), while using bead-by-bead regrow allows one to sample all the states of different compactness from very compact (small R_g interval numbers) to extended (large R_g interval numbers), (Figure 4.5(b)).

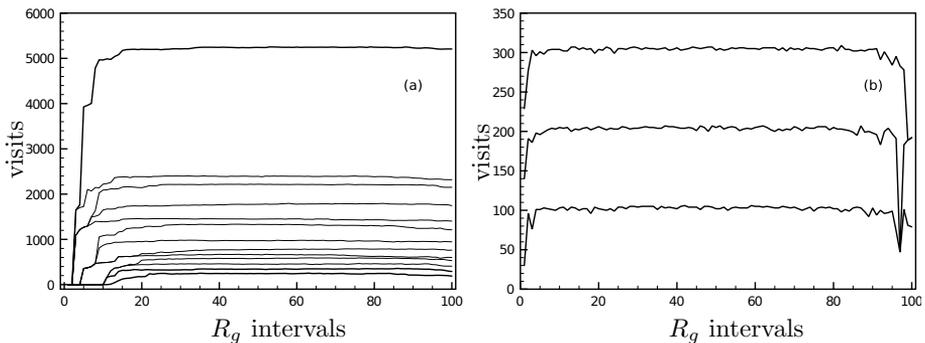


Figure 4.5: (a) Visits numbers of the R_g intervals during a computer experiment with pivot moves, (b) with bead-by-bead regrow. The total number of configurations generated is the number of visits \times 100. The figure is taken from paper III.

An easy way to explain the idea of the CBMC algorithm is to consider a detailed balance condition. The detailed balance condition can be thought of as a configuration flow described by:

$$K(o \rightarrow n) = K(n \rightarrow o), \quad (4.9)$$

where $K(o \rightarrow n)$ and $K(n \rightarrow o)$ are the number of accepted moves (on average) from old, 'o', to new, 'n', and from new to old configurations respectively.

Equation (eq. 4.9) can be factorized according to:

$$K(o \rightarrow n) = p(o) \times \alpha(o \rightarrow n) \times acc(o \rightarrow n), \quad (4.10)$$

where $p(o)$ is the probability for a system to be found in the given state, which is proportional to $\exp[-\beta U(o)]$ for the Canonical Ensemble, $\alpha(o \rightarrow n)$ is the probability to select a new configuration (it is referred to as the Markov's transition matrix) and $acc(o \rightarrow n)$ is the probability to accept a move from an old to a new state.

If we would set $\alpha(o \rightarrow n) = \alpha(n \rightarrow o)$ ¹, it would mean that we change a conformation of the chain in a random manner. In other words, we accept, as a *trial* configuration, any new configuration. In the case of $\alpha(o \rightarrow n) \neq \alpha(n \rightarrow o)$ one would say that some rule for selecting a *trial* configuration is used and this situation is referred to as a configurational bias.

Let us illustrate the idea of configurational biasing for a simple system. We have two oppositely charged ions '+q' and '-q' within a sphere with hard walls. Let us also put the ions initially far away from each other, but assuming that at equilibrium the ions will form a pair, like a dipole. Let the ion '+q' be displaced, while '-q' keeps its position. Assume that '+q' has *several possible random* displacements, and we should choose one of them as a new *trial* position. How can we do this? Since we assumed that at equilibrium the ions will be together, it seems sensible to favour displacements, which move the ions closer and disfavour those which move them apart. So, among several random displacements of the '+q' ion we should select one as a trial position which makes the distance between '-q' and '+q' smaller. In this case the selection rule can be the distance between the ions. For all random displacements we calculate the distance from the fixed position of '-q' and *every random* position of '+q' after displacements: r_1, r_2, r_3, r_4 , if we consider 4 random displacements, (see Figure 4.6). One of the positions then is selected as a trial position according to:

$$p_i = \frac{e^{-r_i}}{\sum_{j=1}^4 e^{-r_j}}, \quad (4.11)$$

where p_i is the probability to select the random displacement number i as a trial position for '+q'. As one can see, the smaller the distance r_i , the larger the probability to select a given random displacement.

Even for a 'simple' system such as an electrolyte in the frames of the restricted primitive model, such a configurational bias will result in much faster convergence in a MC simulation[56].

In our case with a polymer chain we use a bias in two ways. First we introduce a configurational RR-like bias[52] to be able to generate both compact and prolonged structures. Another bias is from the WL scheme, which allows

¹which Metropolis did in his solution

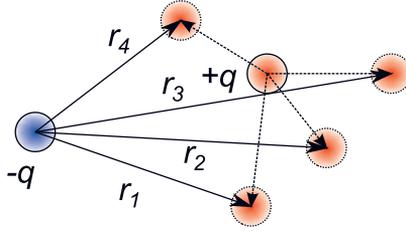


Figure 4.6: One of four displacements is selected as a trial position, according to (eq. 4.11). Random displacements and positions of '+q' are shown using dashed curves. The lengths r_i are the distances between the fixed position of '-q' and 4 random displacements of '+q'.

one to force the polymer to sample the configurations between very compact and more rod-like. The details of the algorithm are given in paper III.

In the computer experiments we used the freely-rotating model. The polymer chain is inscribed into a rigid unpenetrable sphere, mimicking a so called small system[24]. The radius of the sphere is chosen to be larger than the contour length of the chain. The first bead of the polymer is fixed in the center of the sphere. No other components except the chain were considered. To investigate compact structures, Lennard-Jones(LJ) interactions (eq. 4.12) were used for the non-bonded interactions between the beads of the chain:

$$U_{LJ}(r) = 4\epsilon \left[(a/r)^{12} - (a/r)^6 \right], \quad (4.12)$$

where ϵ is the potential well depth and a is the bead diameter.

Reduced dimensionless parameters were used with the size of the bead, a , as the unit of length and ϵ as the unit of energy. In reduced units the LJ interactions are:

$$U_{LJ}(r) = 4\epsilon \left[(a/r)^{12} - (a/r)^6 \right] = 4\epsilon \left[(1/r^*)^{12} - (1/r^*)^6 \right] = \epsilon U_{LJ}^*(r^*), \quad (4.13)$$

where $U_{LJ}^*(r^*) = 4 \left[(1/r^*)^{12} - (1/r^*)^6 \right]$ and $r^* = r/a$.

The torsion energy between the planes formed by bond vectors (\mathbf{r}_i and \mathbf{r}_{i+1}) and (\mathbf{r}_{i+1} and \mathbf{r}_{i+2}) can be written as (see Figure 4.7):

$$U_{tor}^* = \kappa \{ [\mathbf{r}_{i+1} \times \mathbf{r}_i, \mathbf{r}_{i+2} \times \mathbf{r}_{i+1}] / C + 1.0 \}, \quad (4.14)$$

where $[,]$ stands for the dot product, and ' \times ' for the vector product. The normalisation constant $C = [\mathbf{r}_{i+1} \times \mathbf{r}_i]^2 = [\mathbf{r}_{i+2} \times \mathbf{r}_{i+1}]^2$ equals the area of the parallelogram squared. The constant κ is a dimensionless quantity defining the amplitude of the torsion energy. The torsion energy is also shifted, so

that the energy is zero when the chain has its largest end-to-end distance: $R_{ee} = Nl \cos(\theta/2)$, where l is the bond length.

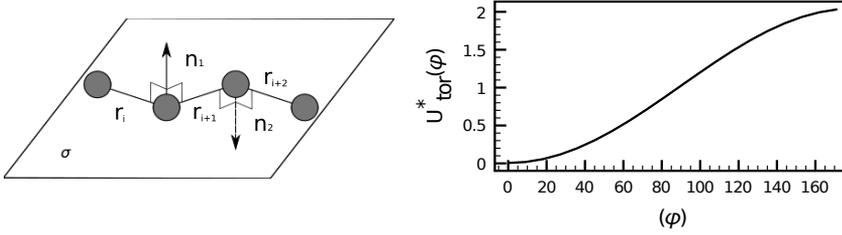


Figure 4.7: An illustration of (eq. 4.14). Left: the direction of the vector product of the r_{i+1} -th and r_i -th bond vectors depicted by as \mathbf{n}_1 . The direction of the corresponding product for r_{i+2} and r_{i+1} is denoted by \mathbf{n}_2 . The normal vectors \mathbf{n}_1 and \mathbf{n}_2 are perpendicular to the plane σ , containing the chain. One can see that for this configuration (eq. 4.14) gives $U_{tor}^* = 0.0$. On the right the graph of (eq. 4.14) as a function of φ is presented.

The full configuration energy in reduced units is:

$$U_{tot}^* = U_{LJ}^*(r^*) + U_{tor}^*. \quad (4.15)$$

For simplicity, we will omit the asterisk sign below.

In our simulations we wanted to construct the configurational energy density of states, $\Omega(E)$, for a wide range of compactions for non-overlapping configurations. Knowing $\Omega(E)$ one can evaluate the average configurational energy $\langle E(T) \rangle$ and heat capacity $c_V(T)$ for a wide range of temperatures T using:

$$\langle E(T) \rangle = \frac{\sum_i E_i \Omega(E_i) e^{-E_i/k_B T}}{\sum_i \Omega(E_i) e^{-E_i/k_B T}} \quad (4.16)$$

and

$$c_V(T) = \frac{1}{T^2} \left(\langle E^2(T) \rangle - \langle E(T) \rangle^2 \right). \quad (4.17)$$

Analysis of the heat capacity, $c_V(T)$, as a function of temperature can shed light on the occurrence of phase-like transitions with changing temperature.

The results of paper III can be summarized as:

1. a new sampling method, combining the RR-like way of geometry changes with the ES sampling with the WL algorithm for a continuum model was developed, tested and applied to the freely-rotating model of semi-stiff polymers including also a torsional stiffness

2. the method allows one to sample very compact and very prolonged structures of a semi-stiff polymer model in a single computer experiment, see (Figure 4.8)
3. the sampling techniques being used and the methods of generating configurations allow a *significant* (more than several times) reduction in simulation time (for compact structures) compared to an algorithm using pivot moves.



Figure 4.8: An example of a compact and a prolonged structure, sampled for a freely-rotating chain with $N = 60$ beads and an angle between the bond vectors $\theta \approx 29^\circ$.

4.3 Growing a polymer chain with a certain degree of compaction

Today it is possible to synthesize polymers with a backbone having a preferred structure. This structure can be long fibers of synthetic silk and UHMWPE which are produced from the reaction bath by pulling a thread line and spinning[57]. Drug delivery, on the other hand, is heavily based on hollow-sphere shaped polymers or capsid-like structures as drug containers[58].

The question then arises: is it possible to construct a recipe to produce an object with a given topology? For example, one has a set of monomers. How should the polymerization reaction be done to obtain e.g. a toroid or something very stretched and rod-like?

In paper IV this question is taken as a starting point to investigate how to devise an algorithm to set up a certain polymer chain structure. As an example, we consider a polyampholyte(PA). Polyampholytes are polymers carrying both positive and negative charges on its backbone. Polyampholytes can e.g. be denaturated proteins like collagen or in their native state, like bovine serum albumin[59]. Polyampholytes can be charge balanced (zero net charge) or carrying a net charge. Among synthetic charge balanced polyampholytes there are several groups depending on how the charges are distributed along the backbone: the charges can be randomly distributed, or one can have an alter-

nating distribution, where positive and negative charges appear in consecutive pairs. The third group is diblock, triblock and zwitterionic distributions. The latter means that each bead carries a dipole. Different charge distributions lead to different conformational properties of the PA[59, 60, 61].

We investigated how the conformational properties of the PA depend on the charge distribution along its backbone. We considered a PA in the frames of the freely-rotating model with a torsional stiffness, with the polymer inscribed into a rigid sphere to mimic a small system[24] in the Canonical Ensemble. We used two types of charges: '-1' and '+4' in a proportion to keep the net charge equal to zero. Multivalent charges ('+4') were used, since they can induce an effective attraction between different coils of the backbone[42, 48]. The MC experiment was conducted in the Canonical ensemble using the entropic sampling method(ES)[32] with the Wang-Landau algorithm[33].

The main idea can be described as follows: consider a chain with $N = 60$ beads, where $N_{+4} = 12$ and $N_{-1} = 48$ are the number of beads with charges '+4' and '-1' respectively. The accessible range of the radius of gyration, R_g , is divided into a number of intervals. Using the ES method with configurational biasing we can sample from very compact (tight toroids, small R_g interval numbers) up to very stretched configurations (large R_g interval numbers). For every configuration we conduct a *short* canonical MMC[29] run, where we exchange positions of '+4' and '-1' charges according to the rule:

$$acc(o \rightarrow n) = \min[1, e^{-\beta\Delta E}], \quad (4.18)$$

where ' o ' and ' n ' are the old and new *charge distribution* states and ΔE is the energy change due to the position exchanges of the charges. Since there are only $N_{+4} = 12$ tetravalent charges, it is enough to perform about 1000 charge exchanges to obtain a Coulomb energy which has *converged for a given configuration* and temperature[52]. For every R_g interval we set up a special counter where we accumulate *averages of averages* for the configurational energy. The first '+4' charge is permanently fixed on the first bead and the relative '+4' charge distribution corresponding to the converged $\langle E \rangle$ is book-kept. We can thus summarize the scheme as follows:

1. grow the polymer and calculate R_g
2. a) for a given configuration run a small cycle of steps according to (eq. 4.18) and calculate the average energy for the given configuration at the given temperature, $\langle E(R_g) \rangle_{can}$
b) update the *average of averages* $\langle \langle E(R_g) \rangle_{can} \rangle$ for the given R_g interval
c) *save* the bead numbers with '+4' charges
3. regrow the polymer.

Steps 2 and 3 are repeated so we accumulate sufficient conformational statistics, until $\Omega(R_g)$ has converged. This radius of gyration density of states, $\Omega(R_g)$, shows the population in a certain R_g interval.

Since, we obtained the average configurational energy for every configuration, we have a curve $\langle E(R_g) \rangle$ at the given temperature. We also accumulated the positions of the '+4' charges along the backbone of the chain after convergence of the $\langle E(R_g) \rangle_{can}$ for every R_g interval, making it possible to answer the question: what *relative* distribution of '+4' charges should one have to observe the chain in a certain R_g interval at the given temperature. The extracted '+4' distribution, ψ , for chains of two different lengths ($N = 40$ and $N = 60$) are shown in Figure 4.9. The distribution, ψ , shows at what bead number we should put the '+4' charges, for the chain to form a compact (small R_g) or prolonged (large R_g) structure at equilibrium.

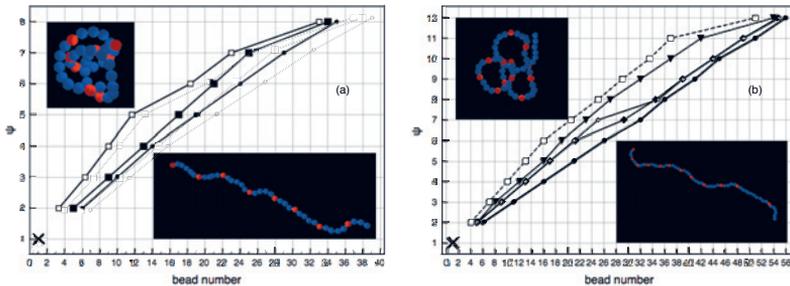


Figure 4.9: Most probable positions of the '+4' charges along the backbone for different degree of compaction: (a) $N = 40$, $R_g \in [2.2 : 10.2]$ in reduced units. Filled circles represent $R_g \approx 2.0$, filled squares correspond to $R_g \approx 4.0$, opened squares are for $R_g \approx 10.0$. (b) $N = 60$, $R_g \in [3.0 : 15.0]$ in reduced units. Filled circles represent $R_g \approx 15.0$, filled diamonds are for $R_g \approx 7.5$, open diamonds: $R_g \approx 7.0$, open squares are $R_g \approx 3.5$. In the insets, a typical chain conformation for $R_g \approx 3.5$ and for $R_g \approx 15.0$ are shown. The position of the first '+4' is marked by a cross. The figure is taken from paper IV.

As we can extract the relative distribution of '+4' charges corresponding to the set of structures for the given R_g interval – we can test this relative distribution. To do this we performed simulations with a frozen positions of all '+4' charges according to the extracted distribution, ψ . As a result one can obtain $\pi(R_g, \beta)$ describing the probability to observe the system with the given R_g :

$$\pi(R_g, \beta) = e^{-\beta \langle E(R_g) \rangle} \Omega(R_g). \quad (4.19)$$

Figure 4.10, illustrating the result from simulations according to (eq. 4.19) can tell us what the probability is to find a polyampholyte in a certain R_g interval at the given temperature in the Canonical ensemble. So, we are able to construct the polyampholyte with the conformational properties of interest.

The results of paper IV can be summarized as follows:

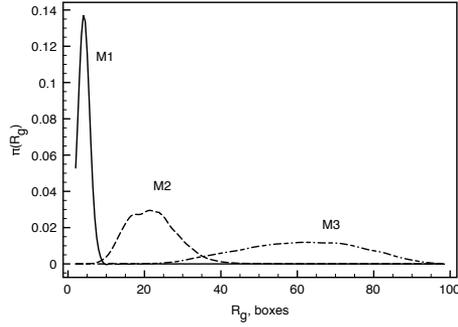


Figure 4.10: The probability to observe the polymer chain with a given R_g , $\pi(R_g, \beta)$, according to (eq. 4.19). The figure shows $\pi(R_g, \beta)$ for different fixed '4' distributions, ψ , resulting in different equilibrium structures for $N = 60$. Thermodynamically stable and highly compact with $\psi_1 = (1, 4, 7, 10, 13, 17, 21, 24, 28, 32, 37, 49)$ shown as solid line ($M1$ region), uncoiled structures with $\psi_3 = (1, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52, 57)$ shown as dot-dashed line ($M3$ region), and intermediate compact with $\psi_2 = (1, 5, 9, 13, 17, 22, 27, 32, 37, 41, 47, 56)$ shown as dashed line, ($M2$ region). The figure is taken from paper IV.

1. we used the simulation scheme developed in paper III to be able to sample configurations of the polymer chain in a wide range of compaction *in a single computer experiment*
2. the radius of gyration density of states, $\Omega(R_g)$, was calculated with high precision
3. the algorithm was developed allowing us to extract information about the *relative charge distribution*, ψ , along the backbone needed to observe a compact or prolonged structure in equilibrium.

4.4 Inducing compaction by nonuniform confinement

Computer simulations of polymer systems have been carried out in many statistical mechanical ensembles and in many different confinements, involving external fields or using special shapes of the simulation cell[62, 63, 64, 65, 66, 67]. For example, if one performs simulations with several chain molecules involved, then it is more reasonable to use *periodic boundary conditions*[20, 21, 24, 26], mimicking a macroscopic system. Periodic boundary conditions can be applied in one dimension, resulting in an infinite system in one dimension, like a tube containing a melt of polymers[66]. If periodic boundary conditions are applied to two dimensions, then one considers a parallel capacitor-like system, which can be used, in computer experiments investigating e.g. surface properties[68]. Periodic boundary conditions extended to three dimen-

sions can be used in computer experiments to investigate bulk properties[65]. Sometimes, however, periodic boundary conditions can be omitted even in the case of long-ranged Coulomb interactions, when one investigates the properties of a *single* molecule in solution[24]. Such a situation can occur in the case of very strong dilution, so individual chains are so far from each other, that *inter-chain* interactions are fully screened by the molecules of solvent, or while conducting simulation in a closed non-Euclidean \mathbb{S}^3 space[69].

In paper V we investigated the mechanism for how a *single* macromolecule can undergo changes in its geometry due to nonuniform confinement, using an external field together with a special shape of the simulation cell. To avoid complications and to understand the important features, we considered a system in two dimensions without excluded volume interactions. As a simulation cell, a two-dimensional cone was used in the Canonical Ensemble. The MMC[29] and the extended ensemble technique[51] were used as simulation method. The *ring* polymer was treated as a sequence of beads, connected by bonds, and the bond length was allowed to fluctuate. The total energy of the system is:

$$U_{tot} = U_{bend} + U_{stretch} + U_{wall} + U_{ext}, \quad (4.20)$$

where U_{bend} is the bending energy, $U_{stretch}$ is the energy due to the bond length fluctuations, U_{wall} is the wall repulsion and U_{ext} is the energy of the chain in the external field.

Specifically for a chain of N bonds,

$$U_{bend}(\theta) = \kappa \sum_{i=1}^N (1 - \cos \theta_i), \quad (4.21)$$

where $\theta_i = \widehat{\mathbf{r}_i, \mathbf{r}_{i+1}}$ (for $i \in [1 : N - 1]$) and $\theta_i = \widehat{\mathbf{r}_i, \mathbf{r}_1}$ (for $i = N$) is the angle between successive bond vectors and κ is a bending force constant.

$$U_{stretch}(b) = \begin{cases} -\gamma \sum_{i=1}^N \ln[1 - ((b_i - b_0)/\Delta b_{max})^2] & , \quad b_i \leq b_{max} \\ \infty & , \quad b_i > b_{max}, \end{cases} \quad (4.22)$$

where γ is a stretching constant, $\Delta b_{max} = b_{max} - b_0$ is the maximal bond fluctuation, $b_i = |\mathbf{b}_i|$, and $b_0 = |\mathbf{b}_0|$ is the equilibrium bond length (a FENE-like potential).

$$U_{wall}(r) = \begin{cases} 0, & \text{bead is inside the cone} \\ \infty, & \text{bead is outside the cone,} \end{cases} \quad (4.23)$$

which describes the hard wall interaction between the polymer and the confining volume.

The interaction with the external field is given by :

$$U_{ext}(x) = \sigma x_{cm}, \quad (4.24)$$

where x_{cm} is the distance between the level of the center of mass of the polymer, cm , and the level of the bottom of the cone, O. A sketch of the system shown in Figure 4.11.

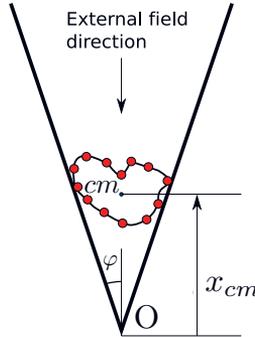


Figure 4.11: A circle-like ring polymer confined inside the cone. The position of the center of mass of the polymer is denoted as 'cm', and x_{cm} is the distance between the level of the center of mass and the bottom of the cone, O.

The main idea of paper V can be formulated: in the absence of an external field, a ring polymer has a circle-like shape due to its stiffness and the random heat vibrations. When the external field is included, the chain will find its equilibrium position and conformation as a result of four potential energy contributions: the bending energy (eq. 4.21), the stretching energy (eq. 4.22), the hard-wall interactions (eq. 4.23) and the external energy (eq. 4.24). The external field pulls the polymer chain down, while the repulsion from the walls has a component pointing upwards and into the cone.

As the chain is *not* flexible, it will try to resist the force, caused by the external field, *up to a certain degree* by shortening its bond-lengths, but keeping a circle-like shape. When the pressure exceeds a certain threshold value, the chain changes its conformation drastically trying to reduce its (Helmholtz) free energy. In the case of a semi-stiff chain, the new stable conformation is similar to the original (fluctuating circle), but increasing the number of loops by one. After forming one additional loop, the chain again accumulates energy if the external field is increased, until the next threshold value, when the next loop is formed. Corresponding screenshots showing the stages of packing of the ring polymer into toroidal-like loops is shown in Figure 4.12.

These drastic changes in geometry can easily be captured while looking at the position of the center of mass of the chain. When a new loop forms, the chain moves a little bit closer towards the bottom of the cone, Figure 4.11,

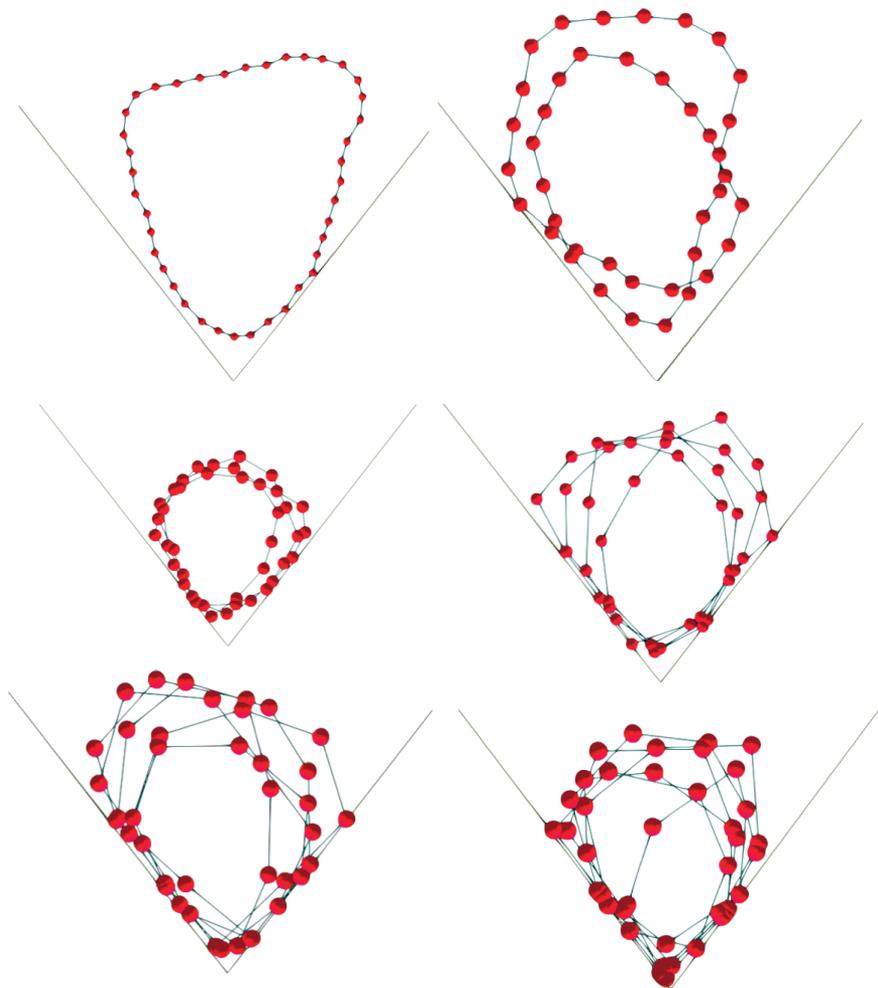


Figure 4.12: Screenshots of different stages of compaction: from one to six loops for a chain with $N = 40$ beads. The figure is taken from paper V.

and the position of the center of mass, x_{cm} , is descending. Another way to see the loop formation is to look at the bending energy, U_{bend} , as a function of the magnitude of the external field. Since the chain is semi-stiff, it tries to keep its circle-like shape as long as possible. Such type of structures being quite uniformly compressed remains circle-like, but with a smaller radius. When the threshold in compression is exceeded, however, a new loop is formed and the bending energy will show a step-like behaviour, since the angles between sequential bonds change abruptly.

In paper V a separate MMC simulation for different strengths of the external field, σ , was performed. As a result we obtained the full average configurational energy, $\langle U_m \rangle$, (eq. 4.20), as a function of the external field strength, Figure 4.13(a), as well as its distribution, $p(U_m)$, where m represents the number of successive increases of the external field, σ_m . Using these data it was possible to investigate the *relative* stability of the equilibrium structures which were observed. This can be done using, for example, the method of extended ensembles[51] and its modifications[70]. A rigorous description of the method and its implementation can be found in the original references[51, 52, 71, 70], while here we will briefly describe the main idea.

Each MMC simulation produces the energy distribution, $p(U_m)$, where $m \in [1 : M]$, $M = 50$. Furthermore, the ensemble for each of the M simulations is considered as a *subensemble* of an *extended ensemble* with an additional *weight function*. In terms of the partition function, (eq. 3.8), we can write:

$$Q(N, V, T) = \sum_{m=1}^M Q_m(\sigma_m, N, V, T) e^{s_m}, \quad (4.25)$$

where $Q_m(\sigma_m, N, V, T)$ is the usual Canonical partition function for subensemble m , σ_m is the extension parameter (the field strength in our work) and s_m is the weight factor, associated with each subensemble. The weight factor, s_m , is the *connection* between the subensembles. So, knowing $p(U_m)$ for every subensemble *and* the connection between the subensembles, given by s_m , we can extract information of how probable it is for the system to occur *spontaneously* in the subensemble number m , relative to the other subensembles. A state which the thermodynamic system will try to obtain *spontaneously* is a more *stable* and has a lower free energy. One can show that the Helmholtz free energy difference for a given temperature is[51]:

$$s_m - s_n = \beta(F_m - F_n), \quad (4.26)$$

where F_m and F_n are the Helmholtz free energies for the m and n subensembles respectively. The weight factors s_m are calculated via a sampling scheme with the Wang-Landau algorithm[70]. We can not determine the absolute values of the Helmholtz free energies without knowing the exact value of F for some reference system, but we can, however, calculate the *free energy differences*

between different systems. We can thus answer the question how the relative stability of the configurations of the ring polymer depends on the strength of the external field. The Helmholtz free energy difference ($\Delta F(m), \forall m \in [1, M]$) is plotted in Figure 4.13(b), showing the local minima of Helmholtz free energy when the ring polymer experiences increased stages of compaction. The local minima correspond to locally stable structures.

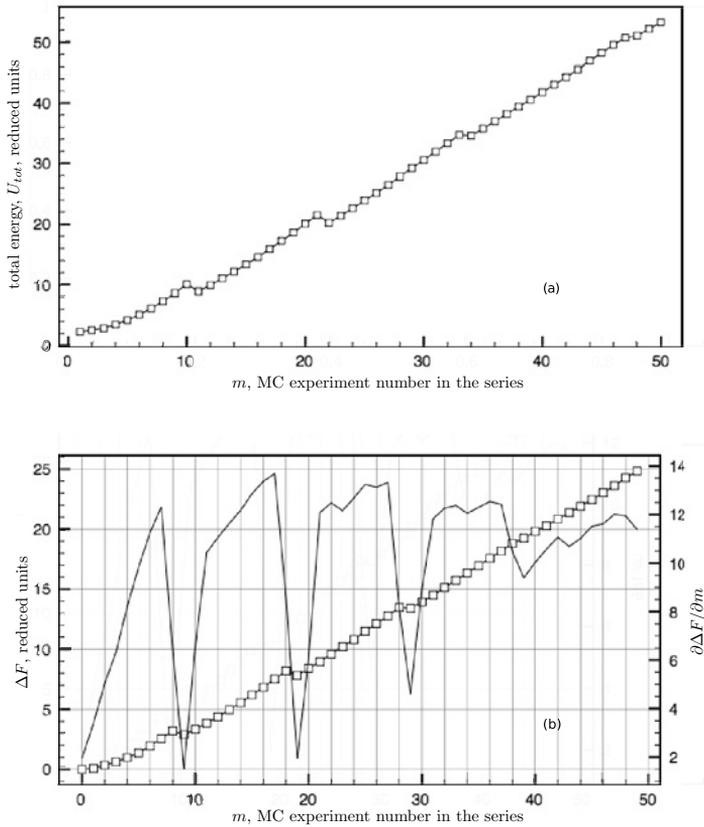


Figure 4.13: (a) The total energy, U_{tot} , and (b) the Helmholtz free energy differences, ΔF , for $N = 40$ as a function of the subensemble number $m : m \in [1 : 50]$. The thin solid line in (b) is a numerical derivative calculated over each 2 points to show more clearly the small minima in the ΔF curve. The free energy for the first subensemble, $m = 1$, is shifted to the zero level. The figure is taken from paper V.

The results of paper V can be summarized as follows:

1. we showed, that a nonuniform confinement, in the form of a cone, together with an external field, is able to induce drastic changes in the shape of semi-stiff polymer chains

2. it was also possible to determine the relative stability of the conformations as a function of the external field strength.

5. Concluding Remarks

The main theme of this thesis is to find methods to study compact structures of semi-stiff polymer chains and how these structures can be generated and modified during Monte Carlo computer experiments. The general idea is that semi-stiff chains do not form random coil-like structures, but more ordered structures, for example toroids or cigar-like shapes. Highly ordered compact structures often have high monomer density gradients, making traditional ways of finding a new trial configuration, like pivot or crank-shafts moves inefficient, since they introduce a piece of a chain which is at least several monomers long. More computationally expensive, but a highly more effective way is to rebuild the chain bead-by-bead from the beginning at every Monte Carlo step. Moreover every monomer position is selected from one of several candidates, in a predefined set, resulting in a so-called a configurational bias. One should pay special attention to the fact that the structures and configurations generated during a simulation are actually model dependent. For example, it is hard to imagine sampling the same configurations for the freely-jointed and freely-rotating model, just because they represent the real polymer on significantly different length scales. Another question which we have not discussed in this thesis and which is also remarkably absent in the literature is how the configurational space of the chain is sampled using different ways to change the geometry of the chain in the frames of the same model.

Nevertheless, the configurational bias only is not enough to investigate conformational properties of semi-stiff chains for a wide range of compactions – from highly packed toroids up to almost stretched. The conventional Metropolis Monte Carlo algorithm is not suitable to generate both compact and prolonged structures, so the Wang-Landau algorithm in the frame of the Entropic Sampling technique was combined in the simulations for the chain to explore a much wider range of compaction, compared to what would have been the case with pure Metropolis Monte Carlo.

Configurational-Bias Monte Carlo and Entropic Sampling techniques with the Wang-Landau algorithm thus allow us to investigate physical phenomena like semi-stiff polymer condensation, where effective attraction between loops of the chain is achieved by van der Waals or by Coulomb interactions in a certain environment. Another way to induce shape transitions in a chain, and which was considered in this thesis is to put a chain into a nonuniform

confinement, e.g. using a special shape of the simulation cell and an external field acting on the molecule.

In all these cases, a semi-stiff chain reveals non-smooth behaviour in its configurational properties, showing the cooperativity of the transitions. For example the radius of gyration distribution function shows that semi-stiff chains prefer to be in a stretched or in a compact conformation in equilibrium, but having a small probability to be found in intermediate conformations.

The simulation techniques used in this thesis also allowed us to use a parallel algorithm, making use of the large computational power of modern computer clusters.

6. Summary in Swedish

I vårt moderna samhälle omges vi av polymera material, i allt från kläder och bildäck till penna och papper. Utifrån dessa exempel förstår vi också att den klass av ämnen vi kallar polymerer består av molekyler med väldigt skiftande egenskaper, både med avseende på storlek och massa liksom variationer i kemisk struktur. Dessa skillnader medför också stora variationer i de fysikaliska egenskaperna hos olika polymerer och bestämmer deras praktiska tillämpningsområden. Den generella beskrivningen av polymer är en molekyl som består av många mindre enheter (monomerer) sammankopplade till en lång kedja. Det kan vara aminosyror i ett protein eller glukosenheterna i stärkelse eller cellulosa liksom vinylkloridenheterna i polyvinylklorid (PVC).

En typ av polymerer som är av speciellt intresse är biopolymerer, eftersom vi är beroende av dem och deras funktion. Till skillnad från många andra makromolekyler är många biopolymerer inte speciellt flexibla utan snarare ganska stela. På molekylär nivå betyder det att orienteringen av en enhet (monomer) i kedjan påverkar orienteringen av nästa enhet. Det finns ett strukturellt "minne" i molekylen och detta kan sträcka sig över många monomerer. Utsträckningen av detta strukturella minne brukar anges i termer av persistenslängden som beskriver hur långt man måste färdas längs molekylen för att korrelationen mellan två monomerer skall upphöra. Om man betraktar en polymerkedja som är åtminstone några persistenslängder lång brukar man beskriva sådana molekyler som "halvstela". För många biopolymerer såsom DNA och många proteiner är denna egenskap viktig för deras egenskaper och funktion. För att bättre förstå och förutsäga egenskaperna hos dessa polymerer är det därför av stor betydelse att utveckla både modeller och beräkningsmetoder för att studera denna viktiga klass av molekyler.

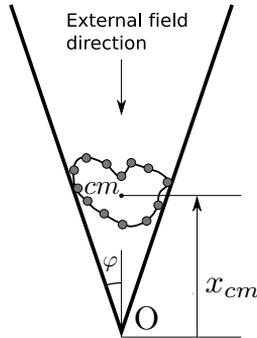
Vissa modeller används mer eller mindre standardmässigt för att undersöka och beskriva icke-flexibla polymerer. Det gäller framför allt den fria-rotationsmodeller och den "masklika kedjan". Båda kan användas för att beräkna storleken hos en polymer som funktion av antalet monomerer eller bindningsvinkeln mellan olika enheter (under förutsättning att respektive modell ger en tillräckligt bra beskrivning av polymeren). Något som dessa modeller emellertid ej tar hänsyn till är mera specifika växelverkningar mellan olika monomerer, såsom elektrostatiske växelverkningar mellan laddade grupper längs molekylen eller att två enheter inte kan vara på samma plats samtidigt (utesluten volym). Om man i en modell för sådana molekyler även tar hänsyn till dessa senare (eller andra) typer av växelverkningar, blir

det oftast nödvändigt att använda datorsimuleringar för att kunna förutsäga egenskaperna hos ett system bestående av en (eller flera) polymerer i något lösningsmedel.

Med hjälp av en beräkningsmetod som kallas Monte Carlo-simuleringar (man använder sig av slumpantal som en viktig del av beräkningarna), har jag ytterligare utvecklat denna metod som en länk mellan de teoretiska modellerna för polymerer och experimentellt observerade resultat. Kortfattat kan man säga att man försöker generera representativa kedjestrukturer som skall motsvara naturliga fluktuationer av molekylernas utseende vid jämvikt, för att sedan bestämma medelvärden av t.ex. form och storlek eller olika termodynamiska storheter. För flexibla kedjor finns det flera väl etablerade metoder som kan beskriva molekylernas egenskaper vid jämvikt. För stelare kedjor måste man använda mera specialiserade simuleringsmetoder. En speciell svårighet är att effektivt kunna sampla kedjor som uppvisar en stor variation i storlek och struktur. Mänskligt DNA har t.ex. en längd på upp till ca. 1 m men kan packas ihop i en cell av storleken $100\ \mu\text{m}$. I avhandlingen har jag koncentrerat mig på att undersöka kompakta konformationer, eftersom dessa är svårare att åstadkomma och även att simulera de strukturella fluktuationer som alltid finns på grund av molekylernas värmerörelse. Konventionella metoder inom Monte Carlo-simuleringar för polymerer fungerar ej så väl för kompakta strukturer. I mitt arbete har jag i stället utgått från en metod för att generera kedjemolekyler som föreslogs för över 50 år sedan och har kopplat denna till moderna simuleringsmetoder som entropisk sampling och Wang-Landau algoritmen. Det visar sig att dessa metoder tillsammans resulterar i en algoritm som är anmärkningsvärt effektiv för att generera kompakta, huvudsakligen toroidala, konformationer för icke-flexibla ("halvstela") polymerer. Genom att på ett kontrollerat sätt variera ett begränsat antal parametrar som beskriver modellen, kan man "styra" hur kompakt eller utsträckt en molekyl är vid jämvikt under olika betingelser. Metoden är också väl lämpad att parallellisera, vilket också bidrar till effektiviteten hos den resulterande algoritmen.

Efter att på detta sätt ha funnit en metod för att generera och effektivt sampla kompakta konfigurationer för icke-flexibla polymerer för en representativ modell av denna typ av molekyler, inriktades arbetet på att förstå och undersöka under vilka betingelser olika kompakta konfigurationer var termodynamiskt stabila, dvs. representerade en jämviktsstruktur. En kompakt struktur (i motsats till en utsträckt) kan ofta induceras av yttre faktorer såsom olika lösningsmedel eller närvaro av olika joner (för laddade polymerer). I det senare fallet kommer närvaro av högladdade joner (i mitt fall tetravalenta joner) att orsaka en kompaktering av en laddad polymer både för en nettoladdad kedja och för en polyamfolyt där molekylerna innehåller både positiva och negativa laddningar. För en icke-flexibel polymer blir den stabila formen en toroidliknande kompakt struktur.

I avsaknad av specifika intramolekylära växelverkningar, kan en kompaktering till en toroidliknande form även induceras av ett yttre fält kombinerat med en icke-symmetrisk form i fältets riktning på den tillgängliga volymen. Det specifika fall som studerats var en cirkulär polymer i en konliknande inneslutning där den potentiella energin ökade linjärt med avståndet till spetsen på konen. Genom att öka styrkan på det yttre fältet kunde man observera



övergångar från en till två till tre etc loopar och med hjälp av Monte-Carlo-simuleringar kunde man jämföra hur den fria energin (dvs. stabiliteten) varierade för de olika toroid-liknande strukturerna som kedjorna bildade.

7. My Contribution

The question what a PhD student has actually been doing during the studies is, without doubt, of big importance. Hopefully, it should clarify that the work is really yours. To that end, I will try to summarize my contribution to the different papers of which this thesis is a summary. Even though I have done most of the work and wrote the first complete draft of all papers (except paper II), there are always programming details, discussion of ideas, and interpretation of results which you discuss with the others in the project. If for nothing else to confirm your own ideas.

- Paper I: I wrote and tested the program, ran the simulations and wrote the first version of the manuscript.
- Paper II: I contributed with results and discussions.
- Papers III-IV: I was the main responsible for developing the project idea. I also did the programming and testing, and wrote the first version of the manuscript.
- Paper V: I was responsible for the original idea and the programming, and I also wrote the first version of the manuscript.

8. Acknowledgements

It is customary that at the end of the piece all the characters come out from the coulisses to greet the audience and thank the spectators for their time and attention. Following this tradition I would like to thank my supervisor from the Saint-Petersburg State University, Pavel Nikolaevich Vorontsov-Velyaminov, for providing me with the potential opportunity to come to Sweden. He, orbiting in science long enough, has created a number of pupils, and some of them are professors themselves.

To absorb new knowledge in Sweden, I was joined up with Malek Khan and Christer Elvingson as my supervisors at the Physical Chemistry section. I would like to thank Malek, who was my main supervisor at the beginning, for his patience, readiness to listen, and his ability to take chances and allowing me to do what I wanted. With Malek I published my first article with colour pictures, but they are available in colour just on the web though. Before Christer became my main supervisor, I thought that to send the manuscript from the supervisor to the student 4-5 times back and forth to correct my bad english grammar and the style would be rather refreshing. But I was too naive and unexperienced, since Christer's approach is to rewrite the manuscript as many times as it takes to also have the language correct (>5). One can only dream about the huge work capacity he has. A special point I want to acknowledge is Christer's remarkable ability to cool students down: the more excited you become during the discussion the more calmly he talks back to you. Probably, he is just very professional.

During all my study period I was taken care of by the Physical Chemistry administrator Laila. Without her help I would definitely have buried myself under the piles of bureaucratic papers needed to be filled in.

Another lady whom I would like to thank is Linda. My wife has truly an angels patience and exclusive abilities to dampen the side effects of my personality. Thanks also to my family in Saint-Petersburg, who allowed me to make my own choices and to the Physical Chemistry department inhabitants for letting me experience different aspects of swedish academic life.

Uppsala, April 2011
Alexey

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