ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

INSTITUTE OF PHYSICS IPHYS

Seminar in Biological and Statistical Physics

Tuesday, January 30th 2018 at 14h00

Room BSP 727, EPFL

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GLOBAL LANDSCAPES OF PROTEIN-RNA RECOGNITION PROVIDE QUANTITATIVE TOOLS TO PREDICT AND ENGINEER SPECIFICITY IN RNA STRUCTURED ELEMENTS

Abstract:

The role of RNA structured elements is fundamental in biology. They help build a network of regulatory interactions that has effects on the most important processes in the cell such as transcription, translation and mRNA decay. A relevant biological phenomenon is the molecular interaction occurring between proteins and these RNA elements. Although such interactions have been extensively studied, the question of how proteins preferentially interact with different sequences but similar structures is still unresolved. Collections of known binding elements are insufficient to characterize the spectrum of potential mutations that contribute to functional RNA molecules. In this work, we developed an integrated framework based on in vitro selection, high-throughput sequencing and global probabilistic modeling to quantify the landscapes of protein-RNA recognition. This approach allowed us to characterize the way that sequence and structural elements confer RNA binding recognition to proteins P22N, 1N and BIV TAT. The parameters of our global model allow us to discern the most important nucleotide sequence interactions that contribute to recognition. By creating a quantitative metric based on such parameter inference, we are able to discriminate between regulated and non-regulated elements in their genomic context as well as the design of functional variants that preserve or enhance specificity. We are able to verify such predictions experimentally and use this framework to quantify pathways that reveal permissive/disruptive evolutionary trajectories. Although we show our results for a finite number of protein-RNA systems, our approach is broadly applicable and easily transferable. Our framework provides a detailed characterization of protein-RNA recognition landscapes with potential applications in unexplored systems.

Host: Prof. De Los Rios
Institute of Physics and Institute of Bioengineering