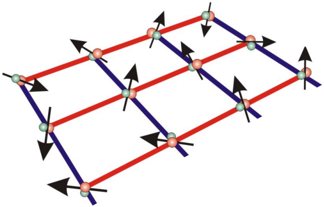
Shortcuts to adiabaticity



adiabatic quantum computing:
maintaining ground state while
driving a quantum system

Demirplak, Rice, JPCA (2003)
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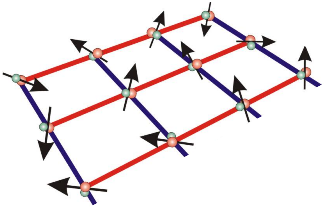

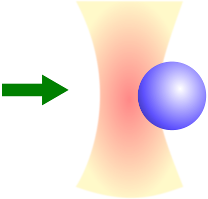

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Brownian motion of
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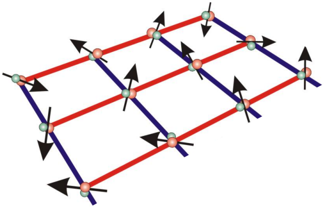

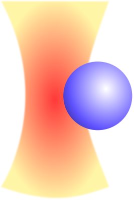

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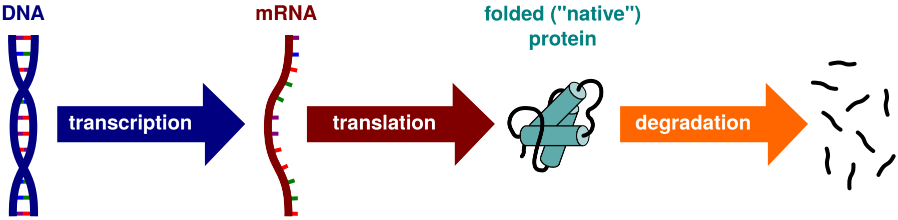
Possible biological
applications:
population genetics
molecular chaperones
force spectroscopy

Traditional view of protein production



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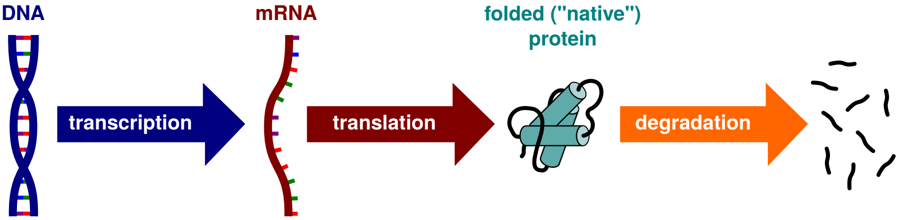

All these processes involve nonequilibrium reaction networks driven by ATP hydrolysis.

The resulting costs of expressing even a single extra protein can be evolutionarily significant for single-celled organisms.

Ilker & Hinczewski, Phys. Rev. Lett. (2019)
Lynch & Marinov, Proc. Natl. Acad. Sci. (2015)

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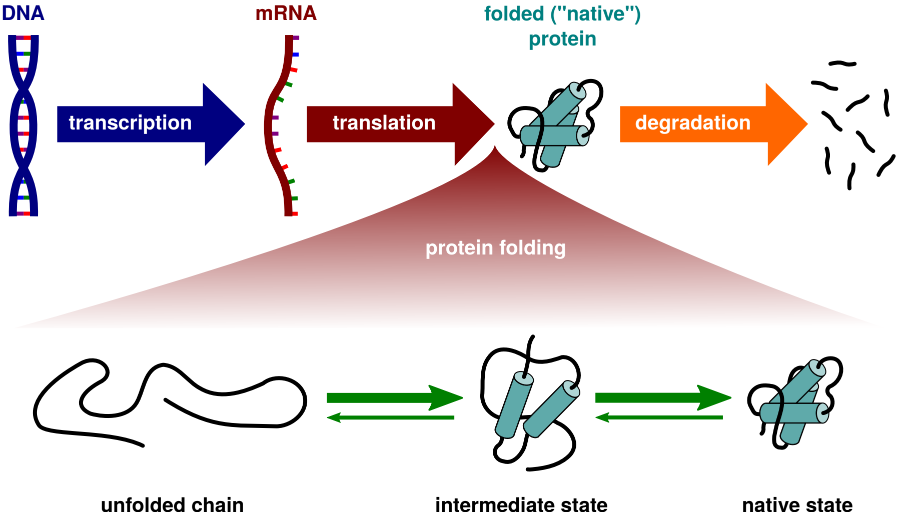
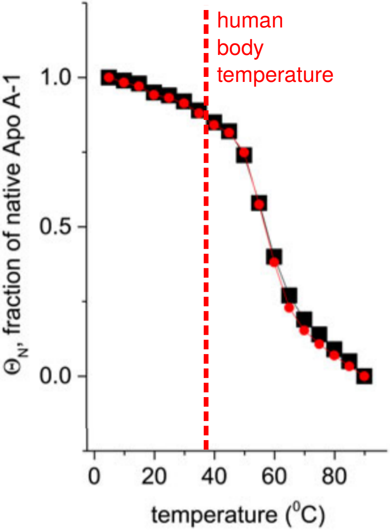


Proteins function at the cliff edge of unfolding



Seelig & Schönfeld, Q. Rev. Biophys. (2016)

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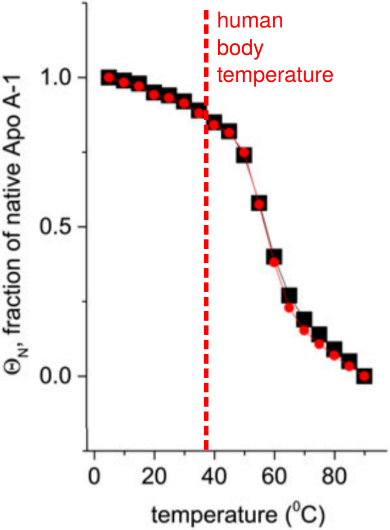

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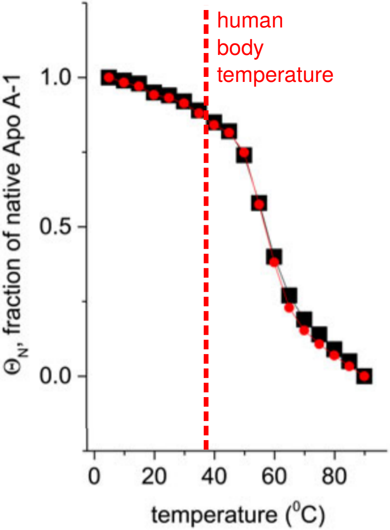
Being on the verge of melting gives proteins the dynamical flexibility essential for their diverse roles as enzymes.

Proteins function at the cliff edge of unfolding



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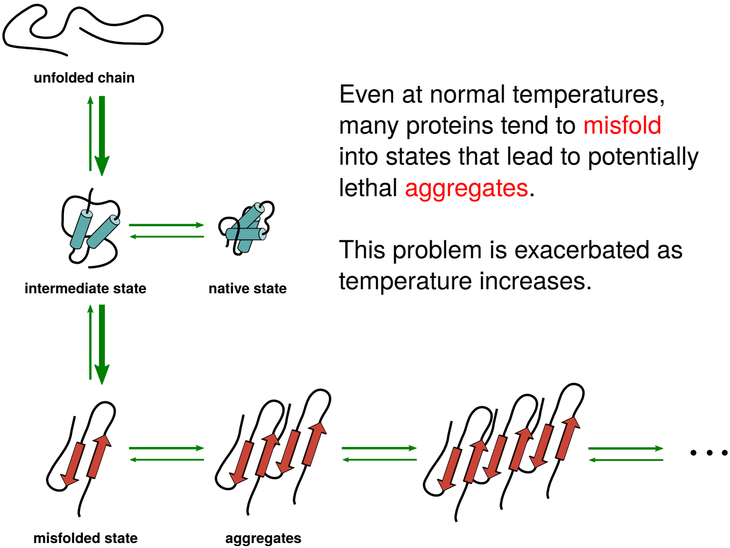
Being on the verge of melting gives proteins the dynamical flexibility essential for their diverse roles as enzymes.

But it also makes them highly vulnerable to changes in temperature (even of a few degrees): heat shock.

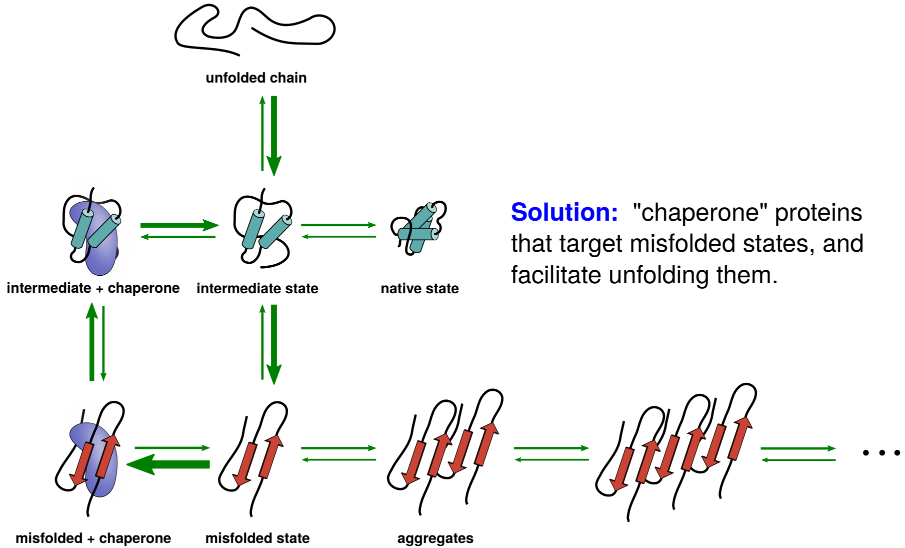
Constant threats: misfolding and aggregation



Even at normal temperatures, many proteins tend to misfold into states that lead to potentially lethal aggregates.

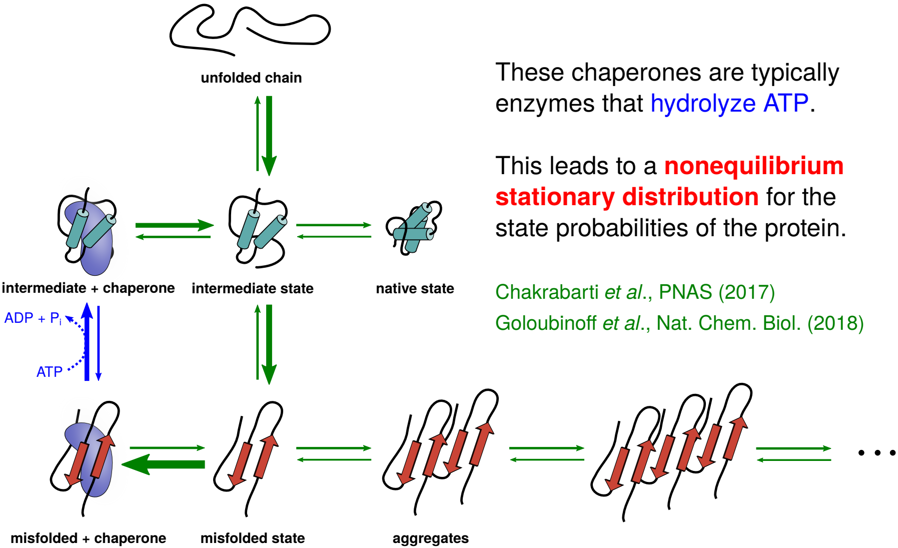
This problem is exacerbated as temperature increases.

Constant threats: misfolding and aggregation



Solution: "chaperone" proteins that target misfolded states, and facilitate unfolding them.

Constant threats: misfolding and aggregation



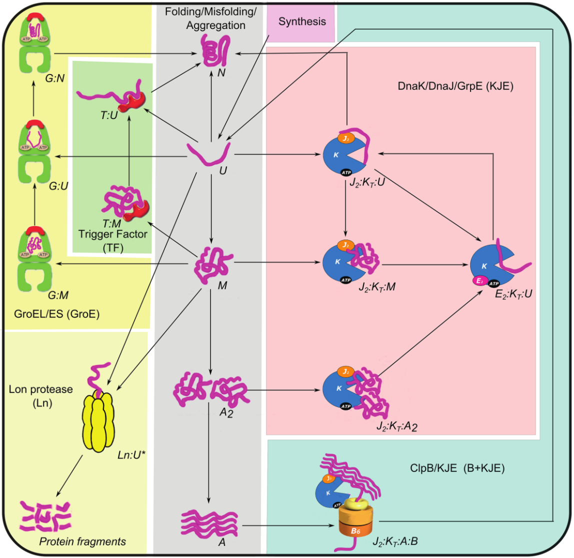
These chaperones are typically enzymes that hydrolyze ATP.

This leads to a **nonequilibrium stationary distribution** for the state probabilities of the protein.

Chakrabarti *et al.*, PNAS (2017)

Goloubinoff *et al.*, Nat. Chem. Biol. (2018)

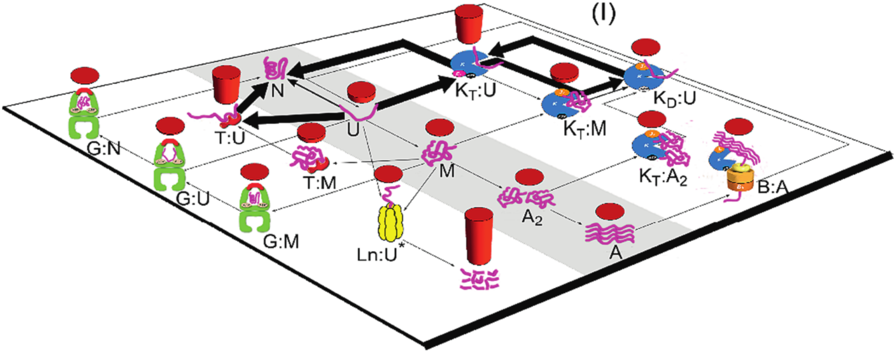
The protein “hospital”: possible chaperone pathways



E. coli chaperone network: Santra *et al.*, PNAS (2017)

The protein “hospital”: possible chaperone pathways

Different classes of proteins interact primarily with different chaperone sub-systems:



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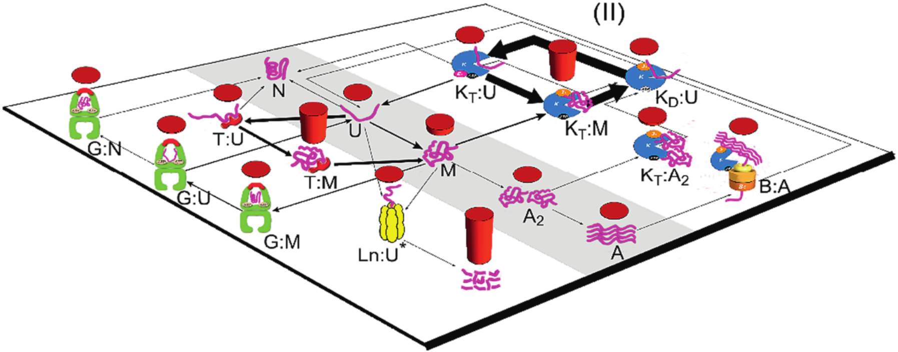

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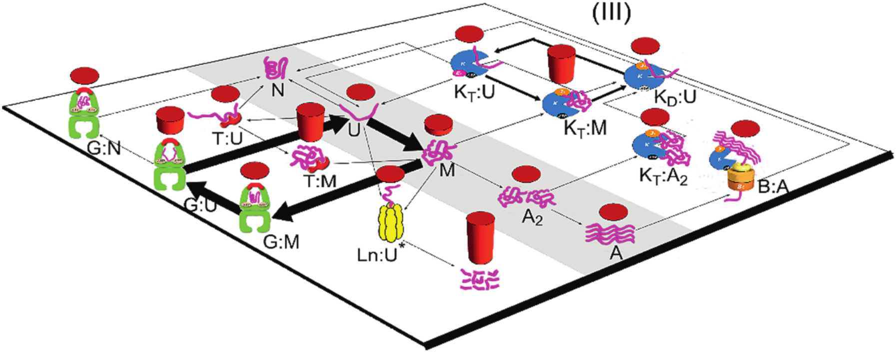

Santra *et al.*, PNAS (2017)

Under optimal growth conditions, chaperones are nearly fully occupied by "patient" proteins: spare capacity is too energetically costly.

Heat shock

What happens when the cell enters a higher temperature environment?

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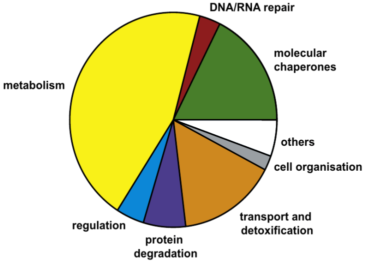
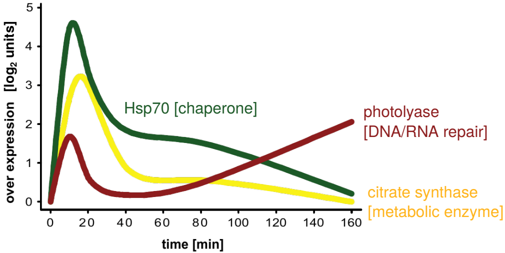
Functional classes of upregulated genes in yeast after a heat shock from 25°C to 35°C over 10 min (out of total of 91 genes upregulated by more than 2.8x):





[Richter *et al.*, Molec. Cell (2010)]

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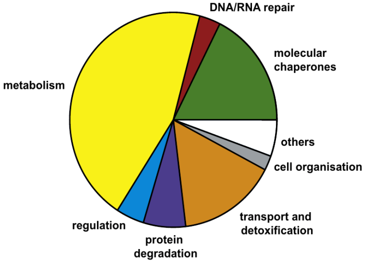
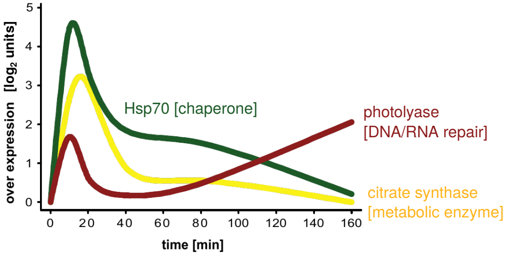
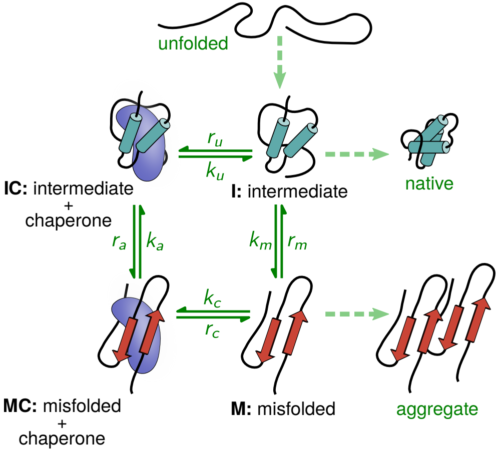




[Richter *et al.*, Molec. Cell (2010)]

Can we understand this upregulation of chaperones using ideas from thermodynamic control?

Markov model for chaperone-protein interaction



Using separation of timescales we can construct a simplified Markov model for a protein that tends to misfold under heat shock, focusing on four key states.