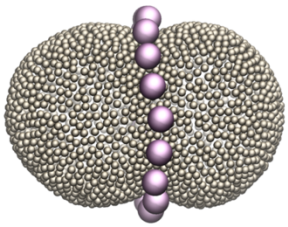
TU Delft

Bionanoscience Department
Think big about life at the smallest scale

Idema group - overview

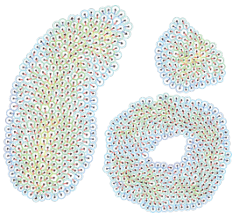
Biology is often highly nonlinear, which is good news for life: nonlinear effects may amplify small signals into global changes, and allow many actors to accomplish together what a few cannot, not just for lack of individual strength, but because the whole really is more than the sum of its parts. In our group, we study these phenomena, along two research lines: (1) the shape and interactions of the cellular membrane with proteins, the cytoskeleton, and other cells, with a particular focus on cell division, and (2) the collective dynamics of many cells, ranging from simple self-propelling spheres to tissues made of cells with internal structure and dynamics.

Membrane-mediated interactions



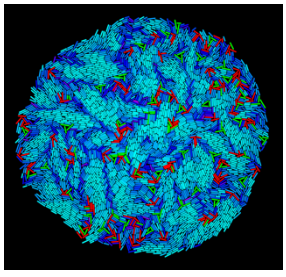
When you put two balls on a mattress, they attract, because they deform the mattress. Two (or more) proteins in a membrane experience similar interactions because of the deformations they impose. Unlike electrostatic interactions, these membrane-mediated interactions are not additive, and can even change 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.

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.

Project 1: Particle-based membrane model

Lipid bilayer membranes can be simulated at the individual lipid level, but this high resolution comes at the price of restricted length and timescales. Alternatively, we can coarse-grain the system, using a single bead to describe multiple lipids. With such a model we can go up to cellular scales, and simulate processes like membrane self-organization and cell deformation. Unfortunately, existing models are highly unstable, making it difficult to draw conclusions. In this project we will implement an alternative model with particle-particle interactions drawn from the theory of liquid crystals, which closely follow the actual deformation modes of the lipid bilayer membrane. We will investigate if this approach yields more stable membranes, and if we can use it to simulate large-scale cellular deformations.

See also

- Yuan et al., Phys. Rev. E 82, 011905 (2010)
- Noguchi, J. Chem. Phys. 134, 055101 (2011)

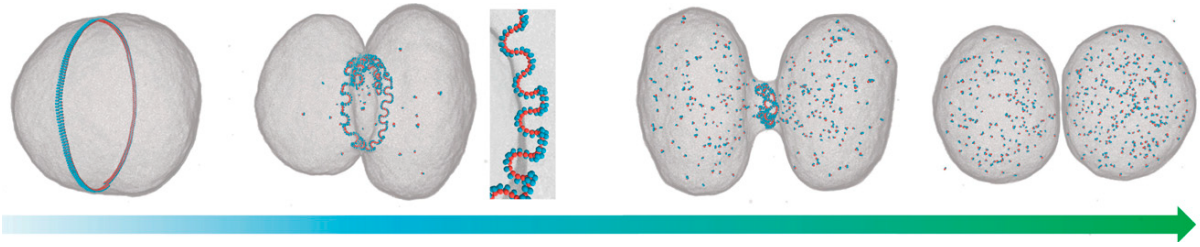


Figure 1 Steps in cell constriction and division, starting from a pre-assembled constriction ring, in the model of Yuan et al. Source: Harker-Krischneck et al., Proc. Natl. Acad. Sci. USA 119, e2107763119 (2022), CC-BY 4.0.

Project 2: Endocytosis in theory and simulation

Endocytosis, the uptake of particles from the environment, is a key process in cellular function. Surprisingly however, a dynamic description of the process, even in the simplest setup where the particle sticks to the cellular membrane, is lacking. In this project, we will combine analytical, numerical and simulation techniques to study this phenomenon, with the aim of arriving at a full dynamic description of the membrane shape and evolution as it wraps around the particle.

See also: Spanke et al., Phys. Rev. Research 4, 023080 (2022).

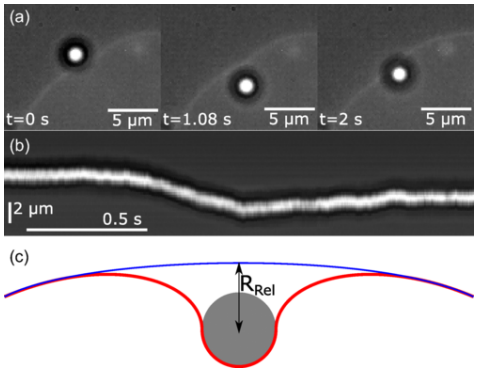


Figure 2 Experimental observation of particle wrapping. From Spanke et al., Phys. Rev. Research 4, 023080 (2022), CC-BY 4.0.

Project 3: Simulating protein-membrane interactions

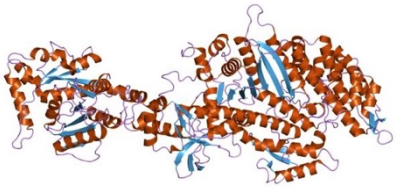


Figure 3: Structure of a fusion of a dynamin I and a myosin II motor. Source: European Bioinformatics Institute, public domain.

Proteins binding to lipid bilayer membranes can change the structure of the membrane by the very act of binding. Inversely, the binding can also affect the shape of the protein. The simple act of binding can therefore have far-reaching consequences, and is likely involved in many cellular processes. To be able to reproduce such processes in artificial cells, we need a better understanding of what happens at the molecular level. In this project, we will use a combination of AlphaFold predictions of protein structures and membrane-protein simulations to see how protein binding can lead to membrane fission, a key step in the reproductive cycle of a cell.

See also: De Franceschi et al., Nat. Nanotech. 19, 70 (2024).

Project 4: Bacterial colony growth and shape

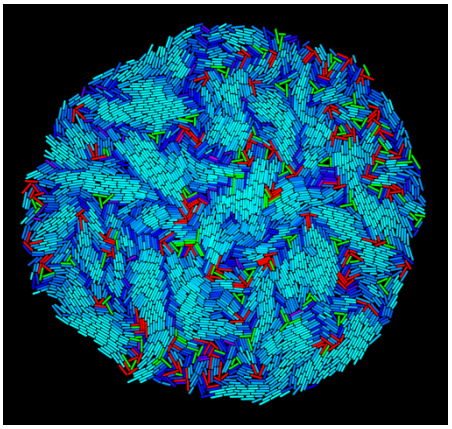


Figure 4 Colony of rod-shaped bacteria, with defects indicated by coloring neighboring bacteria red or green. The shade of blue indicates the local order. Source: R. Los et al., arXiv/2003.10509.

Bacterial colonies grow through repeated growth-and-division cycles. Rod-shaped bacteria do so by elongating along their long axis, defining a clear local orientation. However, after a couple of division rounds, the global orientation is lost, and orientational defects appear. In this project, we'll study how the properties of the colony, like the defect density, correlation length, and colony shape, are affected by the bacterial properties, such as their growth protocol ('adder' and 'sizer' models) and their interactions, to figure out which of these we can induce directly from experimental observations of growing colonies.

See also: R. Los et al., Defect dynamics in growing bacterial colonies, arXiv/2003.10509

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. 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 workspace), and we have a weekly group meeting (jointly with the other theory groups in BN) to which I expect everybody to attend if possible. During group meeting, people take turns giving an 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 someone else out. 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!