

# Stem cell physical

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Stem cells show auxeticity; the nucleus expands, rather than thins, when it's stretched. Credit: Effigos AG

Looking at stem cells through physicists' eyes is challenging some of our basic assumptions about the body's master cells.

One of the many mysteries surrounding [stem cells](#) is how the constantly regenerating cells in adults, such as those in skin, are able to achieve the delicate balance between self-renewal and differentiation – in other words, both maintaining their numbers and producing cells that are more specialised to replace those that are used up or damaged.

"What all of us want to understand is how stem cells decide to make and

maintain a body plan," said Dr Kevin Chalut, a Cambridge physicist who moved his lab to the University's Wellcome Trust-MRC Cambridge Stem Cell Institute two years ago. "How do they decide whether they're going to differentiate or stay a stem cell in order to replenish tissue? We have discovered a lot about stem cells, but at this point nobody can tell you exactly how they maintain that balance."

To unravel this mystery, both Chalut and another physicist, Professor Ben Simons, are bringing a fresh perspective to the biologists' work. Looking at problems through the lens of a physicist helps them untangle many of the complex datasets associated with [stem cell research](#). It also, they say, makes them unafraid to ask questions that some biologists might consider 'heretical', such as whether a few simple rules describe stem cells. "As physicists, we're very used to the idea that complex systems have emergent behaviour that may be described by simple rules," explained Simons.

What they have discovered is challenging some of the basic assumptions we have about stem cells.

One of those assumptions is that once a stem cell has been 'fated' for differentiation, there's no going back. "In fact, it appears that stem cells are much more adaptable than previously thought," said Simons.

By using fluorescent markers and live imaging to track a stem cell's progression, Simons' group has found that they can move backwards and forwards between states biased towards renewal and differentiation, depending on their physical position in their host environment, known as the stem cell niche.

For example, some have argued that mammals, from elephants to mice, require just a few hundred [blood stem cells](#) to maintain sufficient levels of blood in the body. "Which sounds crazy," said Simons. "But if the self-

renewal potential of cells may vary reversibly, the number of cells that retain stem cell potential may be much higher. Just because a certain cell may have a low chance of self-renewal today doesn't mean that it will still be low tomorrow or next week!"

Chalut's group is also looking at the way in which stem cells interact with their environment, specifically at the role that their physical and mechanical properties might play in how they make their fate decisions. It's a little-studied area, but one that could play a key role in understanding how stem cells work.

"If you go to the grocery store to buy an avocado, you're not going to perform lots of chemistry on it in order to decide which is the best one: you're going to pick it up and squeeze it," said Chalut. "In essence, this is what we're trying to do with stem cells."

Chalut's team is looking at the exact point where pluripotency – the ability to generate any other cell type in the body – arises in the embryo, and determining what role physical or mechanical signals play in generating this 'ultimate' stem cell state.

Using fluid pressure to squeeze the stem cells through a channel, as well as miniature cantilevers to push down on the cells, the researchers were able to observe and measure the mechanical properties of these [master cells](#).

What they found is that the nuclei of [embryonic stem cells](#) display a bizarre and highly unusual property known as auxeticity. Most materials will contract when stretched. If you pull on an elastic band, the elastic will get thinner. If you squeeze a tennis ball, its circumference will get larger. However, auxetic materials react differently – squeeze them and they contract, stretch them and they expand.

"The nucleus of an embryonic stem cell is an auxetic sponge – it can open up and soak up material when it's pulled on and expel all that material when it's compressed," said Chalut. "But once the cells have differentiated, this property goes away."

Auxeticity arises precisely at the point in a stem cell's development that it needs to start differentiating, so it's possible that the property exists so that the nucleus is able to allow entrance and space to the molecules required for differentiation.

"There's a lot of discussion about what exactly it means to be pluripotent, and how pluripotency is regulated," said Chalut. "Many different factors play a role, but we believe one of those factors may be a mechanical signal. This may also be the case in the developing embryo."

By bringing together physics and biology, Simons and Chalut believe not only that some of the defining questions in embryonic and adult [stem cell biology](#) can be addressed, but also that new insights can be found into mechanisms of dysregulation in disease, cancer and ageing.

"One of the reasons that this bringing together of disciplines sometimes doesn't work so well is that physicists don't want to understand the biology and biologists don't want to understand the physics," said Chalut. "In a sense, biologists don't know the physical questions to ask, and physicists don't know the biological questions to ask. As a physicist, the main reason I wanted to move my lab to the Stem Cell Institute is I thought there was no point working in biology if I didn't understand which questions to ask."

"There's a real effort being made to combine biology and physics much more than they have been in the past," added Simons. "It takes a bit of a leap of faith to believe physics will enrich the field of biology, but I think it's a very reasonable leap of faith. Scientific history is full of

fields that have been enriched by people coming in and looking at an issue from different directions."

Provided by University of Cambridge

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