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The Wolfson Department of Chemical Engineering

Wolfson Department of Chemical Engineering Seminar

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Sloppy control in bacterial growth and division

Prof. Naama Brenner

Faculty of Chemical Engineering, Technion.

In balanced exponential growth, bacteria maintain statistical stability despite a high level of noise. This "homeostasis" has fascinated scientists for decades. Recent technologies have resurged interest and advanced this problem tremendously, yet much remains unknown. In particular, the control of many coupled variables simultaneously poses a challenge to both data analysis and models: It is not clear, *a-priori*, which variables are under control, and which are stabilized through coupling.

Inspired by the notion of robustness in engineering theory, we addressed this question by measuring the sensitivity of different variables to perturbations. Utilizing the natural variation across experiments, we revealed that some variables are ‘‘sloppy’’ with highly volatile set-points; Other variables are "stiff" and held strictly in place, suggesting that they are under strict control. This effect is manifested geometrically by a nonlinear control manifold with in-plane variability and out-of-plane robustness. Using a recently developed microfluidic device, we quantified the source of sloppy control and found that it mostly comes from high sensitivity to the environment, and only a small fraction from inherited biological individuality. Our method offers a generalizable data-driven approach for identifying control variables in a complex system with many coupled variables.

References:

1. L. Susman, M. Kohram, H. Vashistha, J. T. Nechleba, H. Salman and N. Brenner, "Individuality and slow dynamics in bacterial growth homeostasis”, PNAS 115 (25) E5679-E5687 (2018).
2. Stawsky, H. Vashistha, H. Salman and N. Brenner, “Multiple timescales in bacterial growth homeostasis”. iScience **25**, 103678 (2022).