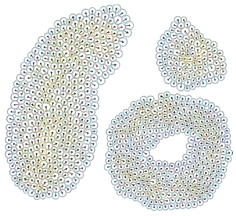
Idema group - overview

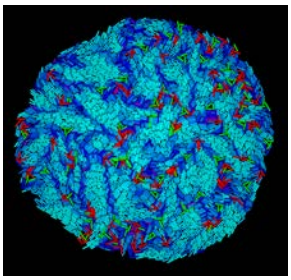
Biology is often highly nonlinear, which is good news for life: many actors together can accomplish what a few cannot, not just for lack of individual strength, but because the whole really is more than the sum of its parts. In our group, we study how collective dynamics of many particles, from protein 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



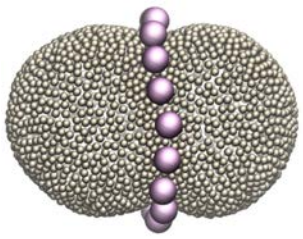
Individual cells and animals behave differently on their own than in a group. Being part of a group is often useful, for protection against outside factors like the weather or predators, or because together cells can achieve more than any single one could alone. We study the collective behaviour of self-propelled 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: 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 have to 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. 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.

Project 2: A model for cellular motility

Individual cells can move around on a substrate by extending a `foot' (known as a lamellipodium) propelled by the active polymerization of a polymer network at the leading end, and disassembling that same network at the trailing end. When two crawling cells meet, they interact and will change their direction of motion. When many such cells come together, they can get stuck ('jammed'), just like grains of sand or rice. In this project, we'll investigate the interactions between relatively large numbers of these crawling cells.

Project 3: Combining mechanics and biochemistry in biofilm development

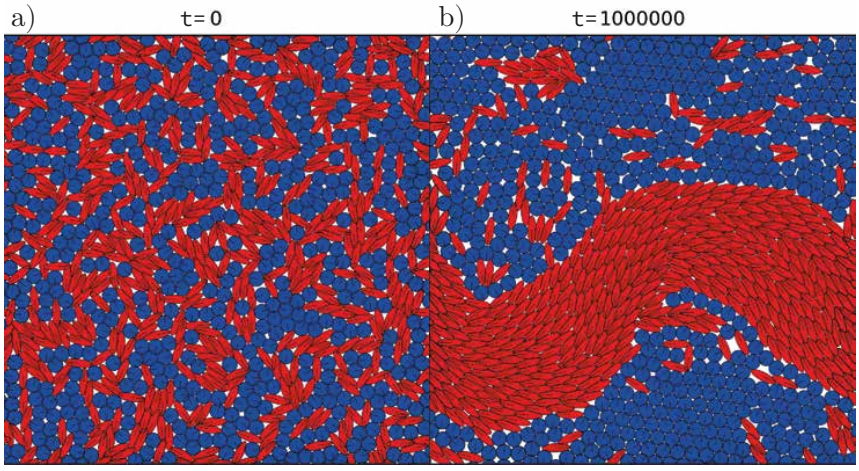
Biofilms are collections of bacteria that grow on surfaces, ranging from your desk and phone to the lining of your gut. Most of them are beneficial, and, for example, help us digest our food. A biofilm consists of both the bacteria themselves and extracellular material that they excrete, which often forms an elastic network that they live in. Most models of biofilm development focus either on the mechanical interactions between the bacteria or the biochemical ones. In this project we will combine them in a single description. We will model the mechanical interactions through repulsion between touching bacteria and the formation of attracting links (resembling the extracellular material and adhesive proteins) between neighbouring ones. We will add biochemical signalling, in which the bacteria produce chemical signalling molecules that diffuse through the medium, and respond to the measured local concentrations by adjusting their growth rate. Finally, we may include an external biochemical nutrient field, that

can affect the growth of the bacteria as well. We will investigate how the biochemical interactions change the properties of the developing biofilm, both on the colony scale and on the local scale, measuring quantities like bacterial alignment and the density of topological defects.

Project 4: Bacterial warfare

Bacteria don't just interact with other bacteria from the same species, they respond to other species as well. These inter-species interactions can be constructive (common examples include symbiotic relationships where they each produce compounds that the other needs) or hostile: some bacteria will go to war. In this project we will study such a bacterial battle, by bringing two colonies of different species together. The bacteria in these colonies can be motile, but their motility will be coupled to the measured concentrations and concentration gradients of biochemicals produced both by same-species and other-species individuals. Moreover, the bacteria interact mechanically, which for this project we will only include in the form of repulsions when they touch. We will investigate under which conditions a 'defending' bacterial colony can prevent an 'invading' colony from growing, which has known applications in biofilm formation but possibly also in tumour development in eukaryotic tissues.

Project 5: The role of interface friction on domain stability in active multicomponent systems



Simulation snapshots at different time points. Figure (a) shows the initial configuration at t=0. One can see that the system was initialized randomly. (b) A state with two domains at a later time point. Once can see that the species are clearly segregated in two domains. However, the domain wall seems to be buckling, which might indicate an instability in the system.

One class of active systems that we study in our group consist of self-propelling subunits or particles. Especially rich and interesting behaviour is observed when one mixes several types of such particles together. The difference in properties can be continuous like size, repulsion strength, or shape. It can also be discrete, like having different types of inter-species interactions. For example, members of same species can align with each other but not with the members of the other species during motion. One widely observed phenomenon in such systems is demixing, i.e. the separation of different species into their own subdomains.

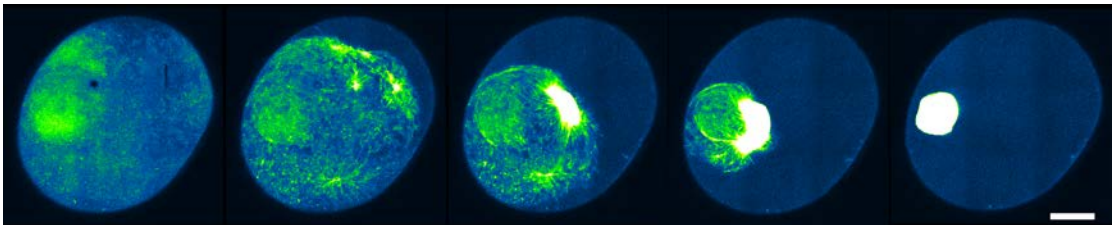
Spontaneous demixing in biological systems has an important role, since this demixing is what causes emergence of spatial order and patterns. Hence the stability of demixed domains is also of interest for us.
In the model that the snapshots are taken from the particles can self-propel and they tend to align their direction of motion with their neighbours. Unless these neighbours are from a different species, then the particles do not influence each other's alignment. This can lead to a mismatch of flow directions at the interface and thus cause friction between the two moving domains. Measuring and quantifying this interface friction and determining its impact on domain stability is the goal of this research project.

Project 6: Simulating multi-component membranes

Lipid bilayer membranes have the special property that they behave like a liquid in-plane (i.e., the particles can move around freely) but like a solid for out-of-plane deformations (i.e., bending them requires work). Thanks to this special nature, membranes in living cells come in many shapes and sizes, from simple spheres to highly connected tubular networks. The membranes in these cells do not consist of a single lipid type, but instead of many lipid species. Some lipid species do not mix well, and will tend to phase-separate, producing patterned membranes. Only for the simplest cases can the shape of such membranes be solved for analytically. In this project, we will use numerical tools to study membrane phase-separation and the resulting membrane shapes. First, we will try to reproduce the known analytical solutions. Second, we will go beyond what is known analytically, and see if we can reproduce some experimentally observed shapes. Third, we will also go beyond the experiments, and predict what other shapes might be possible.

Project 7: How molecular motors work together to remodel the cytoskeleton

MEP; joint project with the Koenderink lab



Eukaryotic cells can undergo dramatic shape changes: they move, squeeze through tight spaces, and even divide themselves. They can do this because they have a highly dynamic actin cytoskeleton, a network of protein filaments which is constantly remodelled by the motor protein myosin. We can capture the characteristic contractile behaviour of the actin cytoskeleton in vitro with just three components: actin, myosin, and a crosslinking protein. It has been shown that the amount of crosslinkers in the network determines the dynamics and length scale of contraction in such a system, but we find experimentally that even small changes in the physiochemical environment can also alter the network behaviour dramatically. We think that this sensitivity comes from an often-overlooked parameter: The self-assembly of individual motor proteins into functional motor filaments, which depends strongly on the environmental conditions. In this project you will set up simulations using Cytosim (Nedelec, 2007 New J. Phys. 9 427) to study how microscopic changes in motor assembly translate into macroscopic changes in network contractility. You will also reconstitute comparable networks in vitro, and systematically study their behavior using fluorescence microscopy.

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!