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Team: Membrane traffic in healthy & diseased brain

<https://ipnp.paris5.inserm.fr/recherche/equipes-et-projets/15-equipe-galli>

Characterization of the synaptic and secretory fusion pore formation on the asymmetric plasma membrane

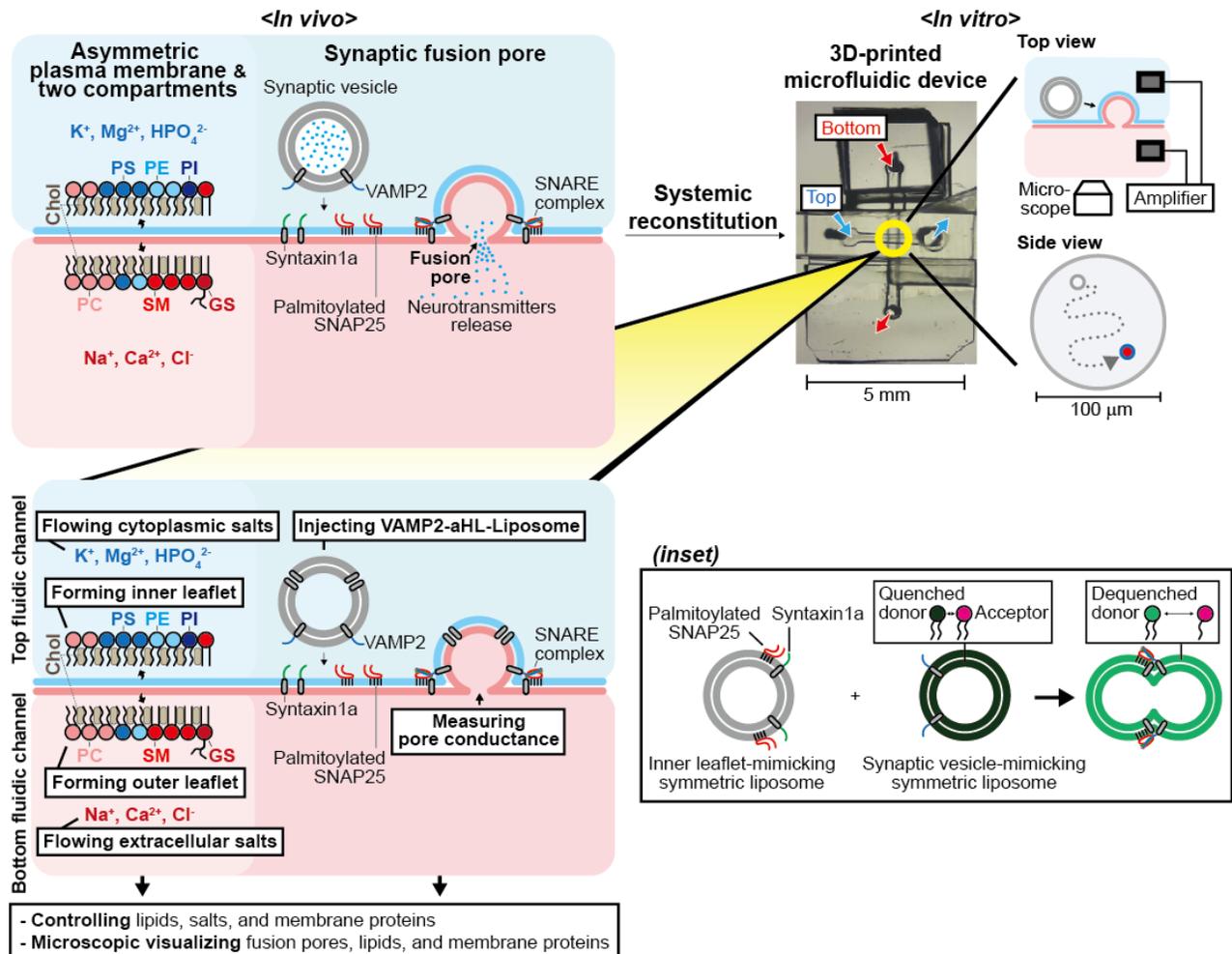
You can find the provisioned long-term topic (total 3 topics) in each paragraph. Please take a look and contact me for discussion.

The cellular plasma membrane is asymmetric, which means, each lipid layer (leaflet) of the bilayer contains different lipid types and distributions. Another asymmetry is across the plasma membrane, which is two aqueous compartments of cytoplasm and extracellular fluid containing different ions, chemicals, and various molecules (e.g., high K⁺ inside/high Na⁺ outside). Those systemic asymmetries are a fundamental and pivotal feature of living cells, however, the fundamental properties have seldom been studied mainly due to difficulty in recapitulation (in recreation) of such asymmetry in vitro. The PI (Paul Heo) developed a **3D-printed microfluidic membrane setup that can reconstruct systemic asymmetries** in the controlled environment. This setup will be used to **address fundamental questions with students**.

How does the asymmetry of the plasma membrane control cellular communication? Using this setup, the PI characterized the dynamics of the nascent synaptic fusion pore that is the passageway to deliver neurotransmitters from the vesicle to the outside of the cell. To mimic physiological neurotransmission in great detail, a student will develop a strategy to conjugate one (SNAP25) of the fusion-mediating components (SNAREs) to the membrane, **called S-palmitoylation** which is seldom studied in the field. Initially, conventional in vitro membranes, such as liposomes and nanodiscs, will be used. Then, the PI's setup will be used to **characterize the dynamics of synaptic fusion pore with controlling asymmetric lipids and salts distribution**.

What about the fusion pore of secretory vesicle on the plasma membrane? Remarkably, vesicle-associated membrane protein 7 (VAMP7) is one of the key players in neurite outgrowth by transporting lipids and various growth factors. However, details of membrane fusion mechanisms are poorly characterized. One of the reasons lies in **the difficulty to purify native full-length VAMP7, which is now solved by PI and can be produced quite an amount in the tube.** A student will characterize the **VAMP7-mediated membrane fusion process and fusion pore formation** using conventional *in vitro* membranes (see above paragraph). Then, the PI's setup will be used to characterize the fusion pore and **to compare how it is different than synaptic fusion pore.**

This interdisciplinary requires your great motivation rather than multidisciplinary backgrounds in biology, biophysics, chemistry, etc. We will build your career together. Welcome you to contact/visit us.



This figure describes the PI's 3D-printed microfluidic membrane setup and an example of application in synaptic fusion pore characterization. Inset figure illustrates one of the conventional *in vitro* membranes that can be used to demonstrate membrane fusion.