Contribution ID : **51** Type : **not specified**

The physics of proofreading mechanisms in cellular signal transduction

Cellular signaling pathways operate as nonequilibrium biochemical networks that transduce directed chemical or mechanical signals across the cell. These cascades, initiated for example by ligand binding to membrane receptors, involve multiple biochemical reactions and complex formations.

Because signaling pathways rely on branched, multiplicative processes, errors can propagate rapidly, threatening fidelity. For instance, incorrect molecular incorporation at any stage can disrupt signal integrity. To counteract this, cells have evolved proofreading mechanisms that ensure remarkable accuracy in processes such as DNA replication and enzymatic reactions.

Since the pioneering work of Hopfield and Ninio in the 1970s, it has been understood that kinetic proofreading (KP) increases fidelity by introducing intermediate chemical steps, powered by nonequilibrium energy sources, at the cost of slower propagation. Later advances showed that catalytic proofreading (CP) can accelerate these error-checking steps, reducing the delay inherent in KP.

An alternative approach involves spatial proofreading, where errors are tested over a finite distance via directed diffusive fluxes, instead of delaying in chemical space, thus achieving high fidelity "at a distance."

This lecture will explore the general physics of proofreading in signal transduction and introduce a thermodynamically consistent model that integrates spatial and chemical proofreading. I will also discuss how these principles apply to real biochemical systems, highlighting potential proofreading mechanisms in G-protein coupled receptor signaling and multi-protein self-assembly.

Role

Professor/PI

Primary author(s) : PIAZZA, Francesco (Università di Firenze); FILLION, Thibault (university of Florence, INFN florence)

Presenter(s) : PIAZZA, Francesco (Università di Firenze)