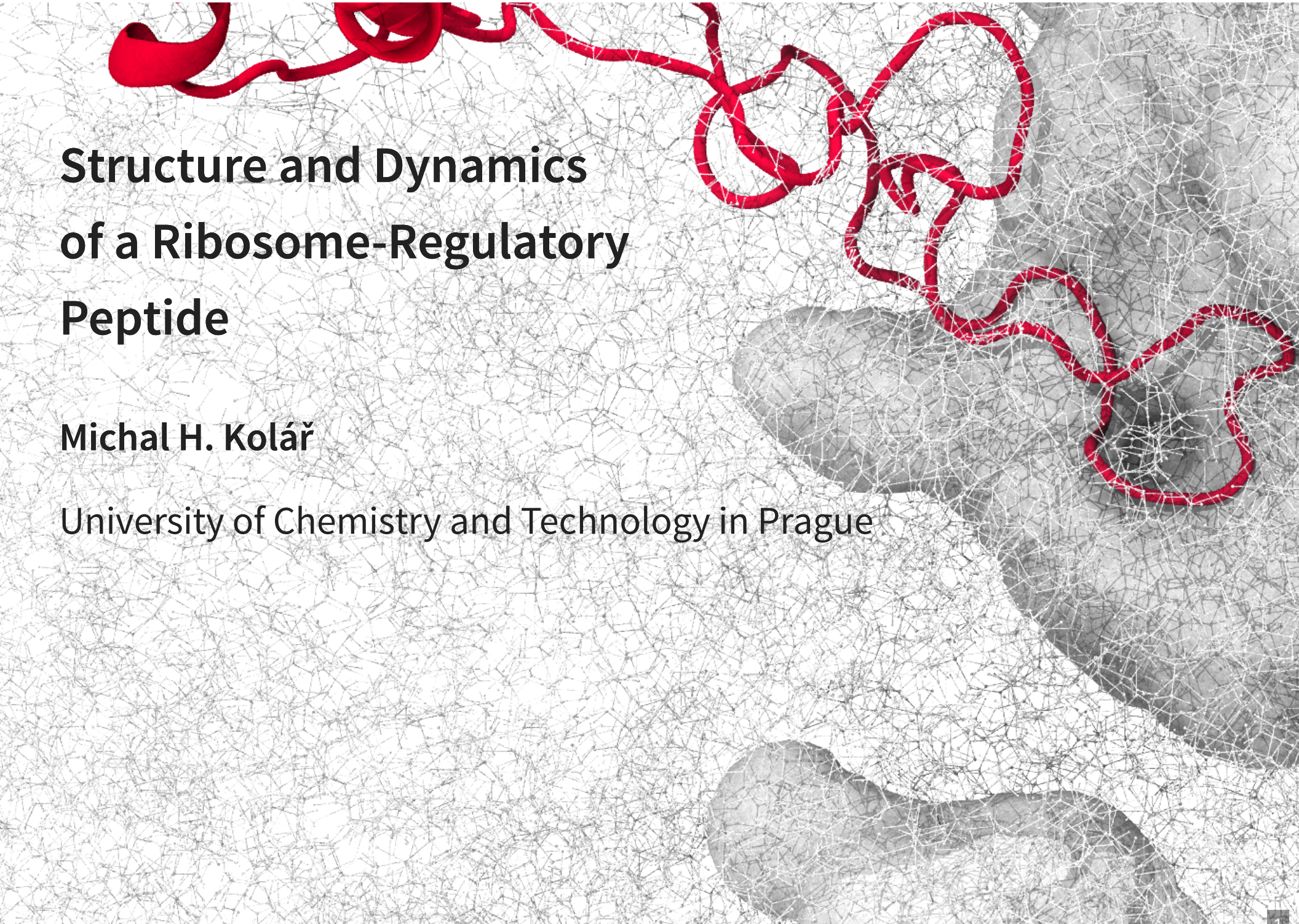


Structure and Dynamics of a Ribosome-Regulatory Peptide

Michal H. Kolář

University of Chemistry and Technology in Prague

People Involved

Lars Bock, Andrea Vaiana, Helmut Grubmüller

from the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany

Ting Su, Roland Beckmann

from the Ludwig Maximilian University of Munich, Germany

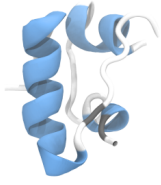
Supercomputers Involved

Leibniz-Rechenzentrum
der Bayerischen Akademie der Wissenschaften

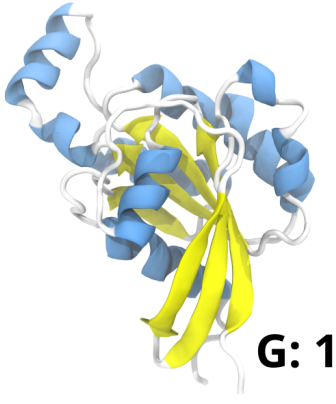
MAX PLANCK COMPUTING & DATA FACILITY
RECHENZENTRUM GARCHING DER MAX-PLANCK-GESELLSCHAFT

IT4Innovations&
národní$$#1!101
superpočítačové
centrum0@!£1€01

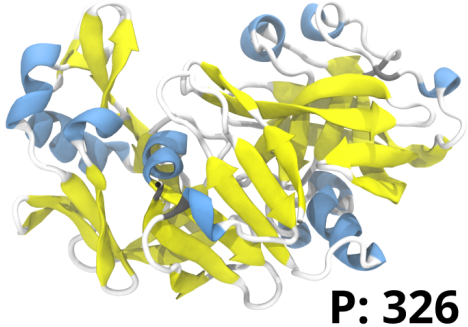
Proteins



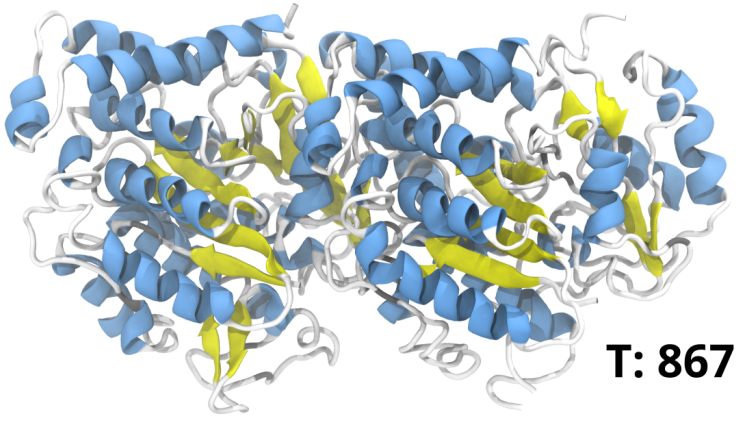
I: 51



G: 186

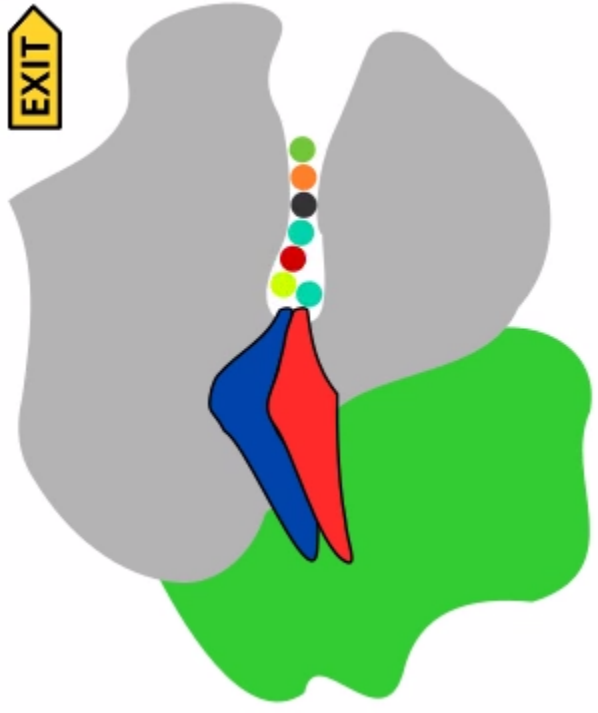


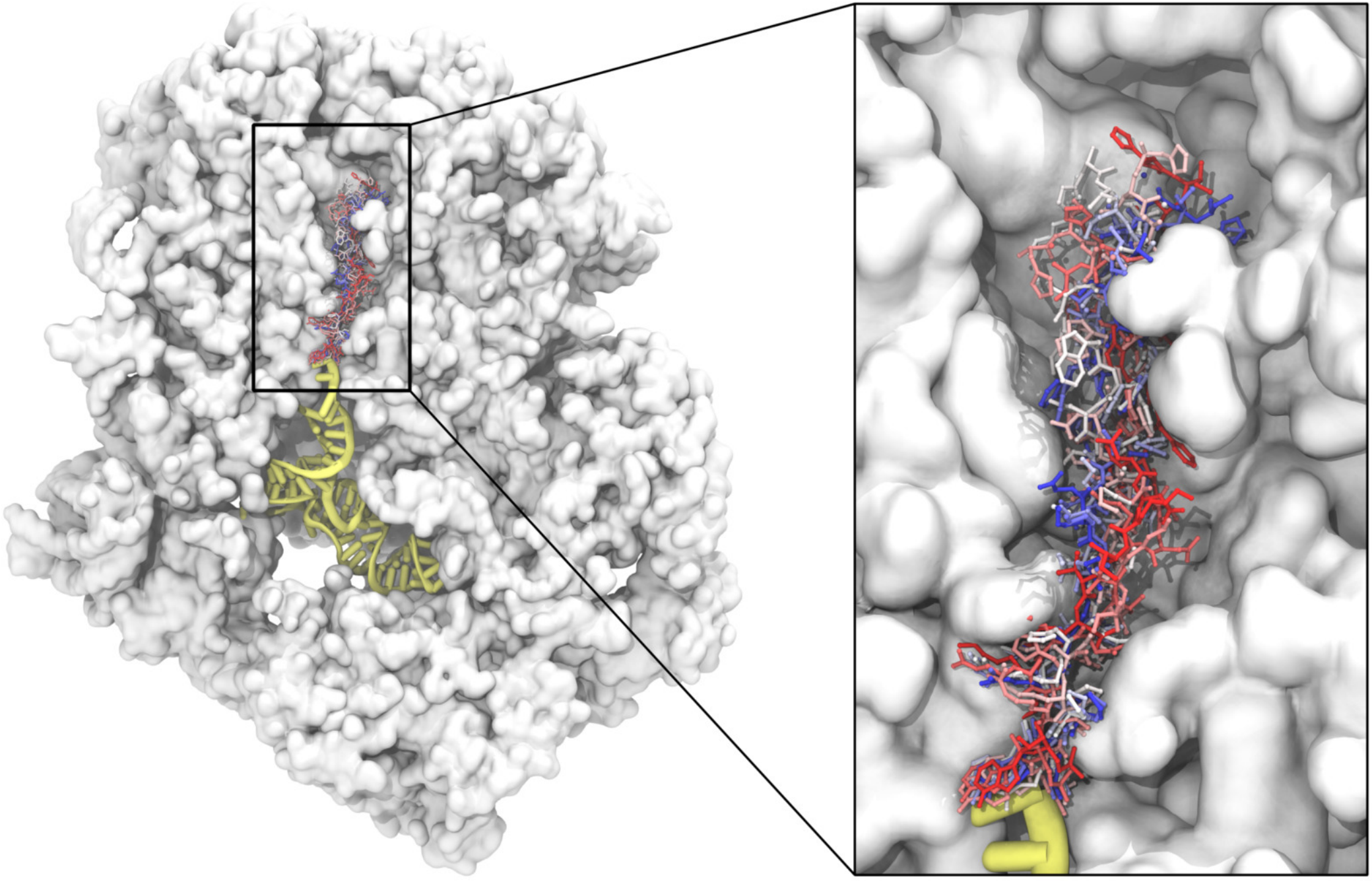
P: 326



T: 867

Peptide Elongation

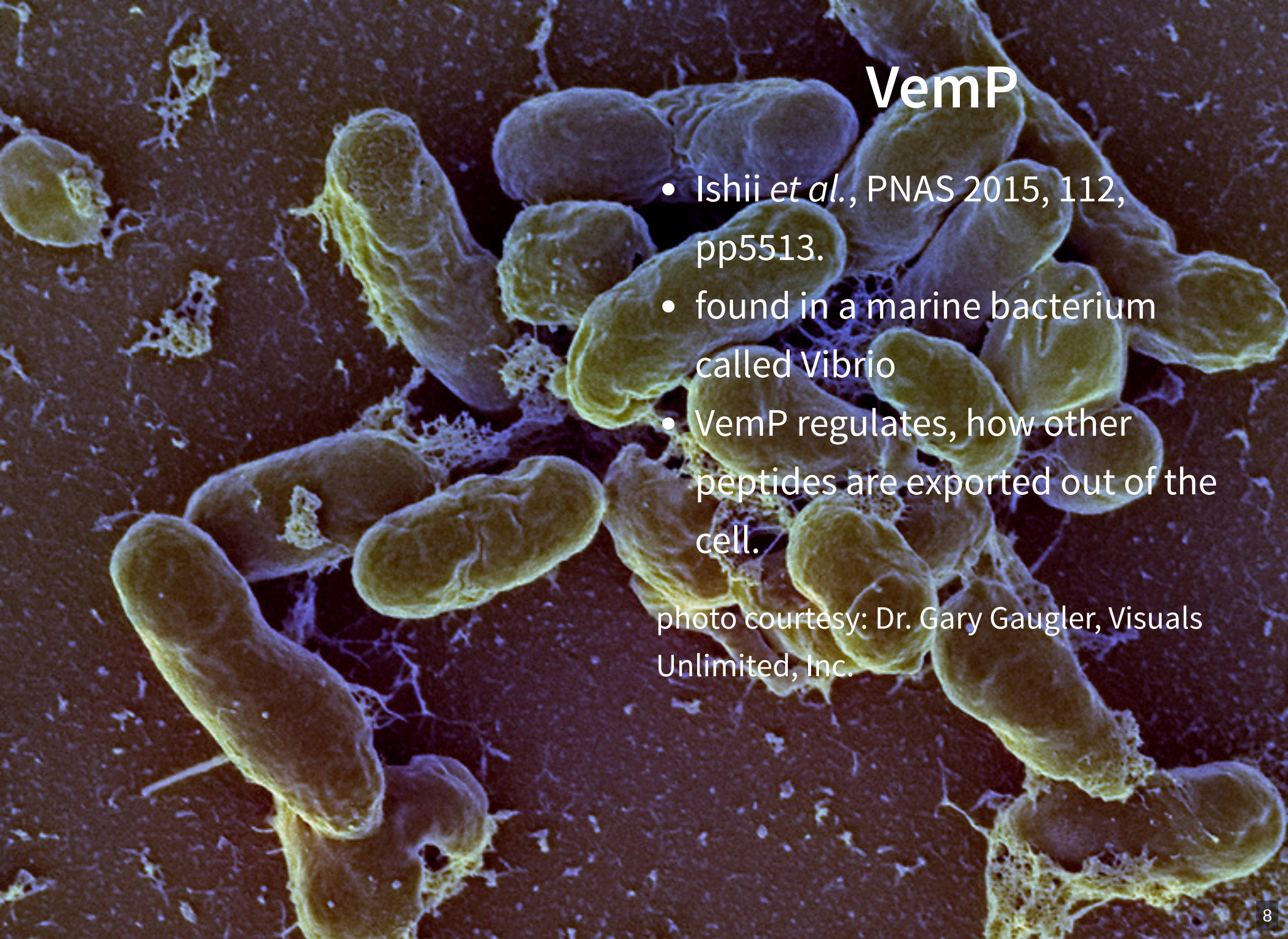




Ribosome Stalling

It is a phenomenon, which nature uses to modulate ribosome function.

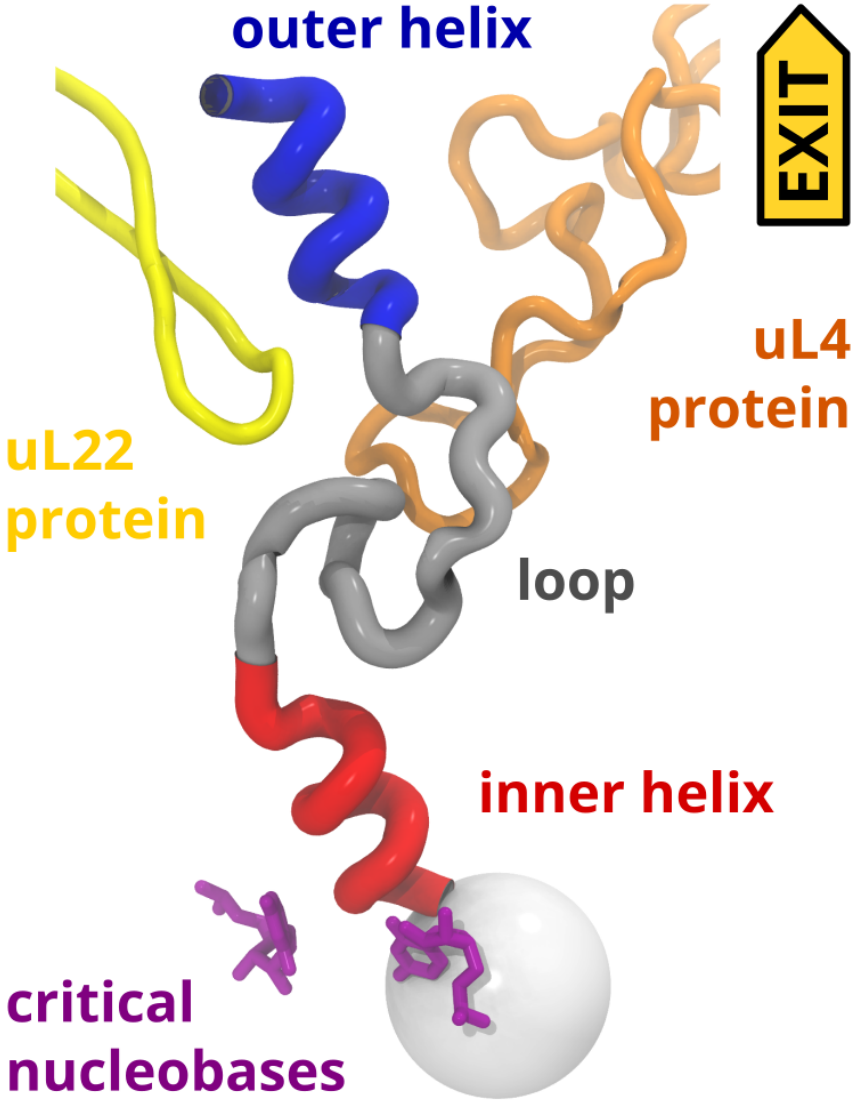
Significant physiologic context (antibiotics, protein misfolding)



VemP

- Ishii *et al.*, PNAS 2015, 112, pp5513.
- found in a marine bacterium called Vibrio
- VemP regulates, how other peptides are exported out of the cell.

photo courtesy: Dr. Gary Gaugler, Visuals Unlimited, Inc.



VemP

- cryo-EM shows extreme compaction in the exit tunnel
- Su *et al.*, eLife 2017, e25642

The inner helix inactivates two nucleobases needed for chemical reaction to occur.

A Puzzle

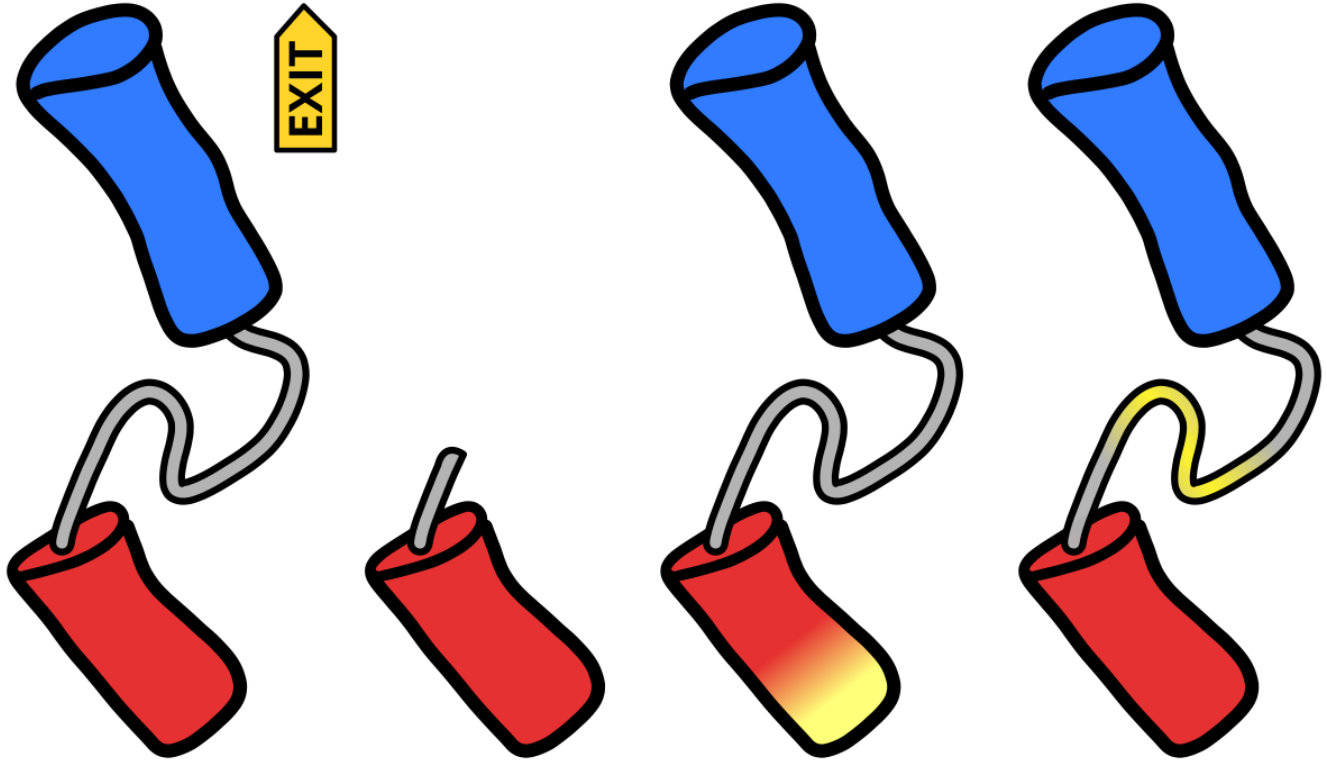
SecM (*E. coli*):	AKFSTPVWISQAQGIRAG'P
SecM (*M. succ.*):	HAPIRGS'P
MifM:	YHRITTWIRKVFRMNSPVNDEED'AGS
VemP:	SDHRISGWKETNAMYVALNSQ'F

from Ishii et al. PNAS 2015, pp5513.

Why are so many amino acids important for VemP stalling?

Strategy

Prepare *in silico* several VemP constructs and study their structure and dynamics by classical molecular mechanics.



Some Technical Details

We solve Newton's equations for about 2 million atoms - entire ribosome, water, ions. (As implemented in GROMACS)

We use classical interatomic potentials.

Typically, we simulate several 800-1000 ns long trajectories.

We analyze structure and dynamics of various parts of the simulated system.

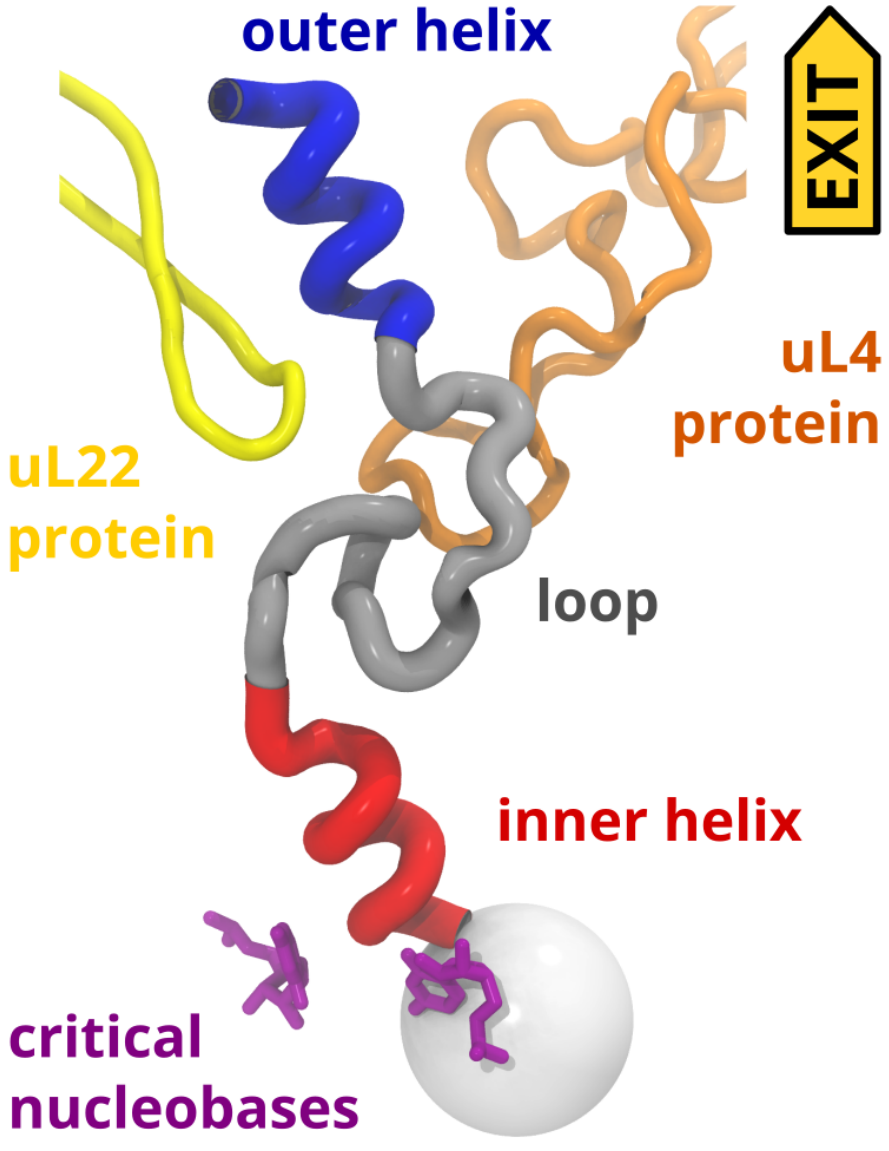
Key Observations

1. Both helices are stable in the tunnel, but unstable outside.

2. The inner helix of the truncated VemP is stable, but moves out of the catalytic site.

3. Mutations in inner helix interfere with the catalytic center.

4. Mutations in the loop help holding the inner helix in place.



Pulling Teaser

EXIT