Modeling of intracellular compartmentalized GPCR signaling

Léo Darrigade*[1]

[1]EPI MUSCA – Institut National de Recherche en Informatique et en Automatique, L'Institut National de Recherche en Informatique et e n Automatique (INRIA), INRAE – France

Résumé

G-protein coupled receptors (GPCRs) constitute a family of cell membrane receptors crucial for intercellular communication. In mammals, they play a pivotal role in regulating fundamental processes, including reproduction and social interactions. Upon activation by hormones at the cell membrane, GPCRs initiate a cascade of intracellular reactions culminating in their internalization. Notably, GPCRs can subsequently transmit signals from intracellular vesicles, with these signals exerting distinct effects on cell physiology compared to signals originating from the membrane (Jean-Alphonse et al. 2014). This study is dedicated to quantitatively analyzing the signals generated by GPCRs within various cellular compartments.

To model the chemical reactions occurring at the membrane and in intracellular vesicles, we construct a measure-valued piecewise deterministic Markov process. The deterministic part encompasses a system of ODEs representing a chemical reactions network (CRN) within each compartment, while the stochastic component accounts for the birth and death of compartments. We study the asymptotic convergence of the process, and we use numerical simulations to glean qualitative insights into the system. We also employ a simpler ODE model to fit longitudinal measures of GPCRs signaling (BRET) under different conditions of perturbation.

References.
(1) Jean-Alphonse, Frédéric et al. (Feb. 2014)."Spatially Restricted G Protein-coupled Receptor Activity via Divergent Endocytic Compartments". In: Journal of Biological Chemistry

Mots-Clés: PDMP, intercelullar communictaion

*Intervenant