AVVISO DI SEMINARIO

Mercoledì 1 Luglio 2015 ore 11:30

nell'Aula Seminari del Dipartimento di Scienze e Tecnologie Chimiche, il

Dr. Ivan Coluzza

University of Vienna, Faculty of Physics
Computational Physics Group
Ivan.Coluzza@univie.ac.at

terrà un seminario dal titolo:

Design and folding of self-knotting bionic proteins

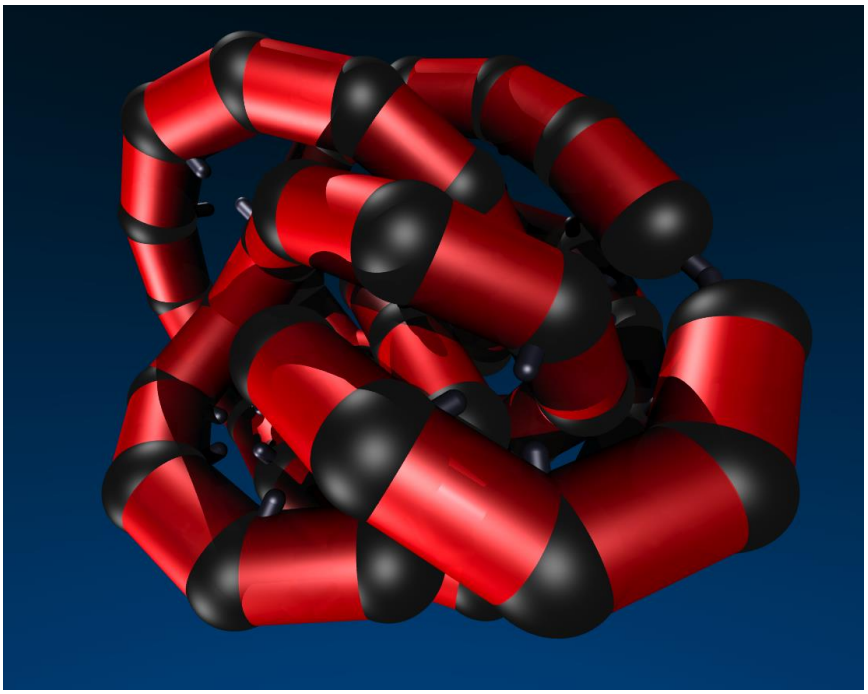
Proponente: ***Dr. Federica Valentini***

Design and folding of self-knotting bionic proteins

Dr. Ivan Coluzza

University of Vienna
Faculty of Physics
Computational Physics Group
Boltzmanngasse 5, 1090 Wien

Tel: +43-(0)1 4277-51176
Fax: +43 (0)1 4277-9511
Ivan.Coluzza@univie.ac.at
comp-phys.univie.ac.at



Self-assembling is the process by which a substance spontaneously reaches a specific long-lived configuration with a well-defined structure. Such structures may be highly inhomogeneous but still strongly differ from random amorphous materials, which are typically dynamically arrested. In fact by having an easily accessible ground state, self-assembling materials have the property of forming structures characterized by few defects, and they often have the capacity to adapt to changes in the environment. In nature proteins are an extraordinary example of self-assembling material. Proteins have two key features: they are all made of sequences of only 20 chemically different blocks, their functions and structures are precisely controlled by the sequence of amino acids. All life that we know of is built upon these elements. In this presentation I will show two breakthrough results that sprouted from the understanding of how the protein features can be transferred to an artificial system that we refer to as Bionic Proteins [1-2]. Bionic proteins are chains of colloidal particles each covered by a chemical layer that gives them different flavors mimicking the amino acids. In addition to the layer each particle is decorated with spots that create a strong preference for specific particle-particle relative orientations. These two elements where enough to allow the design sequences that would self-assemble in a large spectrum of target structures including knotted chains which have important application fro drug design. The Caterpillar protein model [3-4] demonstrated that quantitative protein design could be achieved and potentially used for synthesize novel Anti-cancer drugs (ACD). ACD are identified mainly through large and expensive trial-and-error screenings, with limited help from

computational modeling. In addition, the information provided by pharmacogenomics through wide screening of tumor bio-markers alone is often not sufficient to achieve highly selective ACD, because such markers, or receptors, are also found, though in different concentrations, on healthy cells. Thus, in order to discriminate between tumor and healthy cells, we need a strategy capable of detecting differences in the concentration of such receptors compared to healthy tissue. Such sensitivity to receptor concentration can be achieved using multiple ligands [5-7] that can bind simultaneously to surface receptors and which, analogous to *Velcro*, only bind to target surfaces. Yet, for this strategy to work effectively, we need a control over the binding strength of ligand-receptor interactions that can be achieved by computer protein sequence design. The designed artificial proteins can then be used to decorate nano-particles for target selective targeting, or graphene surface for diagnostic and filtration.

References

[1]. Coluzza, I., & Dellago, C. (2012). The configurational space of colloidal patchy polymers with heterogeneous sequences. *Journal of Physics: Condensed Matter*, *24*(28), 284111. doi:10.1088/0953-8984/24/28/284111

[2]. Coluzza, I., van Oostrum, P., Capone, B., Reimhult, E., & Dellago, C. (2013). Sequence Controlled Self-Knotting Colloidal Patchy Polymers. *Physical Review Letters*, *110*(7), 075501. doi:10.1103/PhysRevLett.110.075501

[3]. Coluzza, I. (2011). A coarse-grained approach to protein design: learning from design to understand folding. *PloS One*, *6*(7), e20853. doi:10.1371/journal.pone.0020853

[4]. Coluzza, I. (2014). Transferable coarse-grained potential for de novo protein folding and design. *PloS One*, *9*(12), e112852. doi:10.1371/journal.pone.0112852

[5]. Dubacheva, G. V., Curk, T., Auzély-Velty, R., Frenkel, D., & Richter, R. P. (2015). Designing multivalent probes for tunable superselective targeting. *Proceedings of the National Academy of Sciences*, 201500622. doi:10.1073/pnas.1500622112

[6]. Dubacheva, G. V, Curk, T., Mognetti, B. M., Auzély-Velty, R., Frenkel, D., & Richter, R. P. (2014). Superselective targeting using multivalent polymers. *Journal of the American Chemical Society*, *136*(5), 1722–5. doi:10.1021/ja411138s

[7]. Martinez-Veracoechea, F. J., & Frenkel, D. (2011). Designing super selectivity in multivalent nano-particle binding. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(27), 10963–8. doi:10.1073/pnas.110535110.

Biography

From 2001 to 2005 I was a Ph.D. student in Prof. Daan Frenkel's group in Amsterdam. Then I moved to Cambridge UK to work with Jean-Pierre Hansen from 2005 to 2008 when I moved to London at National Institute of Medical research for two years. Since 2010 I am working in Vienna as a University Assistant in the group of Prof. Dellago.

During my research experience I developed a deep interest for many different fields, branching from physics to biology, and in problems arising from the interplay of the latter. In particular, as a starting point in my scientific career, I focused on the study of complex biological systems by means of coarse grained models developed in the fields of statistical physics and of theoretical chemistry. Such models are designed to retain crucial system properties that are responsible for the particular phenomena we want to address.