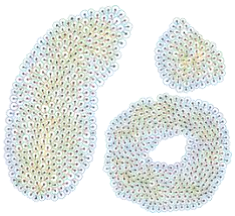
Idema group - overview

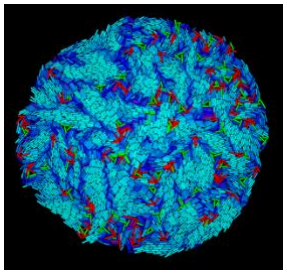
Biology is often highly nonlinear, which is good news for life: many actors together can accomplish what a few cannot, not just for lack of individual strength, but because the whole really is more than the sum of its parts. In our group, we study how collective dynamics of many particles, from protein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



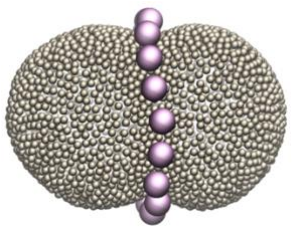
Individual cells and animals behave differently on their own than in a group. Being part of a group is often useful, for protection against outside factors like the weather or predators, or because together cells can achieve more than any single one could alone. We study the collective behaviour of self-propelled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



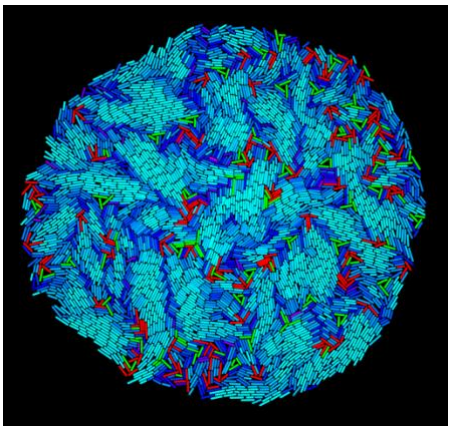
Many bacteria have rod-like shapes, which extend as they grow, and are halved when they divide. Due to this combination of geometry and growth, a bacterial colony becomes an active material with interesting topological properties, including such features as orientational regions and defects. Similarly, 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: Bacterial colony growth and shape



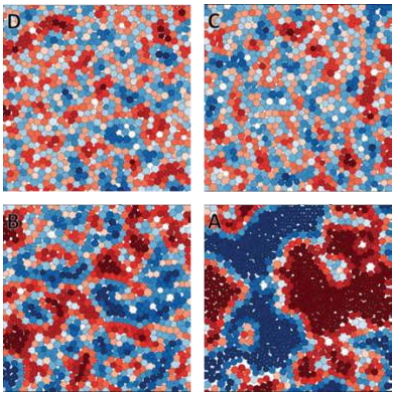
Bacterial colonies grow through repeated growth-and-division cycles. Rod-shaped bacteria do so by elongating along their long axis, defining a clear local orientation. However, after a couple of division rounds, the global orientation is lost, and orientational defects appear. In this project, we'll 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

Project 2: Oscillation-induced phase separation in bacterial colonies

Some species of swimming bacteria can oscillate: they repeatedly flip the direction in which they are moving by 180°. While this behaviour may appear counterproductive for colony spreading, earlier work has shown that it can actually help a colony boundary move faster, by better aligning the bacteria inside. In this project, we'll study what happens when we mix two species of oscillating bacteria together. We expect that under the right conditions, these bacteria can phase-separate, much like the motility-induced phase separation observed in self-propelling systems.

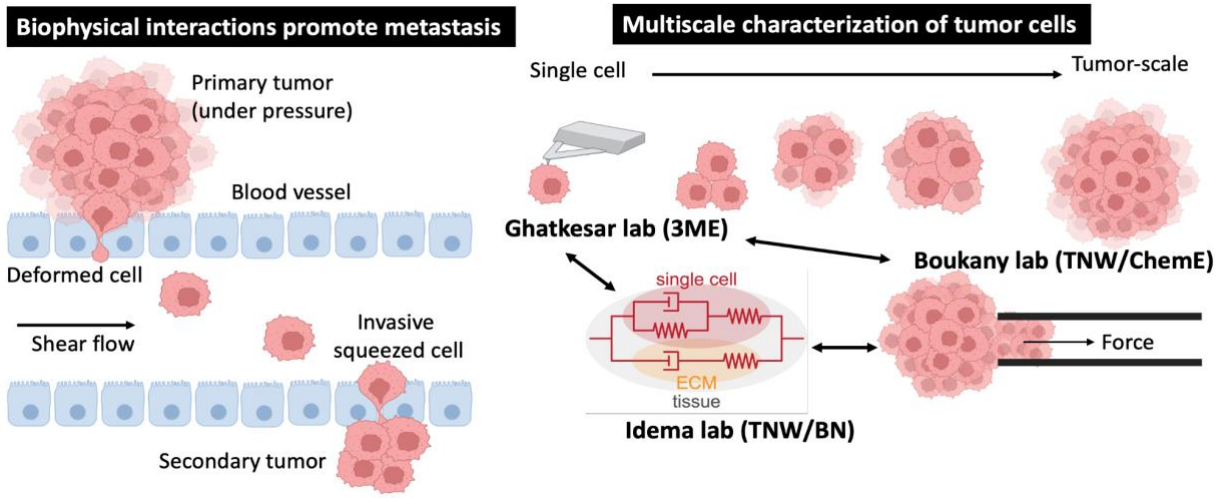
Project 3: Differential alignment



Biological 'particles' (ranging in scale from bacteria to whales) often travel collectively, exhibiting stunning patterns as they do so. Many groups have investigated the properties of collective dynamics of such active particles. Little is known however about what happens in complex (meaning multi-component) active systems. Earlier work in our group suggests that differential alignment and differential repulsion may strongly promote segregation of active particles. In this project we'll study this process in more detail, aiming to predict whether there is a phase transition between mixed and separated states of active matter.

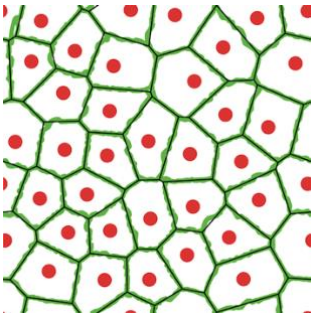
Project 4: Multiscale characterization of tumor cells

Cancer cell invasion into surrounding tissues is a critical step at the early stages of cancer metastasis (responsible for over 90% of cancer-related deaths). Biomechanical processes including cancer cell adhesion, migration, deformation, stiffness, and detachment play key roles in the metastatic process. To understand and ultimately prevent metastasis, we need to understand how tumor cells interact physically with their environment, both as individual cells and collectively. We hypothesize that migrating tumor cells modify the local (ECM and endothelial cells) stiffness both at the primary tumor (to initiate metastasis) and at the new location to be able to invade surrounding tissue and grow to a secondary tumor. To test this idea, we will work with the experimental Boukany (TNW/ChemE) and Ghatkesar (3ME) labs to study tumors both at the single-cell and tissue level, and use multiscale modeling of the tissue to bridge the gap between them.



(Left) Migrating tumor cells initiating the metastatic process via physical interaction with the tumor microenvironment. (Right) We will quantify the biophysical characteristics (size, shape, elastic modulus, and adhesion strength), from single-cells (Ghatkesar Lab) to tumor spheroids (Boukany Lab) and make a theoretical model (Idema Lab) to predict the evolution of physical interactions under various conditions and understand the tumorigenesis. "Created with BioRender.com."

Project 5: Mechanics of tissue development



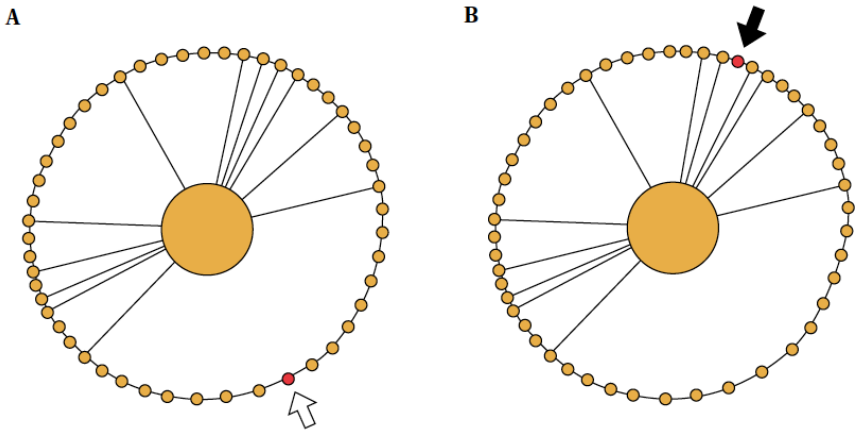
During development, tissues undergo large conformational changes. The most striking one is gastrulation, where a spherical or ellipsoidal shaped embryo inverts to become a toroidal shape, creating the intestinal tract. As part of such changes, tissues sometimes behave as a solid, and sometimes as a fluid. 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, and that non-adhering cells flow like soap bubbles when we shear them. In this project, we will study the effect of cell division on tissue. 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.

See also: 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).

Project 6: Interactions between crawling cells

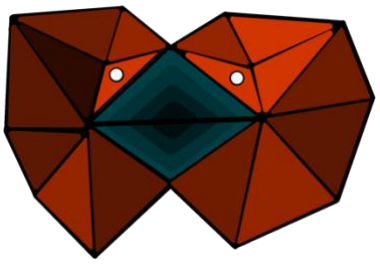
The 'sticks and balls' model of project 6 allows us to create not only growing but also crawling cells. In this project, we will study the interaction between such crawling cells, and see if and how excluded volume and transient adhesion interactions cause the cells to exhibit nontrivial collective dynamics. While we will initially do our simulations in an empty environment, the next step will be to include patterns, resembling extracellular material and ultimately other tissue that the cells are moving through.



Project 7: Three-particle interactions on membranes

Particles embedded in lipid bilayer membranes interact via the deformations they impose. Consequently, embedded particles can attract or repel, depending both on their shape and on the properties of the membrane, including its topology (spheres behaving differently than planar membranes). In this project, we'll study the interactions between three particles on both spherical and planar membranes, and ask whether triangular or linear configurations are more stable.

In this project, we will use "flippy", a software package developed in our group for setting up membrane simulations. We'll combine numerical work with a more analytical approach, expanding the shape of the membranes in Fourier (flat) and spherical harmonic (sphere) modes, and possibly a new hybrid approach where we do simulations based on the Fourier mode expansions.



See also: G. Dadunashvili and T. Idema, flippy: User friendly and open source framework for lipid membrane simulations, arXiv/2301.12305.

Project 8: Interactions between rods and membranes

Next to spherical particles, we can also study the interactions between membrane and rod-shaped particles, both cylinders and spherocylinders. It turns out that when they adhere to the membrane, cylinders can stay both in an upright ('rocket') and flat ('submarine') position on a tense membrane. A floppy membrane will simply wrap the rod. Using a similar combination of numerical and harmonics-based techniques as in project 8, we will determine when we can expect which configuration, and what the various steps in a docking / transition / wrapping process are. For this project we'll collaborate with the experimental Rao group at UTwente.

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!