Metabolic model of E. coli reveals how bacterial growth responds to temperature change

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Bioengineers at the University of California, San Diego have developed a computational model of 1,366 genes in *E. coli* that includes 3D protein structures and has enabled them to compute the temperature sensitivity of the bacterium's proteins. The study, published June 7 in the journal *Science*, opens the door for engineers to create heat-tolerant microbial strains for production of commodity chemicals, therapeutic proteins and other industrial applications.

Students of microbiology learn early that bacterial growth is temperature sensitive. For most pathogens, the optimum growth temperature is approximately the same as the body temperature of humans, or 37 C, but some bacteria, called thermophiles, grow well at high temperatures. Determining what precisely causes some bacteria to be more heat sensitive than others has eluded scientists thus far.

"Evidence has accumulated over several decades that proteins are what limit the heat tolerance of cells, but pinpointing the weak points represented by specific proteins has never before been accomplished except when researchers have engineered certain proteins to be sensitive to temperature," said Roger Chang, the first author on the paper who earned his Ph.D. in bioinformatics and systems biology at UC San Diego in 2012. "Not only have we predicted some of these weak points in *E. coli* but we did so through an unprecedented integrative computational approach drawing from both three-dimensional protein structure analysis

and genome-scale cellular network modeling."

Chang completed his Ph.D. in the Systems Biology Research Group of Professor Bernhard Palsson and is currently a postdoctoral fellow at Harvard Medical School.

Chang said the predictions about thermosensitivity of specific proteins in *E. coli* have been overcome by nutrient supplementation experiments, as predicted by the computational model. The next step is to engineer or evolve thermostabilizing mutations in these proteins to yield genetically thermotolerant strains. The results thus far demonstrate the potential capabilities offered by the emerging field of systems biology, which leverages the power of high-performance computing and an enormous amount of available data from the life sciences to simulate biological activities.

"Broadly speaking, this study demonstrates how fundamental understanding of biology can be revealed by integrating network and structural biology at the genome-scale," said Professor Palsson. "Representing cellular functions in chemically accurate terms enables quantitative computation of cellular behavior. It is quite remarkable how far this field has come in just the past couple of years, and it appears that we can look forward to continuing advances in the near future."

More information: "Structural Systems Biology Evaluation of Metabolic Thermotolerance in Escherichia coli" *Science*, 2013.

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