This is life: some thoughts on self-organized structure formation in active liquids and biological systems

Hoffmann, L.A.

Summary

Walking around outside and looking at different biological systems, three things are easily appreciated: First, biological systems are unfathomably complicated. A detailed understanding of how a tree grows or a deer runs seems impossible. Second, there is a huge diversity, and different biological systems look extremely different. The appearance and movement of bird and a fish share, at first glance, not many similarities. Third, biological organisms vary greatly in length (and time) scale. An elephant is much bigger than a mouse. It then seems almost inconceivable to find general laws which govern the evolution and dynamics of biological systems in general. Nevertheless, despite the enormous diversity, there are some similarities, which gives rise to some hope. For example, different organisms are all made up of cells. More fundamentally, all organisms are subject to, and constrained by, the laws of physics. A human has to spend a lot more energy to fly than a butterfly. Furthermore, while an elephant is much larger than a mouse, when comparing them with the length scales of atoms or the universe, they are almost the same size.

Indeed, in recent years it has emerged that these and other similarities are sufficient to enable one to identify a few general laws and rules that are valid for a large range of biological systems, and that it is possible to ignore many microscopic details. This is in the spirit of a school of physics that aims to identify a minimum number of laws that describe as many different phenomena as possible. The goal in this case then is to find a small set of equations that can be used to describe and explain the dynamics of different biological systems: How do bacteria navigate their environment, how do cells move, how do embryos develop, how do fish swim, how do birds fly, ...?

To put this into context, we can take a step back and look at many-body physics in general. Inherently, one deals with systems where many microscopic constituents are interacting with each other. Through their interaction on the microscopic level, collective dynamics on the macroscopic level may arise. One way of dealing with these large degrees of freedom at the microscopic level is to use computer simulations to explicitly model each microscopic particle and its interactions with other particles. However, analytically this is almost always impossible due to the large degrees of freedom. One would have to solve too many equations simultaneously. Luckily, if we are interested in the dynamics on the macroscopic level, it is often possible to ignore many aspects on the microscopic level. By averaging (coarse-graining) over many particles it is possible to find effective equations of motion that describe the system on the macroscopic level. During the undergraduate physics lectures one often first encounters this strategy when learning about statistical physics and

thermodynamics. In the present thesis, where we are interested in how particles move in space, the effective macroscopic equations of motion we use are hydrodynamic equations like the infamous (Navier-)Stokes equation. This equation is used to describe the dynamics of liquids, e.g., how water flows in a river or how air flows around a driving car. However, we are not dealing with the ordinary Stokes equation. We are interested in "living" systems in the sense that each of the microscopic particles is not just passively reacting to external forces, but is instead exerting forces on its environment. Thus, the systems we are considering are not "just" evolving towards their equilibrium state, but the microscopic particles are constantly converting energy into forces or motion. Such systems are called active. The classical hydrodynamic equations are then expanded to include these additional out-of-equilibrium forces, but the general idea is still the same. A few (think two or three) equations can be used to describe the dynamics of the system on the macroscopic level.

In the field of active liquids there are two equations that stand out, the Toner-Tu equations, and the equations of active nematodynamics. These are a set of two and three equations, respectively. See the Introduction for more details. Importantly, the central equation in either case is a modified Navier-Stokes equation which, compared with the classical Navier-Stokes equation, contains additional terms to account for the active forces . The difference between the two equations is, essentially, that the Toner-Tu equations are used for systems in which the particles are not embedded in another liquid in a "relevant way", whereas the active nematodynamic equations are used if this is the case. Here, "relevant" means that the liquid is mediating interactions, i.e., the dynamics of the liquid is important, and a particle can interact with another particle far away through the presence of the liquid. Thus, for example, a flock of birds is described with the Toner-Tu equations because, while the birds are flying (embedded) in air, the birds are not interacting with each other through perturbing the air. A flying bird perturbs the air around it with its wings, but another bird at a distance will not notice this. On the other hand, cells are embedded in a liquid and when they move they displace this liquid, which other cells further away will notice. Again, see the Introduction for a more precise discussion of this. Thus, one chooses one equation or the other depending on the properties of the system one wants to study. These equations have very rich dynamics. Much research involves studying the same equations (potentially with small modifications like an additional term) in different conditions (different geometry, different boundary conditions, different parameter range, ...), and investigating the resulting dynamics. Once the equations have been solved and analyzed for a given scenario, there is then one last step one needs to take in order to make the connection between the abstract equations and the biological system that we ultimately want to describe. This is potentially the most difficult and controversial step. Namely, identifying certain parameters and quantities in the equations with biological quantities that can be observed experimentally. Ideally, through this process, solving the (relatively simple) hydrodynamic equations yields insights into the dynamics of many different biological systems, as well as experimentally verifiable predictions that can be tested.

We start in **Chapter 2** by going back to the basics. It is well-known that the Toner-Tu equations can be used to describe the collective motion of, e.g., birds or fish. They can be used to show that an initially disordered system of motile particles can organize into a macroscopically ordered state with all particles moving in the same direction. However, how exactly does the system go from a disordered state to an ordered state, what are the dynamics of the intermediate state, and is it possible to identify exactly what drives the transition to order? Chapter 2 is concerned with these questions and we answer them by combining an analytical and numerical analysis of the Toner-Tu equations with an experimental colloidal system. This experimental system is well described by the Toner-Tu equations and can be used as a tractable model system. We find that certain structures, so-called topological defects (see the Introduction) drive the transition to order.

We then turn towards investigating the dynamics of cells and tissues using the active nematodynamic equations. The basic idea is that each cell is imagined to be a force dipole exerting forces on its environment. Combining many cells, like in a tissue, this results in a collective behavior that one is interested in describing. In **Chapter 3** we modify the traditionally used active nematodynamic equations by adding a term to account for chirality. What if the cells are not left-right symmetric but actually are chiral, i.e., the forces they exert on their environment are not mirror symmetric. We investigate how including this effect modifies some well-known phenomena of classic active nematodynamics, namely the motion of half-integer defects and the spontaneous flow transition.

Indeed, there is increasing evidence that some kinds of cells are chiral (that is, only cells of a given chirality are found in nature), and that this chirality is crucial, e.g., during the development of drosophila embryos for them to achieve the correct final shape. Assuming that cells are chiral, these processes could be explained by developing models similar to the one derived in Chapter 3. However, a different problem is the question of how chirality in cells developed in the first place. That is, what is the mechanism that evolutionarily favored one chirality over the other. Is it pure chance or does one chirality have advantages over the other? **Chapter 4** contains a simple model that we developed to explain how chirality might have evolved in certain cells or bacteria. The idea is that from an initial state where both left- and right-chiral particles were present, over time one of the two died out. Thus, after some time the entire system only contains particles of one chirality.

After this brief detour, we return to investigating the dynamics of cells and tissues. The remaining chapters are concerned with understanding morphogenesis, that is the process of shape formation during the growth of tissues and organisms. For example, how does an initially spherical human embryo grow legs and arms? Rather than understanding the details for a single organism, we are interested in uncovering general laws and principles that might be a starting point for answering this question. Again, we use active nematodynamics as the equations to model tissue dynamics. However, whereas in previous chapters we solved equations in flat, two-dimensional space, we now investigate these equations on top of a two-dimensional elastic surface. This surface is allowed to deform such that the active forces could, in principle, deform the surface and create shapes on their own. This

can be used as a first simple model to explain some morphogenetic processes. In **Chapter 5** we develop the model for an active liquid crystal coupled to an elastic surface. We then investigate how an initially flat disk can become unstable due to the presence of active forces. If these forces are sufficiently strong, they can deform the disk to create a protrusion. We analyze this instability both analytically and with simulations, and connect it to some recent experimental observations. Continuing this research, we consider a surface that is initially spherical, not flat. This is closer to the spherical embryos often observed in nature. The results of this study are presented in **Chapter 6**. We find a number of different dynamical regimes, depending on the symmetry of the microscopic particles considered, and the sign and magnitude of the active force. In some cases we again find the formation of protrusions, whereas in other cases we find the opposite, namely the flattening of the sphere. Finally, in **Chapter 7** we present a detailed derivation of the equations used in the previous two chapters. Due to the length of the derivation we present it as a separate chapter, and not merely as an appendix of one of the previous chapters. Furthermore, we present some preliminary results extending and generalizing the results of Chapter 5. Thus, in Chapters 5–7 we develop both an analytical and a computational model which can be used as a starting point to understand some aspects of shape development in organisms and which illuminate some aspects of morphogenesis.