The physics of epithelia (EpiPhysX)

# "If it were easy, it wouldn't be fun"

**The scientists working on the EpiPhysX project seek to find out how skin forms and changes and also how feathers, scales, spines and hairs develop. Their discoveries have even captured the imaginations of fashion designers.**

Every child knows that chameleons change color. These animals use this feature as camouflage against predators, to recruit a mate or to intimidate their rivals. But until now, nobody knew how this color change worked. In March this year, researchers from the EpiPhysX project published the solution to this puzzle: the different colors of the chameleon come about not only due to a yellow pigment and cells which can make the overall color seem lighter or darker, but predominantly due to a regular lattice of intracellular nanoscopic crystals within specialized skin cells. "These cells reflect different wavelengths of light depending on the distance between their nanocrystals. Chameleons are able to tune this distance, generating any color in the whole visible spectrum", explains Michel Milinkovitch, professor in the Department of Genetics and Evolution at the University of Geneva and principal investigator on the EpiPhysX project. Additionally, a second layer of more chaotically-arranged nanocrystals situated underneath the first protects the chameleon from excessive heating.

Michel Milinkovitch investigates how chameleons change their color.

## Chameleons, snakes and crocodiles

The chameleon's ability to change color is just one phenomenon that the researchers are trying to shed light on. They also investigate the formation of skin and its appendages such as hair, spines, feathers and scales. For example, Milinkovitch's team was able to establish that the scales on a crocodile's jaws are not like those of a snake, which are genetically determined. In contrast, physical forces cause the formation of cracks on the stiff skin of the crocodile, similar to those in parched earth. Other matters which the researchers strive to elucidate include why the skin of some lizards is hyperhydrophobic, alterations in a snake's color pattern, or differences in the formation of spines on hedgehogs and tenrecs – spiny mammals which resemble hedgehogs, but are genetically much more closely related to elephants.

"The complexity and diversity of the living world becomes apparent when comparing the different species", explains the evolutionary biophysicist Milinkovitch, whose group works not with the more common model organisms such as fruit flies or mice, but with rather unorthodox creatures like crocodiles and chameleons. However, working with such animals complicates the research process, as the scientists must first establish the necessary basic information on the breeding and development of these species, which have much longer generation times than common model organisms.

In collaboration with Marcos Gonzáles-Gaitán, Milinkovitch is trying to apply some of the state-of-the-art imaging and biochemistry tools available for the fruit fly and zebrafish to his non-model species. It doesn't bother Milinkovitch that everything is a bit more complicated with his exotic research subjects. On the contrary. "If it were easy, it wouldn't be fun", beams the full-blooded scientist.

## Spanning several dimensions

The scientists from EpiPhysX research how epithelia fold and how mechanical forces influence their growth on both a macro- and microscopic scale. While some investigate the formation of crocodile scales or the forces contributing to the development of zebrafish fins, others, including Aurélien Roux, look into what happens when growing tissue is confined inside a small capsule or when dividing cells are physically pulled apart.

Maja Schaffner

In order to collect quantitative data to address these questions, the project members must often think up new methods or develop novel equipment. A prime example is the robot R$^2$OBBIE-3D. “R$^2$OBBIE is able to scan objects up to 1.5 meters long using its moveable arm, which has an integrated digital camera”, enthuses Milinkovitch. “On the resulting 3D model, it’s possible to discern structures as small as 15 micrometers across, over the whole body of a fully-grown snake or lizard, down to the smallest details such as the shape and color of individual skin cells.” This is no mean feat, as imaging methods typically either cover a large area at low resolution or a very small area at high resolution. In collaboration with Bastien Chopard and Andreas Wagner, Milinkovitch uses these 3D images to build cell-based computer models that simulate the development of epithelia.

### Extreme interdisciplinarity

Researchers from disparate disciplines work closely together on this project. To explain the chameleon’s color change abilities, the involved biologists, physicists, engineers and modelers combined multifarious techniques such as tissue probes, electron microscopy, spectroscopy and computational modeling of photon behavior in soft matter.

“Only with the support from SystemsX.ch were we able to realize an interdisciplinary project on this scale”, says Milinkovitch. In his opinion, the research initiative has contributed significantly to a general increase in interdisciplinary research, which he welcomes.

### Basic research with practical potential

“We carry out basic research”, emphasizes Milinkovitch. However, it turns out that some of the project’s findings and developments have great potential for a variety of practical applications. Pathologists and forensic scientists have expressed interest in R$^2$OBBIE the robot for examining their samples.

Even the capsules in which the scientists lock multiplying cells have stirred interest; the EpiPhysX team is growing neurons in capsules that could be smuggled into the brain to produce deficient substances in patients with neurodegenerative diseases such as Alzheimer’s or Parkinson’s.

“Superhydrophobic skin, like a lizard’s, could be used to cover stents which are placed in bodily vessels to keep them open, in order to prevent deposits and blockages from forming”, Milinkovitch adds.

Even the world of fashion is keenly interested. “Since we published our chameleon paper, I’ve received several requests from the textile industry”, says Milinkovitch. “Fashion designers are fascinated by the idea of producing clothes that can change color.”

## EpiPhysX at a glance

Principle investigator: Prof. Michel Milinkovitch

Research groups:

- Prof. Michel Milinkovitch, Laboratory of Artificial & Natural Evolution, Department of Genetics & Evolution, University of Geneva and SIB Swiss Institute of Bioinformatics – Evolution, development and biophysics of non-model organisms
- Prof. Bastien Chopard, Scientific and Parallel Computing Group, CUI, Department of Computer Science, University of Geneva – Numerical modeling
- Prof. Marcos González-Gaitán, Department of Biochemistry, University of Geneva – Development and biophysics of epithelia in *Drosophila* and zebrafish
- Prof. Aurélien Roux, Department of Biochemistry, University of Geneva – Cell and tissue biophysics
- Prof. Andreas Wagner, Institute of Evolutionary Biology and Environmental Sciences, University of Zurich – Robustness analysis of numerical models

Total budget (2013–2017): CHF 7.0 million, including CHF 2.9 million from SystemsX.ch

Project type: Research, Technology and Development (RTD) Project

**EpiPhysX**
The Physics of Epithelia