Temporal cues help keep human looking human

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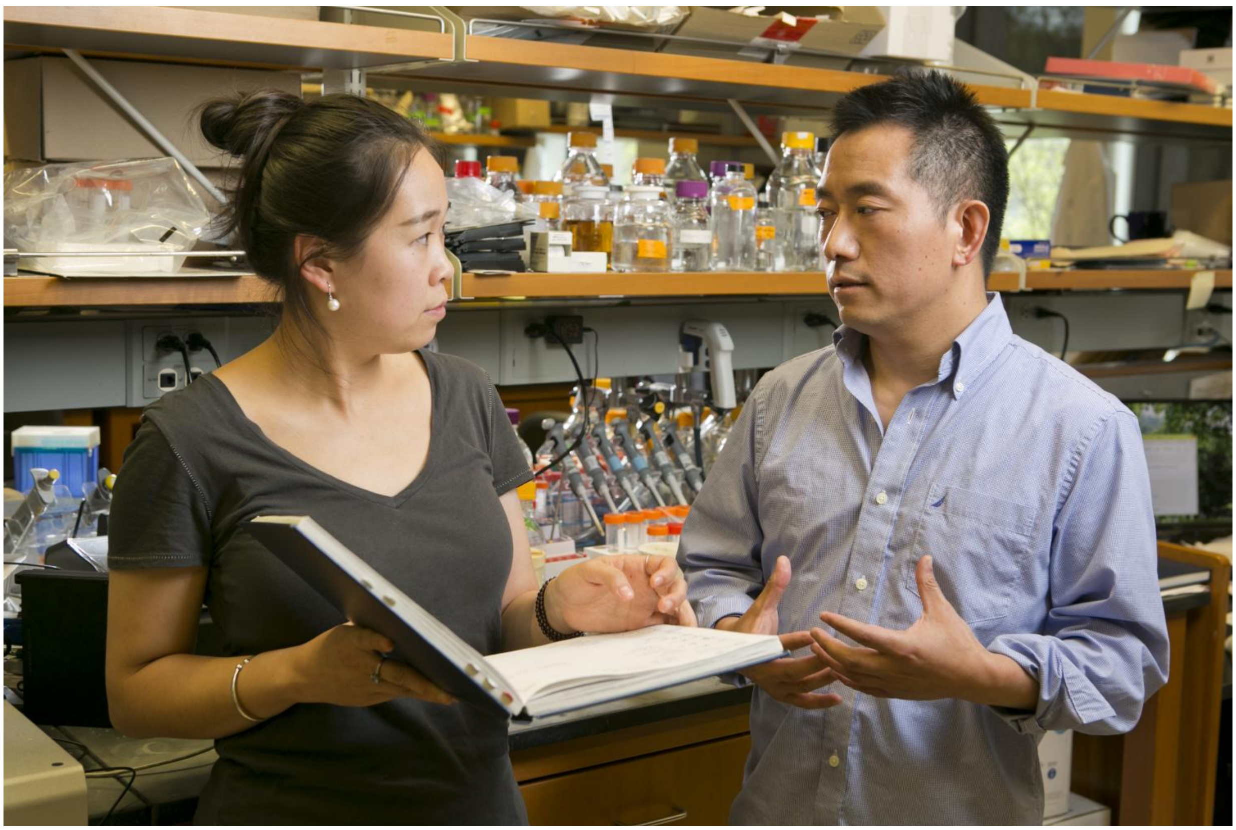

Lingchong You, the Paul Ruffin Scarborough Associate Professor of Engineering at Duke University, and graduate student Will (Yangxiaolu) Cao. Credit: Duke University

Researchers believe that genetically modified bacteria can help explain how a developing animal keeps all of its parts and organs in the same general proportions as every other member of its species.

In 1952, Alan Turing mathematically demonstrated how the nearly endless variety of patterns seen in nature—spots on cheetahs or the distinctive coats of leopards, for example—could be explained by chemicals spreading and interacting by simple rules. Many scientists, however, remained unconvinced, and believed there must be more to the story.

Now, Duke University researchers have discovered another way that patterns can form—through the use of a ticking clock. By combining two chemical signals with a few variables, timing cues emerge. And these timing cues can not only create patterns—they can also make sure these patterns have roughly the same proportions from one colony to the next.

In a study published on April 21 in the journal *Cell*, Lingchong You, the Paul Ruffin Scarborough Associate Professor of Engineering at Duke University, introduced a new genetic circuit into a population of bacteria. You programmed bacteria to produce a protein called T7RNAP (tagged fluorescent blue), which activates its own expression in a positive feedback loop.

As the bacterial colony grows and produces more T7RNAP, it also produces a chemical that triggers the production of a protein called T7 lysozyme (tagged fluorescent red), which inhibits the production of T7RNAP. Wherever the two molecules interact, purple patterns appear in the colony.

Because bacteria toward the outer edge of the colony are more active than those in the interior, this system causes a purple ring to appear like a bullseye. You and his colleagues discovered that they could control its thickness and how long it took for the bullseye to appear by varying the size of the growing environment and amount of nutrients provided.

These variables act as a time cue for the pattern's development. A bigger growth environment or more nutrients causes a delay in the formation of the ring. You speculates that similar timing circuits can operate in other organisms, including animals.

"In our experiment, we get a spatial cue from an unsuspected source. We sort of get it for free from the timing of the genetic circuit," said You. "These two diffusible molecules aren't dictating at what positions cells are going to stop or start producing proteins. Instead, they're telling the cells when to start or stop producing proteins. That's enough to both produce a pattern and to control its scaling, and it's a fundamentally new mechanism."

More information: "Collective Space-Sensing Coordinates: Pattern Scaling in Engineered Bacteria." Yangxiaolu Cao, Marc D. Ryser, Stephen Payne, Bochong Li, Christopher V. Rao, and Lingchong You. *Cell*, 2016. DOI: 10.1016/j.cell.2016.03.006

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