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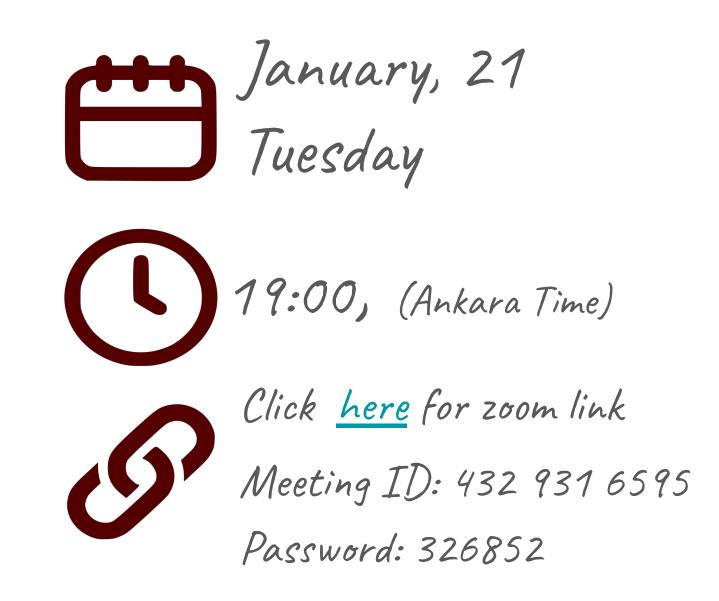
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The price of evolution: how thermodynamics shapes gene regulation

Many of the physical processes in a cell consume energy, but we are only beginning to understand how these costs have influenced the course of evolution. Biology is strewn with counter-intuitively complex mechanisms whose evolutionary predecessors must have consumed significant energy resources without any clear fitness benefit. So how do such mechanisms evolve in the first place, and how strong is the guiding hand of thermodynamic optimization? My talk explores these issues through one specific example: gene regulation in higher organisms (including humans) by microRNAs. These small RNA molecules (only 22 nucleotides long) are versatile tools for controlling the expression of genes into proteins, interfering with the messenger RNAs that are an intermediate step in the expression process. They provide a way of reducing noise in protein population levels, which helps stabilize cells from making sudden random changes in their state. Because a single microRNA type can interfere with the expression of hundreds of genes, this regulation can impose a substantial cost on the cell, since it is forced to compensate by increased messenger RNA transcription. Using a combination of statistical physics, information theory, and population genetics, we argue that the mRNA systems we observe in nature today are a potential instance of thermodynamic optimization: the chemical parameters have been fine-tuned by natural selection to achieve noise control in the most energy-efficient manner. Along the way, we provide insights into one peculiar feature: why we need such short RNA molecules to get the job done, i.e. why the "micro" in microRNA. Reference: E. Ilker and M. Hinczewski, PNAS 121, e2308796121 (2024).



Michael Hinczewski is Warren E. Rupp Associate Professor at Case Western Reserve University. He received his BS degree from Yale University and his PhD from MIT. His research mainly focuses on using statistical physics to understand a variety of biological phenomena across scales, from single molecules to cells and beyond.

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