Lipid-protein machinery mediates plant cell-to-cell communication at plasmodesmata: a multiscale simulation approach

Cuxart, I., [1*] Marien, J., [2] Sritharan, S., [2,3] Bayer, E.M., [4] Sterpone, F., [2] Taly, A. [2]
[*]Lead presenter
[1] irene.cuxart@ibpc.fr
[2] *Université Paris Cité, Laboratoire de Biochimie Théorique (UMR 8266, CNRS), 13 rue Pierre et Marie Curie, 75005, Paris, France*
[3] *(Present address): Computational Structural Biology Research Team, RIKEN Center for Computational Science, 7-1-26, Minatojima-minami-machi, Chuo-ku, Kobe, Hyogo, 650-0047, Japan*
[4] *Laboratoire de Biogenèse Membranaire (UMR 5200, CNRS), A3 - INRA Bordeaux Aquitaine, 71 Avenue Edouard Bourlaux CS 20032, Villenave d'Ornon, France*

Plasmodesmata (PD) interconnect plant cells and enable direct molecular exchange during essential cellular processes, from growth to environmental stimuli responses [1]. PD are a type of membrane contact sites where the endoplasmic reticulum (ER) forms a tubule tethered to the plasma membrane (PM), leaving a space between them for intercellular flow. PD are dynamic and can open or close within seconds to hours to modulate intercellular communication but, although their structure has been characterized, the mechanisms governing their regulation for molecular exchange remain elusive. PD regulation was long associated exclusively to enzymatic modification of the surrounding cell wall. However, a recently identified regulatory mode involving Multiple-C2-domain-containing-Transmembrane-Proteins (MCTPs) challenges previous understanding. MCTPs tether the ER and PM and have specialised C2 lipid-binding domains to respond to cellular stress-associated cues to drive PD opening and closure, and regulate molecular transport [2, 3]. Yet, the current structural data does not explain the mechanisms governing the MCTP-mediated regulation. Here, *in silico* modeling, molecular dynamics and hydrodynamics simulations help uncover this regulatory mechanism: We propose that MCTPs form a flexible and dynamic diffusion barrier within PD, and that by shaping the architecture, electrostatics and dynamics of the cytoplasmic sleeve, MCTPs play a central role in regulating molecular transport by PD. For addressing this, we combine different simulation scales to model a reconstituted *in silico* PD molecular landscape with MCTPs, and the molecular flow trafficking through PD. We present here structural models of MCTPs at the ER-PM interface obtained with deep-learning based tools for structure prediction and molecular dynamics (MD) [4], and the molecular flow through PD with lattice-Boltzmann MD (LBMD) [5,6]. MD simulations elucidate the dynamic landscape of MCTPs and their collective response, as well as their effect on the surrounding membrane bilayers. We seek to integrate these insights into flow modeling of molecules through PD via LBMD simulations to capture how changes in MCTPs and PD geometry affect molecular flow over time. This multiscale approach addresses mechanistic details of plant intercellular signaling in plasmodesmata as response to stress at an unprecedented timescale and spatial resolution.

Bibliography :

[1] Bayer E.M.; Benitez-Alfonso Y. Annu. Rev. Plant Biol., 2024, 75, 291-317.
[2] Brault M.L.; Petit J.D. et al. EMBO Rep., 2019, 20, EMBR201847182.
[3] Pérez-Sancho J.; Smokvarska M. et al. Cell, 2025, 188, 958-977.
[4] Sritharan S.; Versini R. et al. PLOS ONE, 2025, 20, e0326993.
[5] Sterpone F; Derreumaux P. et al. J. Chem. Theory Comput., 2015, 11, 1843-1853.
[6] Timr S.; Melchionna, P. et al. J. Phys. Chem. B., 2023, 127, 3616-3623.