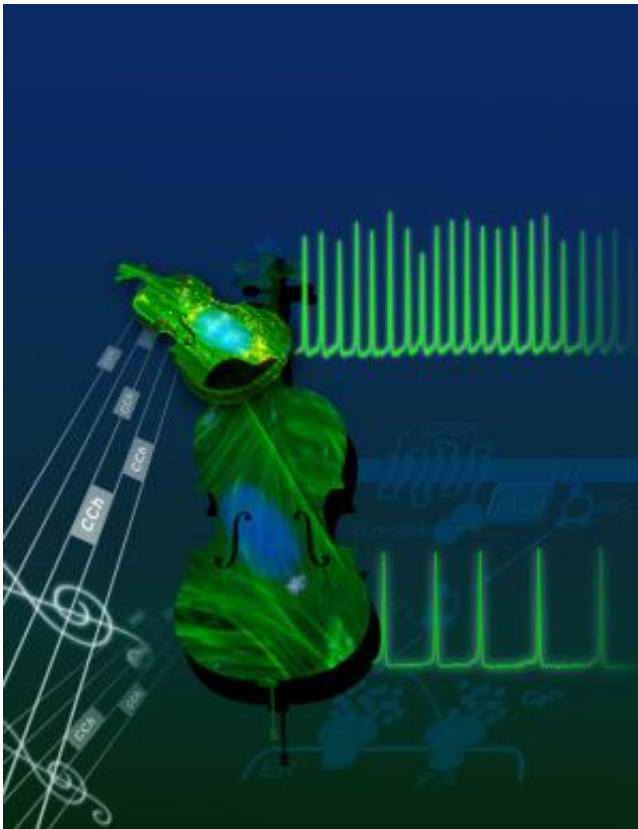


How cells translate signals from surroundings into internal signals

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Signal processing. Credit: LCSB

Every organism has one aim: to survive. Its body cells all work in concert to keep it alive. They do so through finely tuned means of communication. Together with cooperation partners from Berlin and Cambridge, scientists at the Luxembourg Centre for Systems

Biomedicine (LCSB) of the University of Luxembourg have now successfully revealed for the first time the laws by which cells translate signals from their surroundings into internal signals. Like an isolated note in a symphony orchestra, an isolated signal in the cell is of subordinate importance. "What is important is the relative variation of intensity and frequency at which the signals are transmitted from the cell membrane into the cell," says Dr. Alexander Skupin, who led the studies at LCSB. The research group published their results now in the scientific journal *Science Signaling*.

The instruments in an orchestra produce signals – musical notes – by causing the air to vibrate. Inside a cell, calcium ions carry signals. When a piece of information from the environment – say a biological messenger – meets the outer envelope of the cell, [calcium ions](#) are released inside the cell. There, they control various adaptation processes. "At first sight, there is no simple pattern to the ion impulses," Skupin explains; "yet they still culminate in a meaningful response inside the cell, like the activation of a specific gene, for instance."

In order to determine the laws underlying this phenomenon, the researchers studied [human kidney cells](#) and rat liver cells using a combination of imaging technologies and mathematical methods. They discovered that the intensity and frequency of calcium impulses undergo extreme variation – both cell-internally and cell-to-cell. Accordingly, the information they convey cannot be interpreted by analyzing isolated signals alone. "It's like in an orchestra, where studying an isolated note on its own allows no inference of the melody," Skupin continues the musical analogy. "You have to hear how the frequency and volume of all instruments vary and produce the melody. Then you gain an impression of the musical piece."

Now, for the first time, the researchers have managed to gain such an impression of the whole by listening in on the cells' communications.

They discovered that the plethora of calcium impulses vary relatively to one another in a specific relationship: A stimulus from outside does not lead to an absolute increase in calcium impulses, but instead to a change in the frequency at which they occur – in the concert hall, the notes of the instruments rise and fall in symphony. "This pattern is the actual signal that leads to a response in the cells," Skupin says. "With our analyses, we have rendered it interpretable."

"The results are of great importance for analyzing diseases," says Director of LCSB Prof. Dr. Rudi Balling. "We know that, in Parkinson's disease, the calcium balance in the nerve cells is disrupted, and suspect that errant communications between the [cells](#) could play a role in the onset of neurodegenerative diseases. With the discovery of the fundamental laws of these communications, as Alexander Skupin, his team and our cooperation partners have now achieved, we are set to take a major step forward in the analysis of Parkinson's disease."

More information: "Reliable Encoding of Stimulus Intensities Within Random Sequences of Intracellular Ca²⁺ Spikes." Kevin Thurley, Stephen C. Tovey, Gregor Moenke, Victoria L. Prince⁴, Abha Meena, Andrew P. Thomas, Alexander Skupin, Colin W. Taylor, and Martin Falcke. *Sci. Signal.*, 24 June 2014. Vol. 7, Issue 331, p. ra59. [DOI: 10.1126/scisignal.2005237](#)

Provided by University of Luxembourg

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