Thesis proposal: ***Biophysical modeling of postsynaptic domain dynamics***

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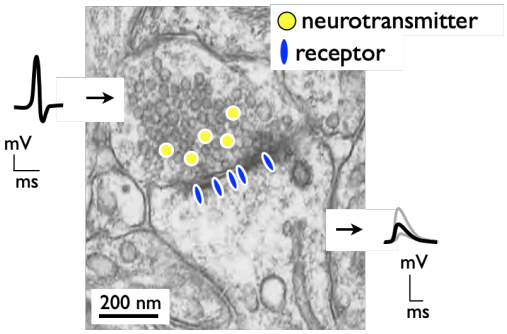
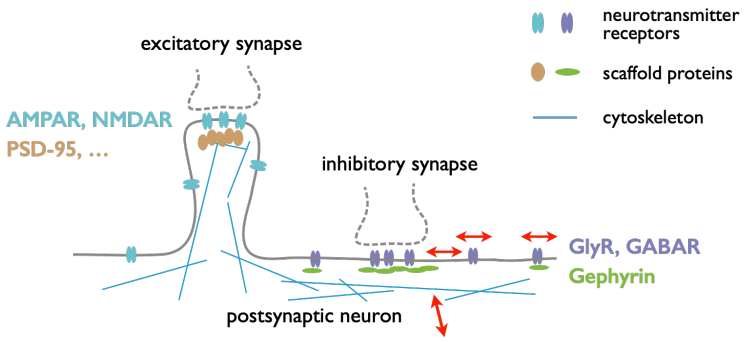
Keywords: postsynaptic domain, aggregation, neurotransmitter receptors, scaffold proteins, synaptic plasticity



10–100 receptors



Synaptic modifications are thought to underlie learning and memory, yet individual synapses often contain only tens or hundreds of copies of neurotransmitter receptors responsible for synaptic transmission. To address how synapses can remain both responsive to meaningful activity-induced plastic changes and resistant to stochastic fluctuations given the relatively low molecule numbers involved, it is important to develop a quantitative understanding of the mechanisms that govern the accumulation of neurotransmitter receptors at synaptic domains. The prospective PhD candidate will **tackle this problem by developing detailed, particle-based computational models** that account for scaffold protein and receptor diffusion and interaction in the postsynaptic membrane, combined with the **mathematical analysis of rate equations** that describe their coupled spatiotemporal dynamics. By addressing the following questions through detailed biophysical modeling, we aim to gain fundamental insights into the organization of postsynaptic domains:

1. **How are synaptic domain sizes regulated in the presence of fluctuations**, and which are the relevant biophysical parameters?
2. **What mechanisms govern the spatial organization of synaptic and extrasynaptic receptor populations**, and what are the implications for interactions between close-by synapses?
3. **What are the biophysical 'handles' that allow plastic modifications of synaptic strength**, and how are they related to known pathways of synaptic plasticity?

The project is part of an ongoing collaboration with the experimental group of Christian Specht at INSERM research unit "Diseases and Hormones of the Nervous System" (Kremlin Bicêtre Hospital, Paris area). The position is fully funded for three years by a French government contract, and will start in October 2024.

For inquiries, please contact Jonas Ranft and/or Vincent Hakim.

To apply, please send a short motivation letter, CV, academic transcript, and two letters of reference to Jonas Ranft and Vincent Hakim.