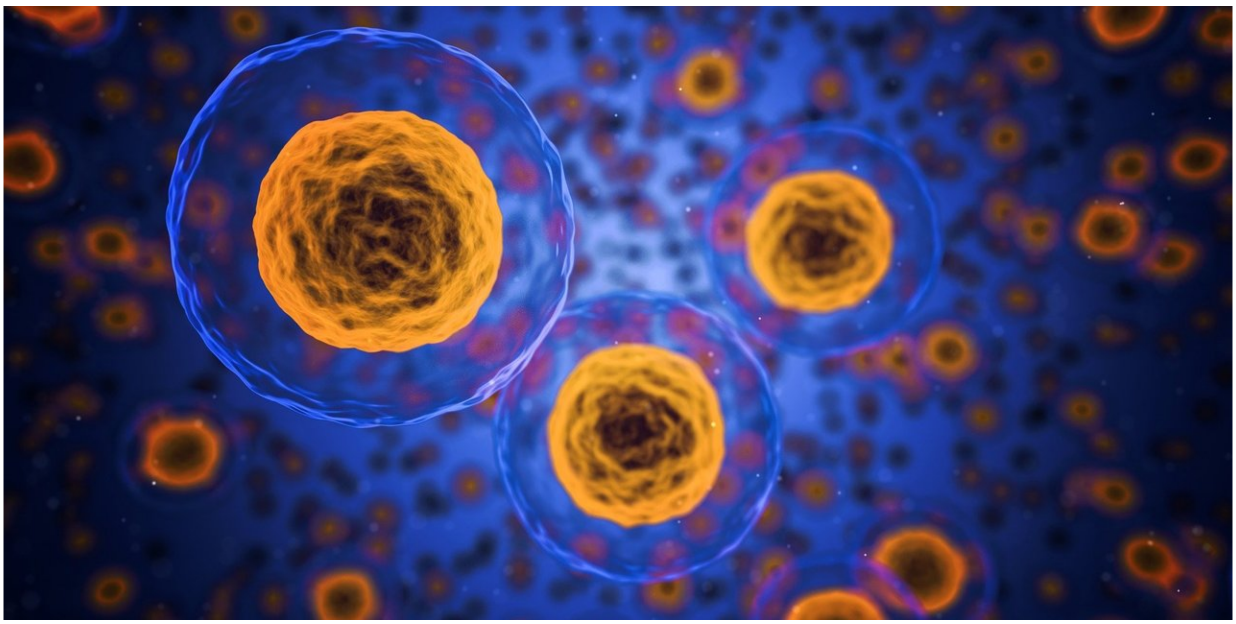
Cellular signaling cascade balances information transmission against energy consumption, study says

July 20 2020



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Cellular signal transmission is not only optimized for precision—it also includes a cost cap. The relationship between information and energy, a concept well established in physics and engineering, is likely to fundamentally shape cellular signaling networks. One of the questions addressed by researchers at the Max Planck Institute for Terrestrial Microbiology, headed by biophysicist Victor Sourjik, is: What enables reliable transmission of signals in the "noisy" cellular environment? The research team is studying signal transmission in baker's yeast (Saccharomyces cerevisiae), combining information theoretical approaches with quantitative experiments.

Precise signaling is crucial for the fitness of every living organism: Whether during development or while communicating with a possible mating partner, only accurate transmission of received signals enables cells to trigger appropriate responses. In biological systems, random fluctuations of signals always lead to background noise, which can impede cell communication. Organisms must therefore have developed strategies to improve the accuracy of signal transmission in the presence of such interference. However, little is yet known about how noise suppression is achieved in cellular networks.

The pheromone signaling pathway of baker's yeast belongs to a class of MAPK (mitogen-activated protein kinase) signaling pathways, which in eukaryotes commonly play a key role in the transmission and translation of extracellular stimuli into intracellular responses such as cell differentiation, proliferation or stress responses.

That the pheromone signaling pathway of yeast contains negative feedback regulations could be seen as clear indication of selection for increased accuracy. Surprisingly, however, both theoretical and experimental analyses of the signaling pathway showed that its accuracy could be easily further improved by increasing the sensitivity of one of the negative feedbacks. So why this discrepancy between the potentially more efficient hypothetical and the natural design? In other words, why didn't yeast naturally optimize the system this way?

Costs versus benefits

The answer seems to lie in the cellular economics. The discrepancy disappears when the energy investment in the operation of the signaling pathway is also considered. "We were able to show that the core of the MAPK signaling pathway, the phosphorylation cycle, has measurable fitness costs. When these are taken into account, and the accuracy of the signal transduction is weighed against the energetic costs of the signaling pathway operation, the naturally observed design appears optimal," explains Alexander Anders, first author of the current publication.

"Here we observe a relation between information and energy, analogous to what is well established in physics and engineering sciences." says Victor Sourjik. "In biology, little attention has been paid to this interplay so far. Our work suggests that cost-benefit trade-off in information transfer must have been important in the evolution of cellular signaling systems. This helps us to better understand the evolutionary optimization of cellular signaling networks." How biology has solved this fundamental dilemma of information costs in other cases remains to be elucidated.

More information: Alexander Anders et al, Design of a MAPK signaling cascade balances energetic cost versus accuracy of information transmission, *Nature Communications* (2020). DOI: 10.1038/s41467-020-17276-4

Provided by Max Planck Society