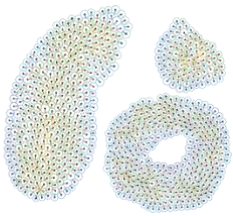
TU Delft

Bionanoscience Department
Think big about life at the smallest scale

Idema group - overview

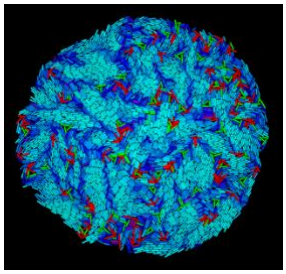
Biology is often highly nonlinear, which is good news for life: many actors together can accomplish what a few cannot, not just for lack of individual strength, but because the whole really is more than the sum of its parts. In our group, we study how collective dynamics of many particles, from protein inclusions in the membrane to growing and dividing cells in colonies, affect the function and behaviour of the living system they are part of.

From single to multicellular behaviour



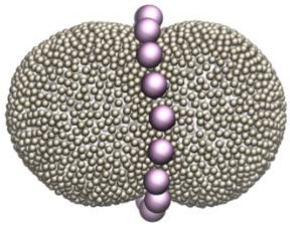
Individual cells and animals behave differently on their own than in a group. Being part of a group is often useful, for protection against outside factors like the weather or predators, or because together cells can achieve more than any single one could alone. We study the collective behaviour of self-propelled soft particles as a model for these systems, looking for a minimal set of rules that allows the cells to create complex patterns.

Development and defects in bacterial colonies and eukaryotic tissues



Many bacteria have rod-like shapes, which extend as they grow, and are halved when they divide. Due to this combination of geometry and growth, a bacterial colony becomes an active material with interesting topological properties, including such features as orientational regions and defects. Similarly, growing and dividing eukaryotic cells form tissues, both healthy and tumour cells. We study the development of both these systems in simulations.

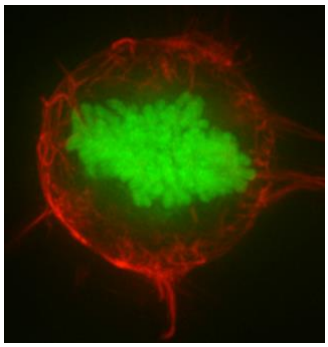
Membrane-mediated interactions



When you put two balls on a mattress, they attract, because they deform the mattress. Two (or more) proteins in a membrane experience similar interactions because of the deformations they impose. Unlike electrostatic interactions, these membrane-mediated interactions are not additive, and can even change sign due to the presence of multiple proteins. Moreover, many membranes in living systems are naturally curved, creating a nontrivial energy landscape that depends on the relative curvature of the membrane and the imposed curvature of the protein. We study the patterns and shapes these membrane/protein compounds form, using both analytical and numerical tools.

Project 1: Exploring the interactions between the actin cortex and the membrane

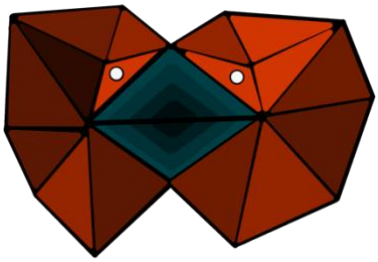
The goal of this project is to further our understanding of the interactions between plasma membranes and cytoskeleton in animal cells. The cytoskeleton is a meshwork of proteins that gives structure to the animal cell. A key part of the cytoskeleton is the actin cortex, that resides below the membrane of the cell and plays a key role in large scale membrane reshaping during cell migration and division; the physics of these reshaping is however not yet fully understood.



Actin (red) and DNA-histones (green) in a HeLa cell [1].

To mimic or study simple properties of cells, giant unilamellar vesicles (GUVs) are often used. Observing how these vesicles respond to external stresses, or simply how they fluctuate when left unperturbed can teach provide us information about their mechanical properties. A combination of a GUV which contains an actin network on its inner leaflet, can be used as a simple model system to study the interactions between plasma membranes and cytoskeleton. Such systems can be made experimentally by our collaborators in the Koenderink lab.

In this project, we will use "flippy" [2], a software package developed in our group for studying membrane simulations, to study how the interaction between actin network and membranes can be modelled in simulations. The goal of the project is to explore a new computational model of such interactions and see if it captures the fluctuation behaviour of the GUV + actin system.

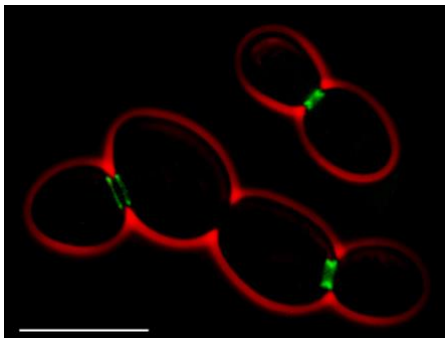


Although the interactions between the actin cortex and the cell membrane are our current focus of interest, we are also interested in other systems with membrane protein interactions. Interested students are welcome to propose and explore new project ideas.

[1] Wikimedia commons, CC-BY-SA 4.0, https://commons.wikimedia.org/wiki/File:Actin-cortex.png

[2] G. Dadunashvili and T. Idema, *Flippy*, gitlab.tudelft.nl/idema-group/flippy

Project 2: Collar-to-double ring transition during cytokinesis of budding yeast



Septins (green) in budding yeast (cell outline in red) [6].

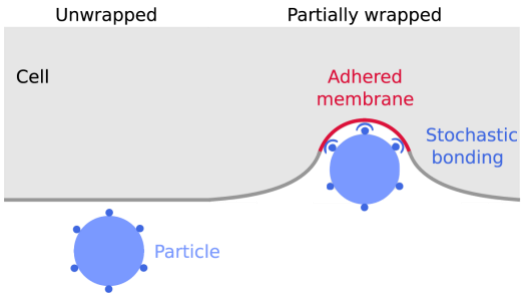
Cell shape control is fundamental when cells move or divide. It is mainly determined by the plasma membrane and the cytoskeleton. Septin filaments, sometimes called the 'fourth component' of the cytoskeleton, are relatively unexplored compared to the better-known actin, intermediate and microtubule fibers.
Septins form non-polar complexes of various sizes (typically hexamers or octamers) in different species. They can also assemble into higher-order structures including filaments, bundles and rings, and interact with the plasma membrane [3]. For example, during cytokinesis of budding yeast, membrane bound septin filaments form layered filament networks, that undergo a dramatic reorganization [4]. First, during the initial formation of the bud, septins filaments run in parallel with the mother-bud axis. Then, as the bud evolves a collar-like structure is formed, where paired filaments run in parallel with the mother-bud axis and single filaments run perpendicular to the mother-bud axis. Finally, when cytokinesis starts, the collar-like structure disappears and a double ring of filaments appears, where filaments only run perpendicular to the mother-bud axis. Although we know that filaments rearrange on the membrane, it is still unclear how the collar-to-double ring transition occurs.

In this project, we want to investigate different scenarios that might explain how the collar-to-double ring transition occurs. We will therefore develop a theoretical framework that takes the configuration energy of septin filaments and the plasma membrane into account [5]. Based on the developed energetic model we will identify the most likely mechanism that can explain the collar-to-double ring transition.

[3] S. Mostowy and P. Cossart, Septins: the fourth component of the cytoskeleton, Nat. Rev. Mol. Cell Biol. 13, 183-194 (2012).
[4] K. Ong, C. Wloka, S. Okada, T. Svitkina, and E. Bi, Architecture and dynamic remodelling of the septin cytoskeleton during the cell cycle, Nat. Commun. 5, 5698 (2014).
[5] A. Beber et al., Membrane reshaping by micrometric curvature sensitive septin filaments, Nat. Commun. 10, 420 (2019).
[6] Philippsen Lab, Biozentrum Basel, on Wikimedia commons, public domain, https://commons.wikimedia.org/wiki/File:S_cerevisiae_septins.jpg

Project 3: Virus particle motion on 2D membranes

The first step of a viral infection is the virus entry into the host cell. Prior to the actual uptake process the virus particle binds to receptors of the host cell's plasma membrane,
which then can lead to complete particle uptake into the cell. Since the receptors diffuse within the plasma membrane and the virus particles can also unbind from receptor, the virus particle shows distinct modes of motion, as experimentally observed [7,8].



Virus particle adhesion and uptake [9].

In this project, we will develop a stochastic lattice-based model that considers receptor diffusion, receptor binding kinetics and particle uptake. We will simulate trajectories characterizing how the virus particle moves along the plasma membrane. Our goal is to determine under which conditions the virus particle will move along the plasma membrane and under which conditions particle uptake is more favorable.

[7] P. Kukura, H. Ewers, C. Müller, A. Renn, A. Helenius, and V. Sandoghdar, High-speed nanoscopic tracking of the position and orientation of a single virus, Nat. Methods 6, 923 (2009).
[8] C. J. Burckhardt and U. F. Greber, Virus movements on the plasma membrane support infection and transmission between cells, PLoS Pathog. 5, e1000621 (2009).
[9] F. Frey, F Ziebert, and U. S. Schwarz, Dynamics of particle uptake at cell membranes, Phys. Rev. E 100, 052403 (2019).

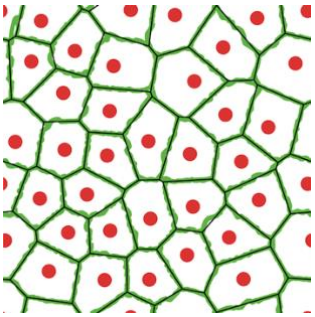
Project 4: Statistics of filament growth

Septin filaments can be considered the 'fourth component' of the cytoskeleton (see project 2). Currently it is under debate whether septins are isodesmic or cooperative polymers. While isodesmic polymers can fragment and show an exponential filament length distribution, cooperative polyermers typically do not fragment and show a peaked filament length distribution [10].

In this project we want to theoretically investigate filament growth processes. We aim to predict how the filament length distribution depends on kinetic growth parameters and the possible growth modes. Therefore, we will develop a filament growth model that is based on the Smoluchowski coagulation-fragmentation equation [11]. We will study the deduced model and the resulting filament length distributions in different limiting cases.

[10] B. L. Woods, I. Seim, J. Liu, G. McLaughlin, K. S. Cannon, and A. S. Gladfelter, Biophysical properties governing septin assembly, bioRxiv (Cell Biology, 2021).
[11] J. A. Wattis, An introduction to mathematical models of coagulation-fragmentation processes: a discrete deterministic mean-field approach, Physica D 222, 1 (2006).

Project 5: Mechanics of tissue development



During development, tissues undergo large conformational changes. The most striking one is gastrulation, where a spherical or ellipsoidal shaped embryo inverts to become a toroidal shape, creating the intestinal tract. As part of such changes, tissues sometimes behave as a solid, and sometimes as a fluid. The characteristic difference between solids and fluids here is their response to shear: solids will elastically deform, while fluids will flow. In this project, we'll study the mechanics of a developing tissue, built from cells that we describe with a 'sticks and balls' model (where the 'balls' are the nucleus and part of the cortex/plasma membrane, while the 'sticks' are fairly stiff springs that connect the balls to each other, giving the cell rigidity while also allowing it to grow). We already know that this model can correctly predict the geometric pattern of the cells in an actual tissue [12]. Here, we will first actively deform it by shearing, to see whether the resulting tissue is fluid or solid, and which parameters determine that. Second, we will punch a hole in the tissue, and see how it responds, both on short (mechanical response) timescales and on longer ones (where dividing cells can fill up the hole). As always, we will aim to predict the outcome of similar tests in experiments.

Possible extensions of this project are the inclusion of multiple cell types, and studying the onset of the buckling (the first step of gastrulation) for the tissue when put on a cylinder.

[12] R. van Drongelen, T. Vazquez-Faci, T. A. P. M. Huijben, M. van der Zee, and T. Idema
Mechanics of epithelial tissue formation, J. Theor. Biol. **454**, 182-189 (2018).

A few notes on working in the Idema group

As a BEP or MEP student in any group, you'll get your own specific project which is usually a part of a larger research line going on in the group. Your direct supervisor can either be a "junior scientist" (a PhD student or postdoc) or the group's PI, depending on the project. Since we're a theory group, our methods differ somewhat from those of the experimental groups: rather than going into the lab, most of the projects we have involve building and running simulations, sometimes complemented with analytical work. We'll give you some training in how to do this, but you probably already know the basic idea (there are things like "for loops" and "if statements"). The results of the simulations you analyse and interpret just like you would experimental data. Also, you're supposed to put your results into context, which means that you (with some help) have to look for and read the relevant literature and discuss your results compared to those of others. For our specific case, when possible comparisons to experiments are especially valuable. At the end of your project, you write a thesis and give a presentation. On both of these, we'll give you feedback on the initial version, which you can incorporate in the final version that will go to the thesis committee and your friends and parents. In the evaluation, we look at the presentation and thesis, but also at the quality of the work, your level of independence, creativity, communication, and understanding of your topic.

Nobody in science works alone – even though everyone has their own project, it is very useful to discuss them with others. In fact, you can only claim you understand something if you can explain it, and by explaining, you often realize new things (or that you didn't understand something). To that end, I encourage people to talk to the other students in the group (and perhaps find a shared work space), and we have a weekly group meeting to which I expect everybody to attend if possible. During group meeting, everybody gives a brief update on their project, especially focussing on the things you are working on or struggling with right then; it happens frequently that someone else in the room has encountered the same problem and can help you out - or you can help out someone else. In the department, we have forum meetings every Monday, in which PhD students and postdocs present their work; there are also regular seminars by visiting scientists from other universities and research institutes around the world. Attending (some) of these gives you a first-hand view of how people work (and struggle) in science.

In addition to these planned meetings, you can have one-on-one meetings with me to discuss your project in detail when needed (this varies widely). We're there to help, so please don't hesitate to ask for it when necessary. Most importantly though, pick a project that appeals to you, and make sure you have a good time working on it!