Direct simulation of DNA strand–lipid layer interactions

Epitopemeap Project Report – Paulo Pinto

Introduction

The understanding of protein and polymer adsorption phenomena is fundamental for the development of a complete and systematic description of many biological mechanisms. It is today understood that biomaterial surfaces, when in contact with a biological media, are immediately coated by proteins, changing the external characteristics of the material. A complete, qualitative, picture of the processes by which proteins adhere to materials is thus of the utmost importance.

Also in a large number of technological processes, such as pharmacology, adsorption processes onto lipid monolayers and bilayers is of fundamental importance. For example, the adsorption of macromolecules onto surfaces of substrates is an intermediate step in fabrication of drug and gene delivery vehicles.

The group of Prof. Alberto Pais at the University of Coimbra in Portugal has extensively published on the subject of polyelectrolyte complexes in solution (Dias & Pais, 2010) (Dias, Linse, & Pais, 2010). We followed up on this expertise to create a working model of complex molecules and their interactions with a surface when in a medium.

In a recent work (Dias R. , Pais, Linse, Miguel, & Lindman, 2005) exactly such system was modelled and several features studied. DNA molecules were modelled as spring-bead chains: a sequence of negatively charged hard spheres (beads) connected with harmonic bonds with the chain flexibility regulated by angular force terms. The surface is composed of a hard planar wall with embedded positively and negatively charged hard spheres. Furthermore, different mobilities of the charges present in the membrane and its consequences were investigated.

In this project we aimed at introducing a model system where a polymer solution comes in contact with a surface where we have deposited (and fixed) a pattern of charged particles. A negatively charger polyelectrolyte is modeled as interacting cations with a stable distance of 6A. The surface is made up as an hard potential where there is embedded (fixed in the simulation procedure) a square pattern of positive charges separated by 8A intervals. The adsorption criteria is described in Fig. 1.

The simulation is set up by setting the frozen surface in place and then placing the chain randomly in a position close to the wall. The simulation is run until the chain is adsorbed and the radius of gyration and end-to-end distance distributions are smooth. After this a production run is performed as to obtain the final results.

We studied the effect of chain length and of the size of the square pattern patch in quantities such as the abdorbed chain particle number, the chain radius of gyration and others. Simulations were performed using the MOLSIM package (Linse, 2001).
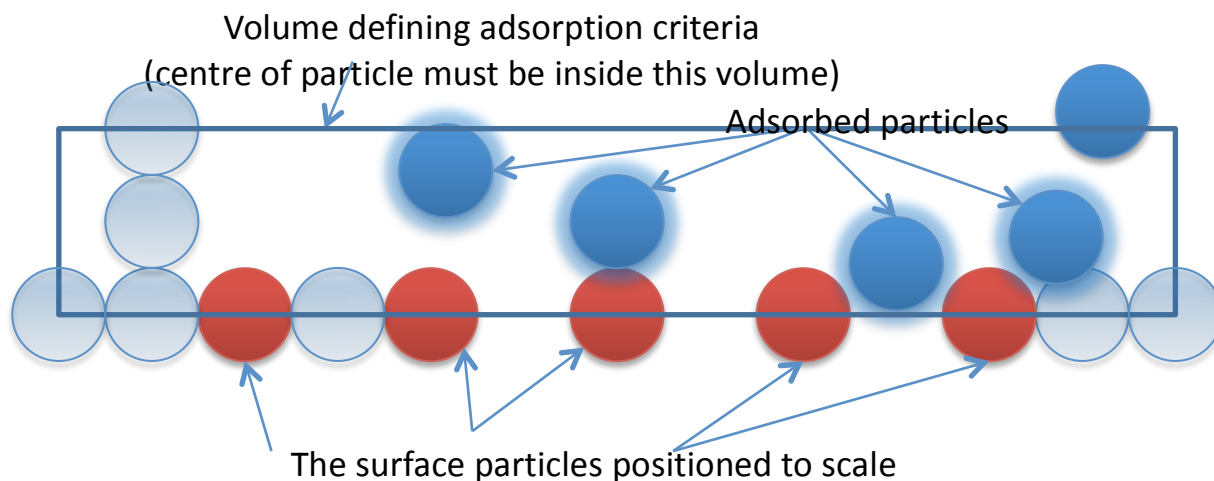
FIGURE 1: Cross section of the sytem under study. The red particles are fixed to the surface while blue particles represent the polycation particles. The polycation paticles within the box are considered adsorbed to the surface. All sizes are to scale, the diameter of the particles is 4A.

Global behaviour

We started by studying the radius of gyration of the polycationic chain. If Fig. 2 we present how this quantity changes with the square root of the patch area and the chain length. First and foremost, we found that the longer chains only "feel" larger surface charges. In fact, there is a reasonable expectation, confirmed in our results, that the reduction of the radius of gyration occurs for a surface patch area less than the square of the chain length ($area^{1/2} < chain\_n$). However, as seen for smaller chains, there is a sweet spot after which the chain no longer collapses so much. This result is particularly promising when considering this system as a possible sensor array for molecules in a solution. The results for longer chains and larger areas are less robust as further thermalization of the system seems to yield results with a larger radius of gyration – we leave this study as future work.

Given the same set of variables as in Fig. 2, we proceeded to study the number of chain particles adsorbed to the surface. These squences of adsorbed particles are commonly refered to as "trains". The results are shown in Fig. 3.

Once again we should make the caveat that for longer chains and larger areas the results are not very robust and we expect a depression on the *train_n / chain_n* ratio. Given this, however, we found that for longer chains, their conformation prevents them from being completely adsorbed to the surface. For all patch sizes, bigger chains are less adsorbed and bigger patches adsorb (almost) completely bigger chains.
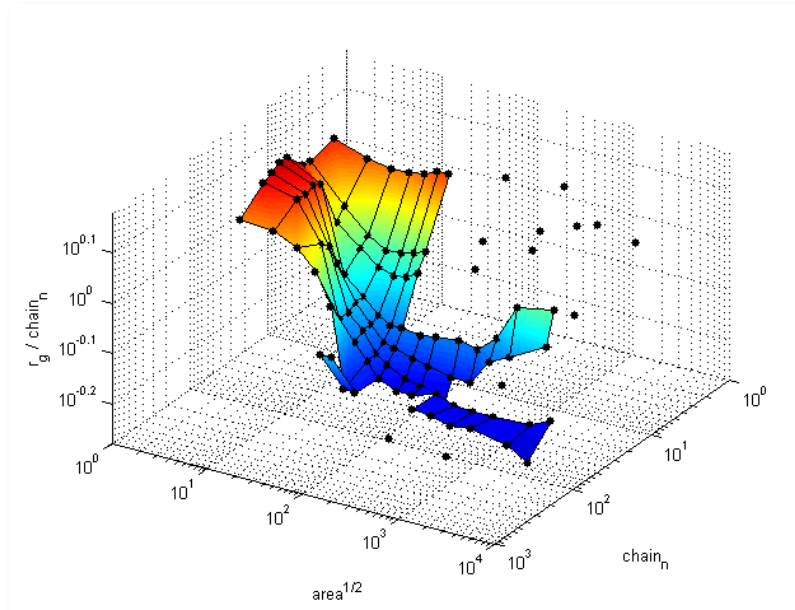
FIGURE 2: Conformation of the adsorbed chain as measured by the radius of gyration. The reduction of the radius of gyration occurs for a surface patch area less than the square of the chain length (*area^1/2 < chain_n*).
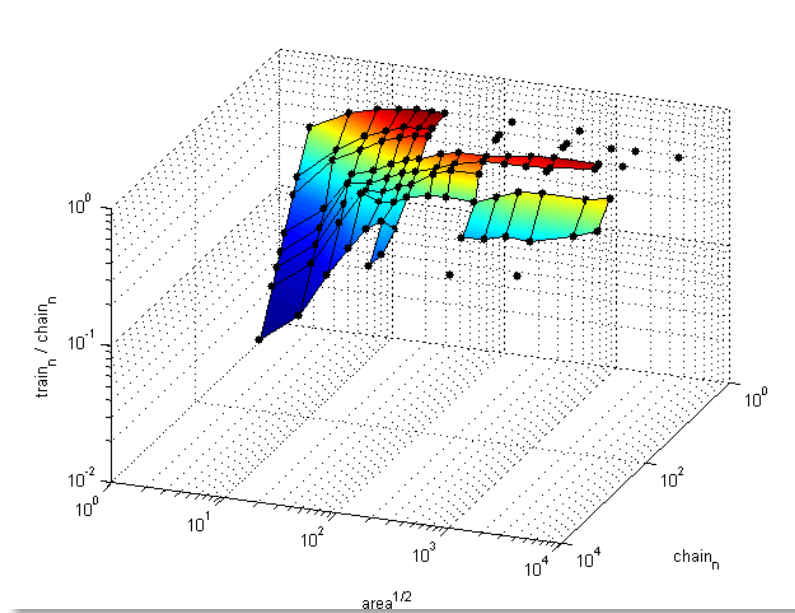

FIGURE 3: The number of absorbed chain particles (*train_n*) divided by the length of the chain length itself, as a function of the chain length and square root of the patch area.

Conclusion and outlook

The plan of action for this visit was to pursue different alternatives for expanding on this topic while serving as training period with an experienced group in a different set of computational skills and packages. This objective has been completely fullfiled and set up the problem for a future fruitful colaboration.

A proper theoretical treatment can provide possible explanations in this problem: "matching in polymeric systems requires both (i) a reduction of the entropically favored loops and (ii) ensuring self-correcting by selecting the proper range of polymer-pattern interactions…". Some of the results obtained are very promissing results in regard to the field of pattern recognition (McNamara, Kong, C. Y., & Muthukumar, M., 2002).

Further studies were performed in this model, however they lay outside the scope of this report. In the future we expect to deepen our understanding of the topic with the objective of publication in relevant journals in the field.

Bibliography

Dias, R., & Pais, A. (2010). Polyelectrolyte Condensation in Bulk, at Surfaces, and Under Confinement. *Adv. Colloid. Interf. Sc. , 158*, 48-62.

Dias, R., Linse, P., & Pais, A. (2010). Characterization of Polyelectrolyte Complexes in Solution. Compaction and Intra-Chain Seggregation.

Dias, R., Pais, A., Linse, P., Miguel, M., & Lindman, B. (2005). Polyion Adsorption onto Catanionic Surfaces. A Monte Carlo Study. *J. Phys. Chem. B , 109*, 11781-11788.

Linse, P. (2001). MOLSIM.

McNamara, J., Kong, C. Y., & Muthukumar, M. (2002). Monte Carlo studies of adsorption of a sequenced polyelectrolyte to patterned surfaces. *The Journal of Chemical Physics , 117*, 5354.