

On-chip fertilization: Making a controlled microfluidic environment to decipher fertilization mechanisms

Location: École Normale Supérieure (Paris), Departments of Chemistry and Physics
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Context and objective

Fertilization, the union of a sperm and an egg, is the founding event of life. Its success requires the fusion of one—and only one—sperm with an egg, as fusion of multiple sperm leads to pathological polyspermy. Despite decades of research, the mechanisms governing gamete fusion and subsequent block to polyspermy remain poorly understood. This limited understanding largely stems from the specificities of the gametes and the complexity of their mode of interaction. Eggs are enclosed within the fluid-filled perivitelline space (PVS), surrounded by the zona pellucida (ZP), a glycoprotein envelop that sperm has to traverse to interact and fuse with the egg plasma membrane. Advanced real-time imaging approaches of the gamete contact zone before and after fusion—including bright-field, confocal, and super-resolution microscopy such as STED—are essential to resolve the spatiotemporal sequence of transient events underlying sperm–egg fusion and the establishment of the block to polyspermy. However, under physiological in vitro fertilization conditions, the large number and high motility of sperm contacting the zona pellucida render both the identity of the sperm penetrating the PVS and the exact site of interaction with the egg plasma membrane unpredictable, thereby limiting the applicability of high-resolution real-time imaging. The objective of the internship is to overcome this limitation by creating a biomimetic microfluidic environment that faithfully reproduces physiological conditions while allowing real-time imaging.

The internship

The intern will make and test the first prototypes of a new microfluidic device, which uniquely integrate a tightly controlled biomimetic microenvironment with the use of native biological gametes to study fertilization. With this chip, we will control the timing and location at which a sperm reaches the egg plasma membrane while immobilizing the egg to enable spatiotemporal imaging of the interaction site. The egg ZP will be removed and functionally replaced by a microfluidic valve that regulates sperm access and constrains sperm head movement by trapping the flagellum. This chip will open avenue to study the remodeling leading to fusion by imaging relevant fusion protein reorganization on the gamete. At the same time, this chip will permit to immerse sperm for a controlled duration in the PVS of unfertilized or fertilized eggs before being allowed to reach the plasma membrane of a ZP-free egg. It will thus enable investigation of the polyspermy block induced by PVS content.

An interdisciplinary partnership

We are seeking a highly motivated M2 student who wishes to work on this interdisciplinary project, which combines biophysics, biology, and microfluidics. The project will benefit from the rich environment of the Synthetic and Living Soft Matter (SOFT) team in the Department of Chemistry, the Molecular Membrane Mechanisms team in the Department of Physics, both at École Normale Supérieure–PSL University, and the technological platform of the Institut Pierre-Gilles de Gennes. The successful applicant will work closely with researchers from the SOFT team (microfluidics) and the Molecular Membrane Mechanisms team (leading specialists in fertilization mechanisms), located in the same building.

Applicants are invited to send a CV and contact references to the 3 supervisors.