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Cells must use their brakes moderately for effective speed control

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How cells regulate their own function by "accelerating and braking" is important basic knowledge when new intelligent medicines are being developed, or when plant cells are tweaked to produce more bioenergy. In a study published by *Nature Communications* on May 14, researchers at Uppsala and Umeå universities show a model of how cells' regulatory systems work.

All living cells have a regulatory system similar to what can be found in today's smartphones. Just like our phones process a large amount of information that we feed them, cells continuously process information about their outer and inner environment. Inside the cells, information is sent and processed via a large network of interactions between signalling molecules.

In electronic circuits it is common with negative feedback, inhibiting functions, to make signals clearer and to reduce noise that can obscure important information. Cells also use this technique for reducing unwanted noise. Almost half of all signalling molecules that regulate which genes should be on or off, regulate their own genetic expression through biochemical reactions acting as inhibitors.

"If the number of signalling molecules is more than necessary, they shut down their own production for a short while, to later resume it. The difference between feedback in electronic systems and biological systems is that biological systems are much more imprecise and slow", explains Andreas Grönlund, lead author, currently active at Umeå

University.

Together with professors Per Lötstedt and Johan Elf, both at Uppsala University, he has used new data and mathematical models to calculate how long the molecules must remain in their binding sites to make the feedback exactly strong enough to reduce noise as much as possible.

The calculations showed that the molecules ideally should bind significantly weaker than previously believed, a characteristic that turned out to correspond well to the binding strength found in global regulatory molecules in *E. coli* bacteria.

"A car driver needs to know when and how hard to press the brake in different situations and which way to turn the steering wheel in a left turn. In the same way, we need to increase our understanding of regulatory systems in cells to be able to develop new intelligent medicines when the regulation system doesn't work or to be able to control plant cells to produce green energy through more efficient production of bio mass", says Johan Elf.

More information: Andreas Grönlund, Per Lötstedt & Johan Elf. Transcription factor binding kinetics constrain noise suppression via negative feedback. *Nature Communications*.

Provided by Uppsala University

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