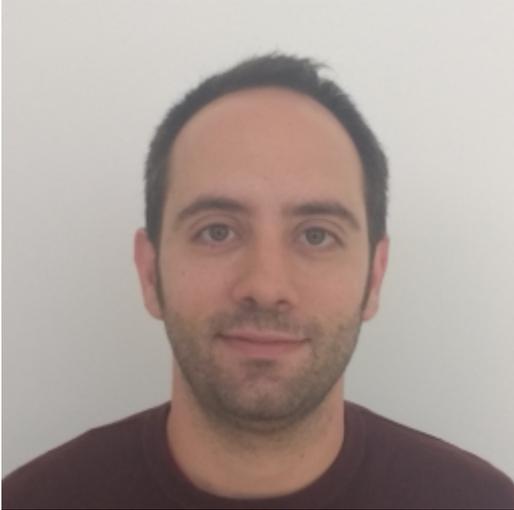


SORS: Coevolution and epistasis in antibiotic-resistant beta-lactamases

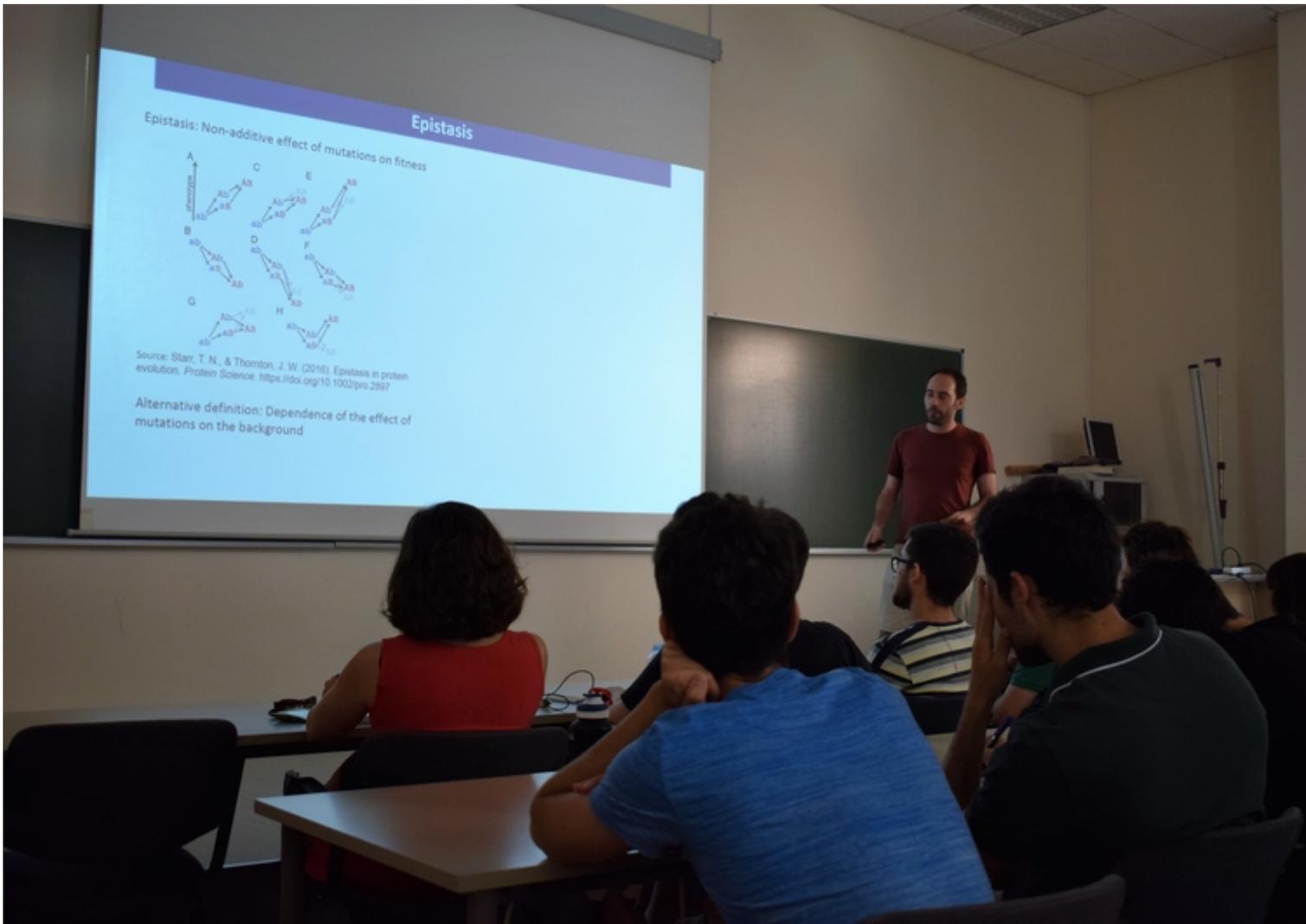
Objectives

Abstract: The effect of mutations depends on the context where they appear due to epistatic interactions. For instance, a mutation can be neutral only if another specific mutation has occurred previously, and detrimental otherwise. Similarly, from a long-term evolutionary perspective, a mutation can be detrimental in a protein but not in a homologous protein due to their differences in amino acids, even if they perform the same cellular function. The appearance of deep mutational scanning techniques in recent times, that allows researches to measure the effect of tens of thousands or even hundreds of thousands of combinations of mutations, have finally permitted systematic studies of epistasis in proteins. At the same time, there have been breakthrough improvements on the computational modeling of coevolution in proteins, i.e. the interdependencies between positions, that arise from epistatic interactions coming from functional and structural constraints that are present in every protein. During this collaboration with the Statistical Genomics and Biological Physics group of the Sorbonne University of Paris, we have combined both computational models and experimental data to unveil the functional and structural constraints are present and shapes the evolutionary paths of beta-lactamases, an important family of antibiotic-resistant proteins. We are able to detect and characterized constraints in beta-lactamases coming from epistatic interactions and their dependency on the context. These results provide insights into the function and evolution and beta-lactamases, and could be useful for the development of new antibiotics and against the emergence of antibiotic resistance.



Short bio: Juan Rodriguez-Rivas is currently finishing his PhD

degree in computational biology at the Computational Biology group at BSC. During his PhD, he has studied coevolution within and between proteins, a field of study at the interface between protein sequences and structures. Previously he worked in software development and deployment in the private sector. His formal training comprises Computer Science (University of Seville), Bioinformatics and Computational Biology (Complutense University of Madrid) and Biophysics (Autonomous University of Madrid).



Speakers

Juan Rodriguez-Rivas is currently finishing his PhD degree in computational biology at the Computational Biology group at BSC.

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