

Designing Robust Biomolecular Control Systems for Perfect Adaptation

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by **Mustafa Khammash**

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- Wednesday
- Building 5 Paraninfo (Envases de Cartón)
- 8:45 – 9:45

Adaptation is a recurring theme in biology, offering vital survival mechanisms in dynamic environments through precise regulation of physiological variables. In this talk, I will present the fundamental theory and concepts needed for designing biomolecular control systems that achieve robust perfect adaptation (RPA). RPA is a biological process through which a specific variable of interest is maintained at a desired setpoint despite persistent perturbations in the underlying network. From a theory perspective, I will elucidate how RPA imposes critical structural constraints on the underlying networks that can be characterized by simple linear algebraic conditions. These conditions in turn impose an integral feedback structure on RPA achieving networks, a fact that yields insight into how RPA mechanisms can be realized with biomolecular reactions. Building on these insights, I will introduce a novel internal model principle (IMP) tailored for biomolecular networks, akin to celebrated IMP in control theory. Finally, I will relate these theoretical developments to practical implementation of RPA-achieving controllers and their applications. I will demonstrate the implementation of genetically engineered synthetic RPA controllers in living cells and showcase their tunability and adaptation properties.

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