Coarse-grain modeling of systems with biological and technological relevance

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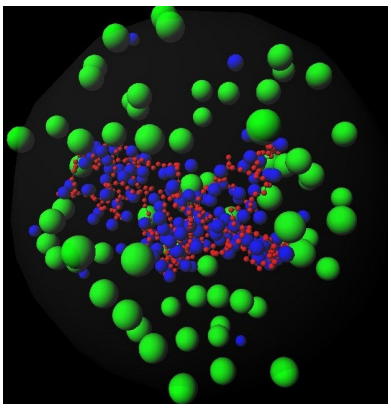
Background

Soft matter physics approach to biological systems have received increasing interest. Chromatin condensation and dynamics in eukaryotic cells, for example, have been studied using a range of approaches including experimental, theoretical and modeling techniques.
Coarse-grain modeling, in particular, has been used, in what would be considered "a priori" very complicated systems, with surprisingly good results. Examples are (i) chromatin condensation and structure, (ii) the effect of nucleoid proteins on the structure and flexibility of DNA and (iii) relative positioning, and concomitant activation, of chromosomes in the nuclei.
Monte Carlo simulations of coarse-grain systems will be used in a number of projects that investigate, using simple models, systems of biological and technological relevance.

Genome condensation on simple bacterial cell models

Bacterial genome is folded in a compact structure called the nucleoid which, and contrarily to the nucleus in eukaryotes, is not enclosed in a lipid membrane but phase separated from the cytoplasm.
Several mechanisms are believed to contribute to the compactness of the DNA (nucleoid), such as molecular crowding and nucleoid-associated protein binding.
In this work we will probe the compaction of DNA, distribution of and competition between the different components confined inside a spherical cell, using Monte Carlo simulations. The components will consist primarily of a polyelectrolyte chain (DNA molecule), crowding agents and dimers (nucleiod-associated proteins).
Previous results have shown no significant condensation of a confined DNA molecule using solely crowding agents, irrespectively of their number of charge. In this work, we will include model nuclei-associated proteins. These will be described as charged dimers, i.e. two particles connected by a harmonic spring. We will start by studying the interaction between such dimers and the DNA molecule. Afterwards, crowding agents will be added to the model to assess the influence of both mechanisms on DNA condensation.



Representative snapshot of a model bacterial nucleoid composed of a 400-monomer long ‘DNA’ (Z_{mon}=-1e, red), 70 neutral crowding ‘proteins’ (green) and small proteins (Z_{prot}=3, blue) that ensure the neutralization of the system.

DNA melting in the presence of oppositely charged lipid aggregates with different morphologies

The melting or denaturation of DNA is important for the biological function of DNA molecules in vivo and for technological applications, such DNA sensors.
The melting temperature is known to vary with, for example, the length and base sequence of the DNA molecules, the ionic strength and pH of the solutions, and the addition of co-solutes. As a general rule, the addition of positively charged co-solutes to the DNA solution leads to an increase of the melting temperature due to the screening of electrostatic interactions between the two DNA strands. However, the single-stranded DNA is much more flexible than the double-helix (persistence lengths of about 2 vs. 50 nm). We speculate that this might have an impact on the preferred interaction of one form of DNA over the other when dealing with positively charged objects with different morphologies.
In this work we will probe the melting temperature of a simple DNA model, where each individual strand is described as a sequence of charged monomers connected by harmonic springs and possessing an attractive potential to form the duplex, in the presence of oppositely charged structures, mimicking the lipid aggregates, with different morphologies.
Experimental work may also be conducted throughout the project, using UV-vis spectrophotometry or fluorescence spectroscopy for DNA melting determinations in the presence of different lipid aggregates.

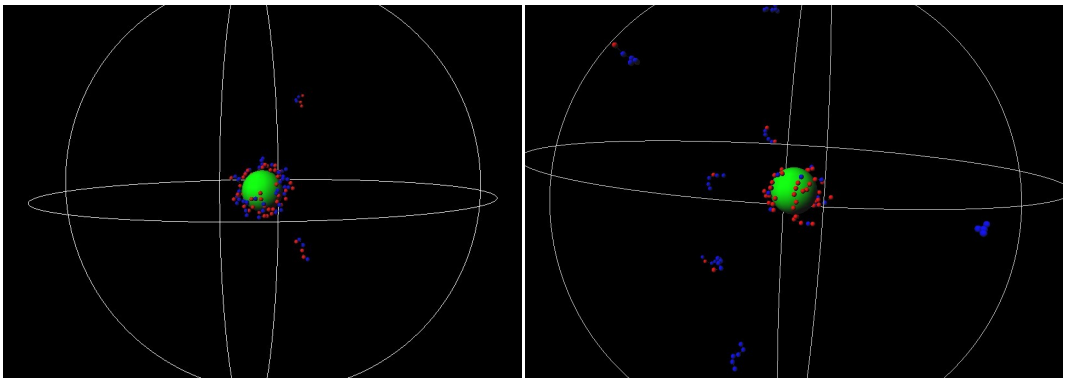
Polyplexes in solution. Effect of charge mobility

The interaction between DNA and oppositely charged polyelectrolytes and consequent formation of polyelectrolytes complexes (polyplexes) attracts much interest, partially due to the fact that polyplexes are considered promising gene delivery vehicles in gene transfection. It is thus not surprising that a vast amount of experimental and theoretical work has been performed in these systems.
In this project we will probe the effect of charge mobility along positively charged chains on DNA condensation and polyplex structure and topology.

Nanoparticle – poly-acid interactions. Effect of pH and charge mobility

Systems comprising of nanoparticles and oppositely charged polyelectrolytes are of great technological interest. The stability of colloidal suspensions is a major priority of companies producing formulations that range from paints, cosmetics, detergents and food. On the other hand, the controlled deposition of such suspensions on surfaces is highly desirable in some of the same applications: paints, conditioners, and other surface enhancing agents.
It has been observed experimentally that, in concentrated polyacid-surfactant systems, an annealed polyion is more efficient in stabilizing the long-range ordered phases than a quenched polyan ion, in which the charges are fixed along the backbone .
This is very interesting both from a scientific and technological view-points. The charge of weak polyacids can be easily tuned using pH variations, and it is unclear how such changes will influence the local polyion-nanoparticle interactions as well as the global phase behavior.
Proton migration along and between the poly-acid chains brings both complexity and numerous possibilities.
Preliminary results have shown that when the charges are allowed to migrate between polyions we obtain highly charged polyions that are strongly bound to the nanoparticles and nearly neutral polymers

that are free in solution.
In this project we will continue this study, probing the effect of pH and charge mobility on the interaction of a charged nanoparticle and oppositely charged polyelectrolytes.



Representative snapshots showing the adsorption of poly-acid chains (red and blue spheres represent charged and neutral monomers, respectively) to an oppositely charged nanoparticle (green). On the system to the left, the charges of the monomers are allowed to move solely within the chain (intramolecular diffusion); on the right-hand side the charges are also able to move between chains (intermolecular diffusion).