Consider this scenario: in your haste to grab the latest issue of *Physics World*, you scrape your hand on your postbox. It’s nothing severe, just a little scratch, but if your immune system is functioning as it should, your body will perform an amazing feat of microscopic organization. Your body assesses the level of damage and threat from infection, sending security cells to the site to hoover up intrusive bacteria and seal the wound. Within a few days you’d hardly know the scrape was ever there: your skin and blood vessels repair themselves.

Except of course there’s no mind behind this repair. Your brain isn’t required to heal a wound: there’s no local oversight from any intelligent agent, and the cells involved don’t think. Instead, cells interact with their neighbours, and a larger pattern emerges from those small-scale interactions. That’s the key to “self-organization”, whether it occurs in the human immune system, swarms of locusts, water molecules in a snowflake or electrons in a magnetic material.

For that reason, researchers studying biological self-organization draw heavily on physics. Some directly investigate the physical interactions between cells and their environments; others use theoretical models drawn or adapted from physics to understand emergent behaviours in biological systems. It’s an interdisciplinary field, involving physicists, computer scientists, biologists, mathematicians and medical doctors.

“Physics defines how things can interact,” says Herbert Levine, a professor of bioengineering at Rice University in Texas, US. “Biology defines what interactions were chosen by evolution to actually give rise to some functional capability.” Understanding cellular self-organization is key to grasping how healthy bodies function, including immune system response, the menstrual cycle, the growth of cells in the brain and more. It’s also essential for studying cancer, autoimmune diseases and other illnesses associated with healthy functions breaking down.

While biological self-organization research is appealing for pure curiosity alone, its importance to medical applications also gives it a sense of urgency lacking in most physics studies. Scottish mathematician Alexander Anderson, for example, focuses on how cancers evolve and progress, and how they respond to treatment. Tackling these questions requires a range of expertise and so the department Anderson runs at the Moffitt Cancer Center in Florida, US, includes computer scientists, physicists and mathematicians. “We’re focused on trying to use mathematical computational models and physical laws to define and understand how cancers evolve and progress, and how they respond to treatment,” he explains.

Amina Qutub, a bioengineering professor at Rice University, focuses less on the mechanical side and more on graph theory and machine learning to understand how cells self-organize. In physics, graph theory is used to describe possible networks of atoms in solids, among other things, without immediate reference to the forces involved. Similarly, machine learning enables computers to learn and make predictions without modelling all the detailed interactions between proteins. “What we’re trying to figure out is what are the seminal properties of what makes a cell cancerous versus healthy,” says Qutub.

**Levels of organization**

Both physics and mathematical models in biology involve different degrees of abstraction. Water molecules don’t co-ordinate intelligently to make snowflakes; they simply form beautiful patterns via ordinary intermolecular forces, temperature and pressure. Cells are more complicated than water molecules, but they aren’t much smarter – the difference lies in the ways they interact with each other and their environment.

Whether trying to understand magnetism or cancer, researchers can focus on individual interactions on the level of cells or electrons, or they can look at the larger-scale behaviours that emerge from those interactions. The goal in all these cases is to find a mathematical model that – in as simple as possible a way – reproduces the behaviour you want to study, and excludes unnecessary details. In analogy,
think of the difference between studying the bond between two atoms and the thermodynamics of a gas. The second arises from the first, but you don’t need to know every detail about inter-atomic forces to describe the relationship between temperature, density and pressure.

Some researchers, including Levine, try to identify the physical interactions governing cells and molecules. This is akin to “first principles” calculations in condensed-matter physics, which attempt to derive the properties of materials using the equations of quantum mechanics. Another approach called “agent-based systems”, used by Anderson, is more like statistical mechanics in that it treats cells like particles in an ensemble. “These little agents have a rule-set that drives their behaviour, and then collectively you see these emergent phenomena,” he says. A sufficiently abstract or general model can be applied to extremely different systems. For instance, a statistical mechanics theory originally proposed to describe ferromagnetism, known as the Potts model, is now used to describe a wide range of phase transitions in physics, chemistry and biology – including the transition from random configurations to structured growth in cells.

On the highest level of abstraction, there’s little attempt to model the biological system using the equations of physics. Instead, researchers use machine learning and higher mathematics, including graph theory. While it’s the branch of mathematics that calculates your connection to Kevin Bacon, graph theory also describes networks of self-organized cells.

Cell signalling
On the scale of cells, the forces most relevant to their movement are of the electromagnetic variety. Where ions are involved, electrostatic forces are the most important, whereas for electrically neutral objects it is van der Waals forces. These intermolecular forces are so strong that unless cells in motion exert themselves, they tend to come to a standstill.

That environment also affects communication. On macroscopic scales, sound and light waves reliably travel in straight lines. The best analogy for cells, on the other hand, is smell. A cell ejects a wave of molecules, which bounce around randomly; the net result is diffusion into the surrounding medium. “If you want to find a good restaurant by walking around the streets and sniffing, that is sort of the equivalent of what many of these microbes do,” says Levine. “The signal is propagating as some spreading cloud of molecules being emitted by the kitchen, and then you have to home in on where that is.”

Even the wave nature of signals is different on the macroscopic scale. While light and sound are (mostly) linear waves, passing through each other and interfering by simple wave addition and subtraction, molecular diffusion waves combine nonlinearly. Instead of crossing each other and travelling long distances, the waves stop each other and create a boundary where they meet, which results in less cross-talk and redundant information. What remains is a small number of molecules, and the direction from which they came can be more easily identified. “The physics of the problem comes about by understanding how this collective secretion of all these chemicals creates patterns,” says Levine. “The cells do this collectively: each one just responds to its local measurements and its local machinery, but the net effect is to create a chemical roadmap.”

Inside a human (or other animal) body, these roadmaps can be very complicated. For that reason, Levine and other biophysicists look at the relatively
If you consider cancer as a complex evolving system, it really matters which scale you’re looking at when you choose what sorts of equations or model approaches you might try.

Cancers do have common features. “If there’s a fundamental theory of cancer or at least of cancer biology, what would that be?” asks Anderson. “In some sense it really boils down to evolution.” He adds that if you consider cancer as a complex evolving system, it really matters which scale you’re looking at when you choose what sorts of equations or model approaches you might try.

Those scales include cell-level – how individual cancer cells interact with each other and surrounding healthy tissues – and population-level. On the population level, for instance, how cancer cells react to treatment can be modelled using systems that look at how many cells die or otherwise respond to the treatment. “You might be looking at boundaries that are deforming and changing as the tumour invades,” says Anderson. “There’s obviously physics you can write down for that.”

From computers to chemotherapy

Whether driven by curiosity or a desire to save lives, understanding the physics of cellular self-organization is both an old and a growing field. Computer processors and algorithms are now so sophisticated that many of the earlier simplifications are redundant: new models can get much closer to descriptions of real biological systems.

That’s absolutely essential, when doing experiments on living organisms isn’t possible. “What controls the fate of a single cell and multiple cells in a community?” Qutub asks. “These are questions that computational modelling can help address, where experiments can’t.”

For Anderson, the big picture in the physics of biology is saving lives and improving medical treatments. His belief is that this can be achieved only via an interdisciplinary approach, and he feels so strongly about this that he even moved his group from his maths department on the east coast of Scotland to a cancer centre in the heart of Florida. “I really believe,” says Anderson, “that multidisciplinary team design is the future of cancer research, and the future of how we should be treating cancer patients.”