Second Year PhD in Physics Report

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1 Research Summary: Project and Side-Project

1.1 Main Project: Chromatin Compaction; a combined computational and experimental approach

Understanding the mechanistic details underlying DNA compaction is a very important question in Biophysics. In order to fit in the cell nucleus, the DNA winds itself around proteins, the histones, to form nucleosomes, which are the building blocks of chromatin. While the first level of compaction, the nucleosome, has been studied in atomic resolution, the topology of the chromatin fibre remains debated. We propose a mesoscale bottom-up model: starting from the all-atom human nucleosome crystal structure, we move on to a coarse-grained approach where nucleosomes and linker DNA are each represented as three interacting centres. In order to parametrise our model, we combine long-range interaction energies between nucleosome core particles (NCP) and linker DNA at different positions and orientations with short range interactions forces obtained from all-atom Molecular Dynamics (MD) simulations on NCPs, linker DNA, and NCP with linker DNA. Besides measuring the point-by-point electrostatic interaction energy between NCPs, this approach gives us information on the feasible NCP positions in close range. We are also developing an analytical expression for the electrostatic interaction between two nucleosomes, which will provide the large-distance expression for electrostatic interactions. In our mesoscale force-field we consider three main kinds of interaction: mechanical, (de)solvation and electrostatic. This simplified model allows the study of larger conformations of the chromatin fibre, beyond the oligonucleosome level.

We perform accompanying and complementary experiments, focusing on non-invasive methods that do not require aggressive sample preparation that could perturb the topology. For the moment, we have performed experiments using Differential Scanning Calorimetry, Zeta Potential measurements, and plan on performing Small Angle X-ray Scattering and Atomic Force Microscopy experiments. We explore conformational states and changes depending on the variation of parameters such as monovalent ion concentration, NCP number, and temperature. We validate intermediate results comparing them to existing oligonucleosome models in literature and to our own experiments, aimed at providing structural, electrostatic, and thermodynamic information. Overall, we propose a cohesive mesoscale bottom-up model, combining simulations and experiments, thus testing different hypotheses in order to shed light on the determinants of chromatin conformation.

1.2 Side-Project: Theoretical Mueller Matrix Microscopy

In collaboration with Dr. Aymeric Le Gratiet and Prof. Colin J. Sheppard.

We study the Mueller matrix and the Coherency matrix (a linear combination of the Mueller matrix and the Pauli matrices) in the context of light propagation and the application of these matrices in label-free microscopy. We investigate the properties of the Coherency matrix and interpret the physical information on light and physical samples that can be extracted from it. We study different matrix forms in transmission, backscattering, and reflectance configurations, for different kinds of media. We apply the Coherency matrix on zebrafish samples in different stages of development and show that the contrast is improved using the information gathered by the elements and eigenvalues of the Coherency matrix (paper in preparation). Both in a theoretical and in an experimental framework, we compare the Coherency matrix method with the Lu-Chipman decomposition of the Mueller matrix, the most commonly used decomposition in microscopy, and show that the Coherency matrix method is more general and does not require a priori information on the sample.

2 List of Publications and Conference Communications

2.1 Publications

- Artemi Bendandi, Silvia Dante, Alberto Diaspro, and Walter Rocchia
  "Chromatin Compaction Multiscale Modelling: A Complex Synergy between Theory, Simulation and Experiment"
  Submitted
- Aymeric Le Gratiet, Marta d'Amora, Marti Duocastella, Riccardo Marongiu, Artemi Bendandi, Silvia Giordani, Paolo Bianchini, and Alberto Diaspro,
  "Zebrafish structural development in Mueller-matrix scanning microscopy"
  Submitted
- Colin J. R. Sheppard, Artemi Bendandi, Aymeric Le Gratiet, and Alberto Diaspro,
  "Eigenvalues of the coherency matrix for exact backscattering"
  J. Opt. Soc. Am. A 36, 1540-1550 (2019).
  DOI https://doi.org/10.1364/JOSAA.36.001540
- Colin J. R. Sheppard, Artemi Bendandi, Aymeric Le Gratiet, and Alberto Diaspro,
  "Coherency and differential Mueller matrices for polarizing media"
  J. Opt. Soc. Am. A 35, 2058-2069 (2018).
  DOI https://doi.org/10.1364/JOSAA.35.002058

2.2 Conference Communications

- **Oral Presentation** School "BImBS 2019 - BioInformatics meets BioSimulations in protein and DNA studies: from theory to practice".
  5-12/10/2019. Lugano, Switzerland

- **Poster** Italian Celebration Day for the 50 Years of CECAM.
  7/7/2019. Bologna, Italy
  Winner of Poster Competition
- **Invited Poster** Workshop "Computational mathematics for model reduction and predictive modelling in molecular and complex systems".
  21-29/05/2019. Lausanne, Switzerland
- **Oral Presentation** Workshop "Biophysical Society Thematic Meeting: Multiscale Modelling of Chromatin".
  31/03-05/04/2019. Les Houches, France

3 List of Courses Followed

During the second year, I followed two courses, having successfully completed four courses during the first year.

- Metodi di Simulazione, Prof. Paolo Saracco
  Exam Passed on 08/07/2019
- Advanced Computational Physics, Prof. Riccardo Ferrando
  Exam Passed on 08/07/2019