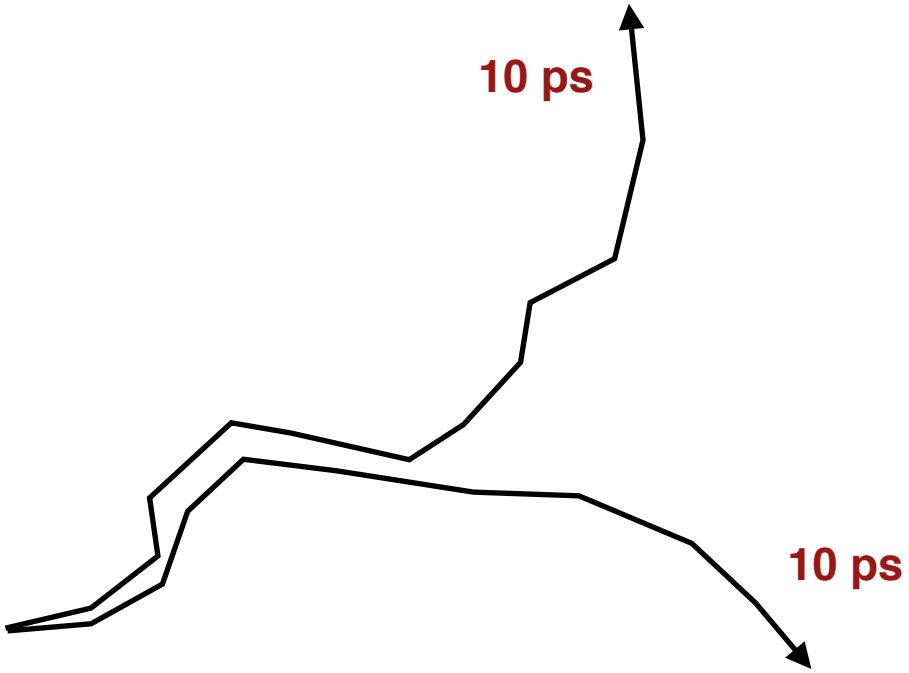
Reproducibility of molecular simulations

Helmut Grubmüller, Göttingen, Germany

Issues to discuss:

(1) Chaoticity of molecular dynamics



Start: differs by 0.000001 A

Issues to discuss:

(1) Chaoticity of molecular dynamics

(2) => What do we mean by "reproducibility"?

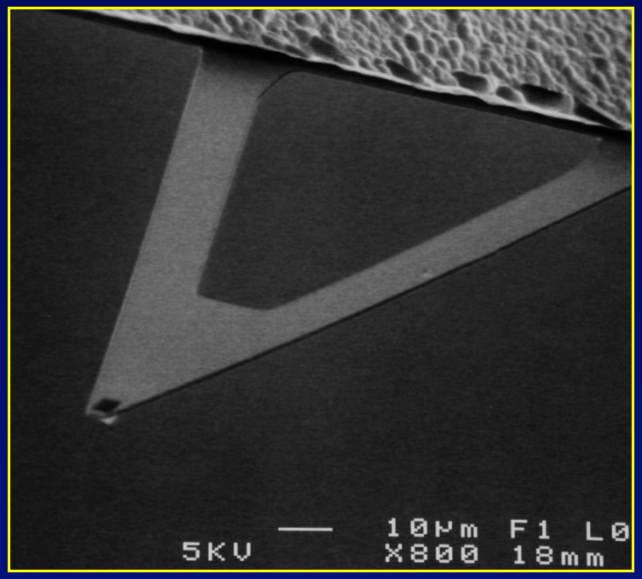
H. Grubmüller, P. Tavan,
J. Comp. Chem. **19**, 1534 (1998)

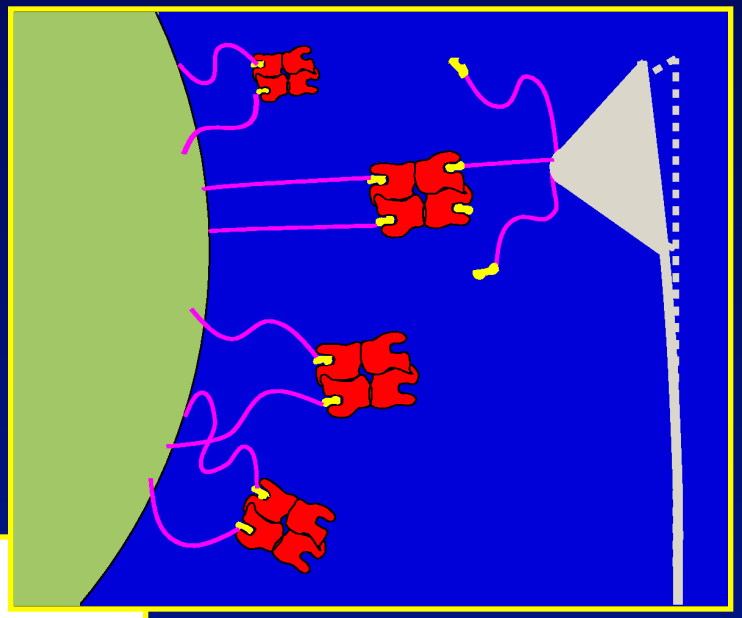
--> Relevant Observables

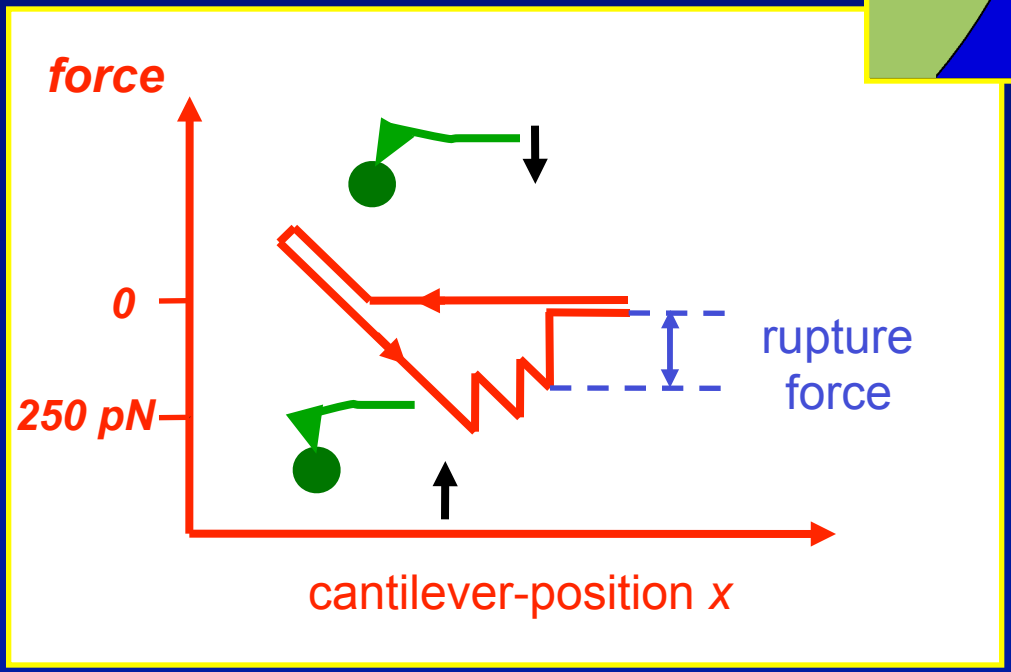
$x_1(t)$ ... $x_n(t)$ vs:

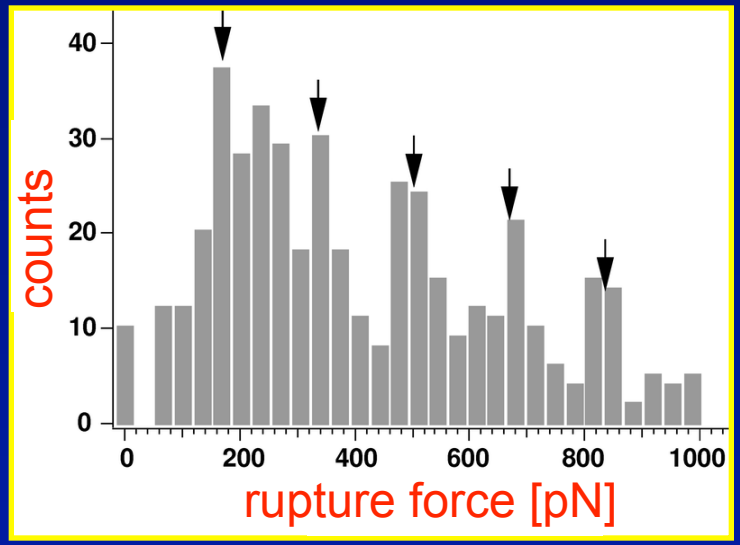
$\langle |x_1 - x_2| \rangle$,
rmsf,
PCA,
FFT(x(t)),
mean transition rates
FRET-efficiencies,
rupture forces
functional mechanisms
...

Single Molecule Force Spectroscopy



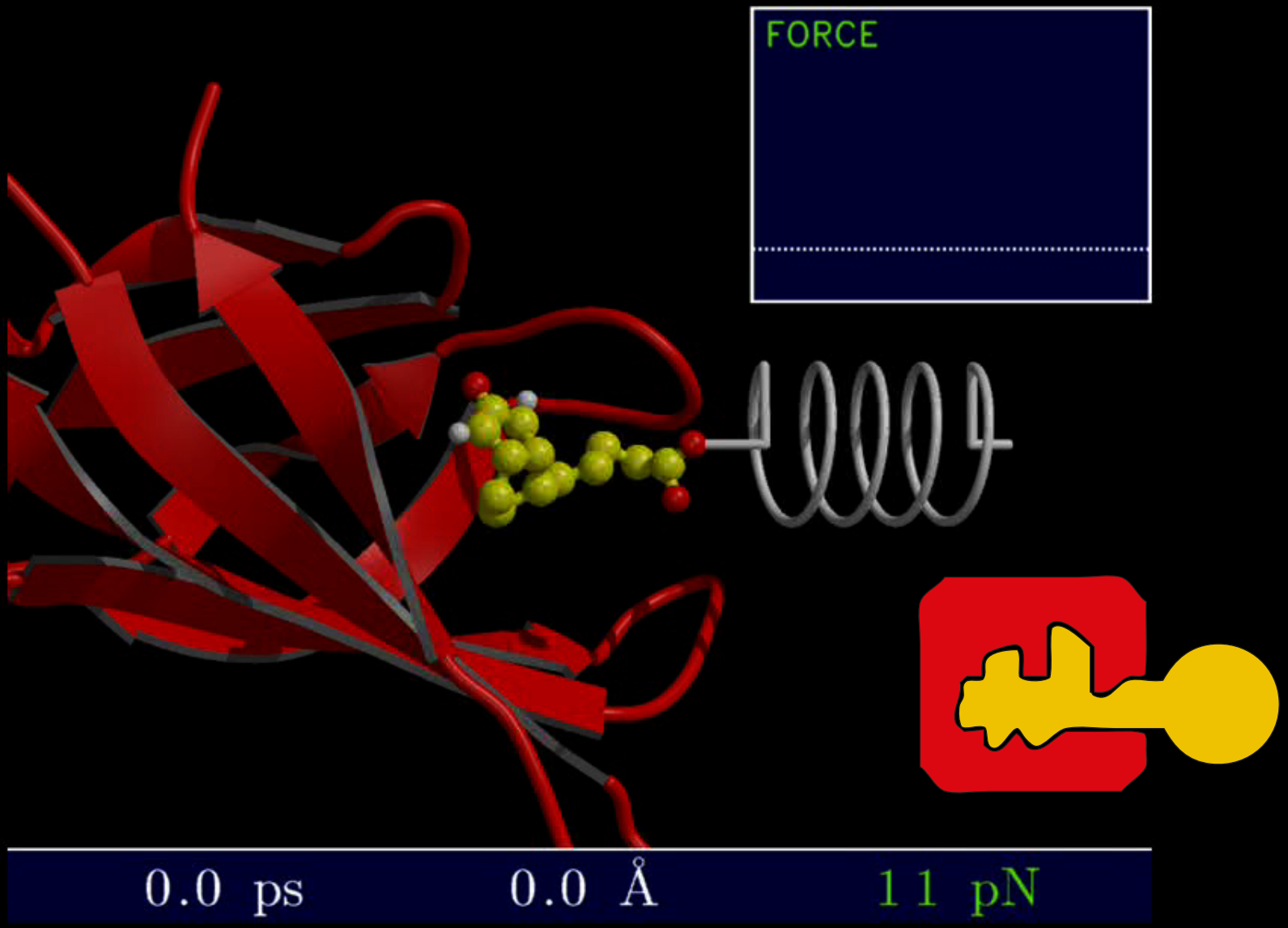






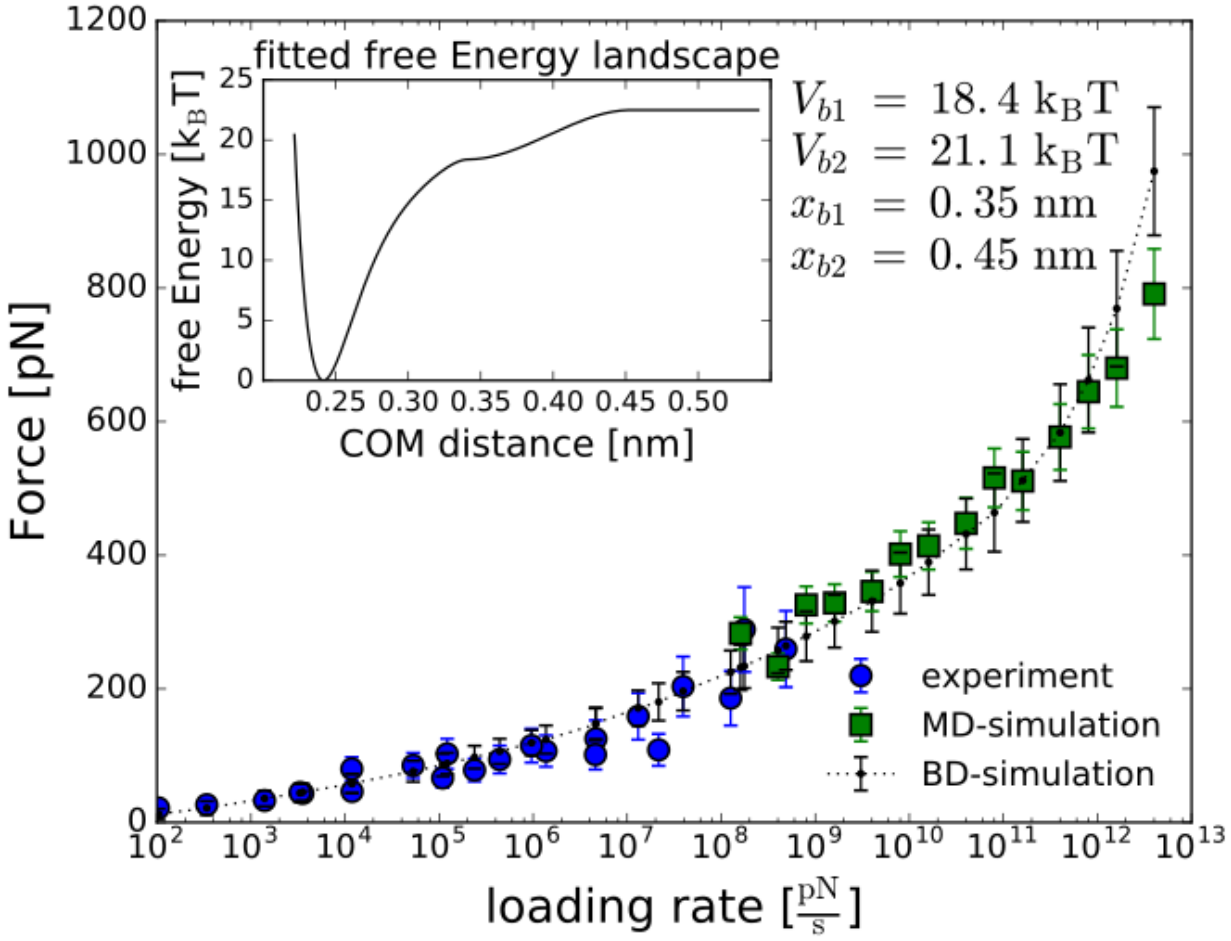
E.-L. Florin, V. T. Moy, H. E. Gaub, *Science* **264**, 415 (1994)

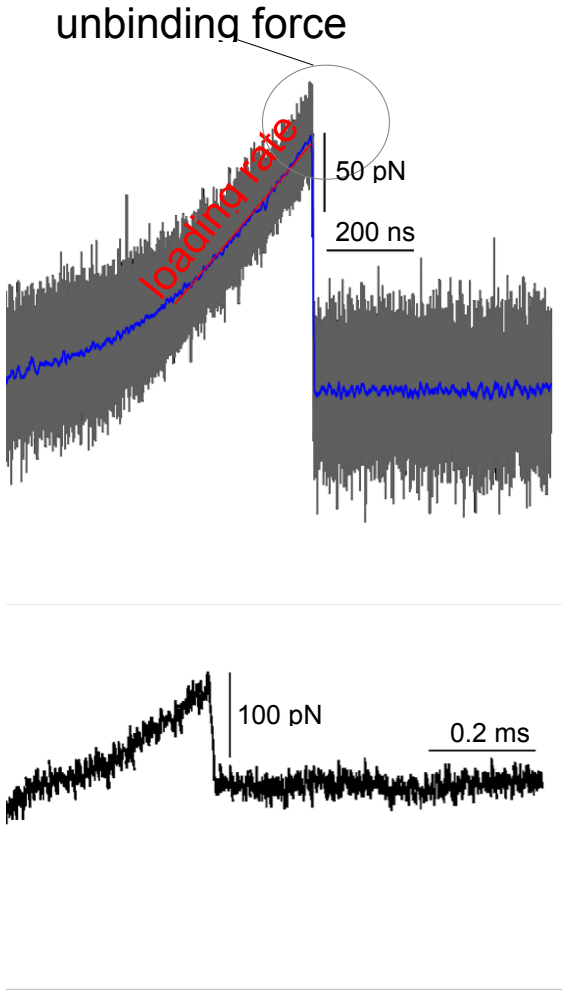
Force probe simulations



H. Grubmüller, B. Heymann, P. Tavan, Science 271, 997, 1996

Exp + Sim -> Free energy landscape





A. Russek, F. Rico, S. Scheuring, H. Grubmüller (in preparation)

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(3) Is nature reproducible anyway?

Statistical Mechanics: environment

Quantum mechanics!

===> Biomolecular function better be robust!!

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(4) Numerical reproducibility

-- use of random numbers

-- single/double etc

-- sequence of operations (parallel...)

-- different CPUs/GPUs

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(5) Software versions, different codes, different approximations

PME, FMM, multistep, v-site....

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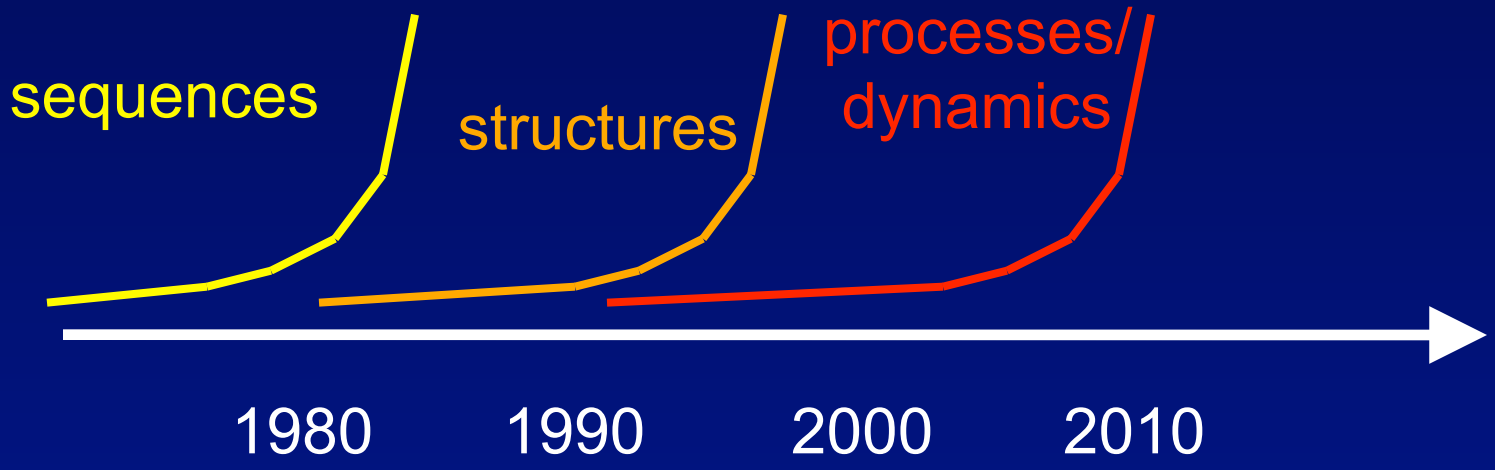
(7) Practical reproducibility: Nobody re-runs a 6 month 100,000 core simulation!

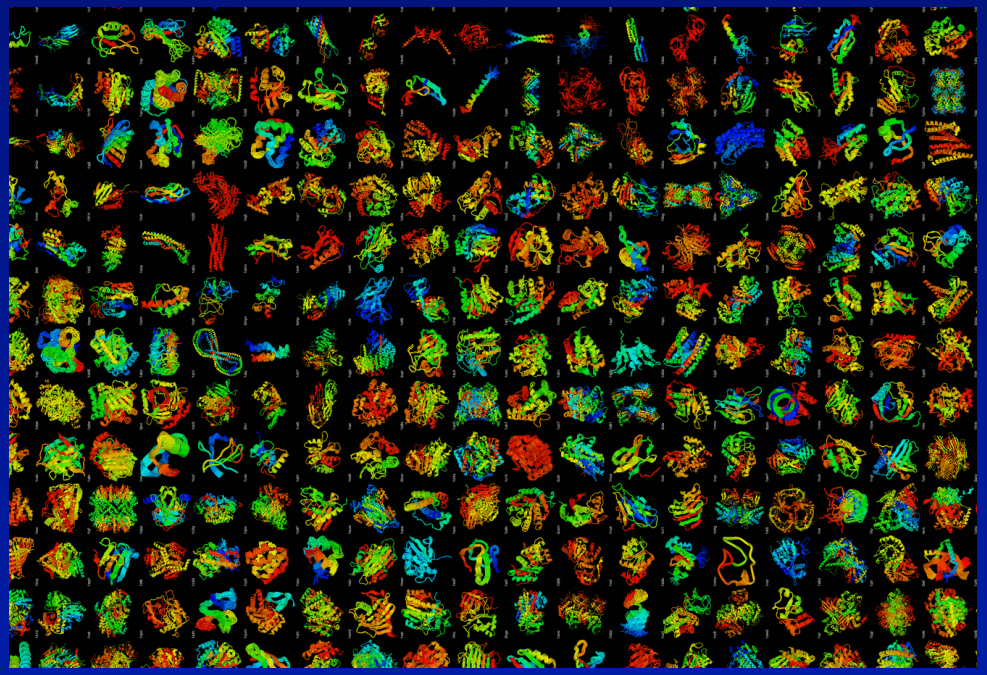
Perspective: The ‚Dynasome‘



Phylogenetic trees

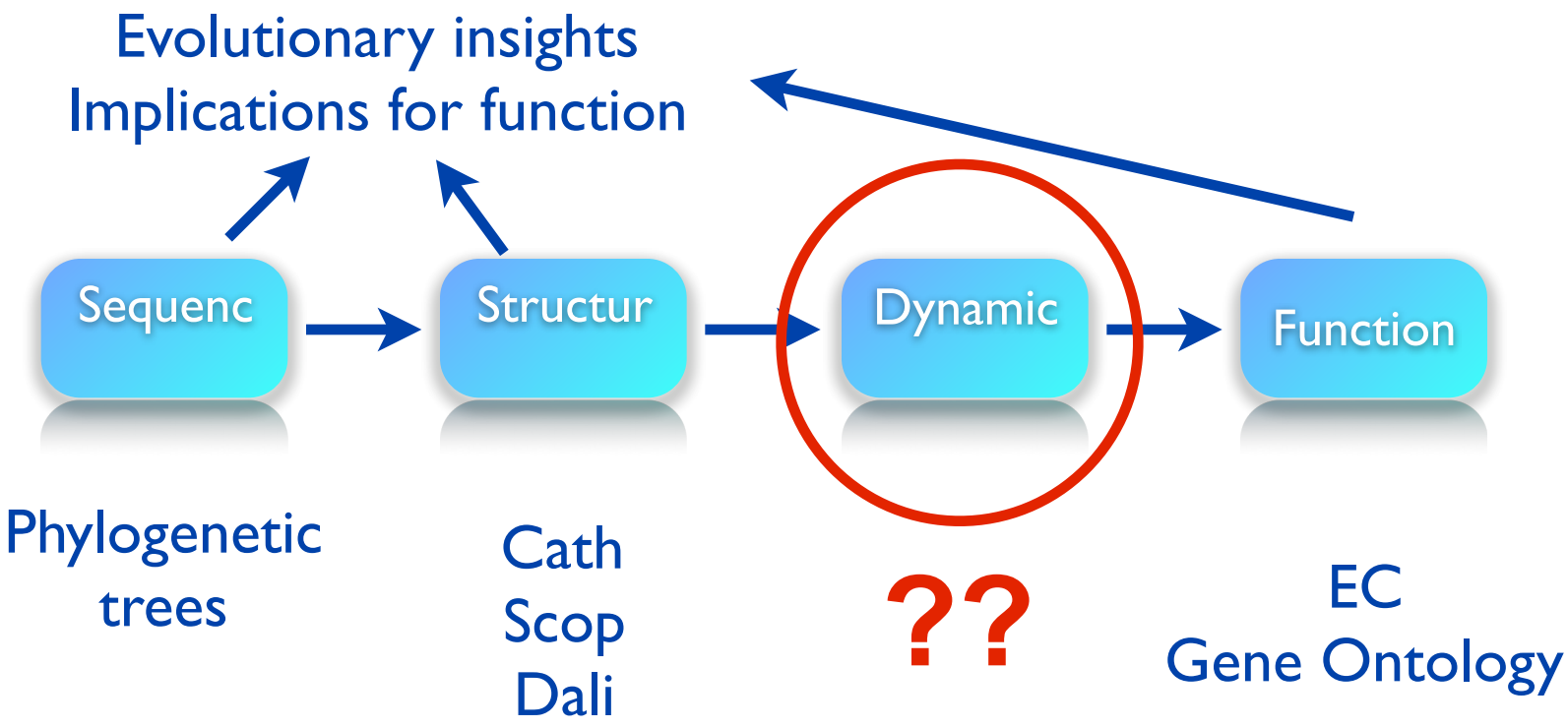
Protein structures fall into families

-> Can we also identify and classify dynamics motifs?



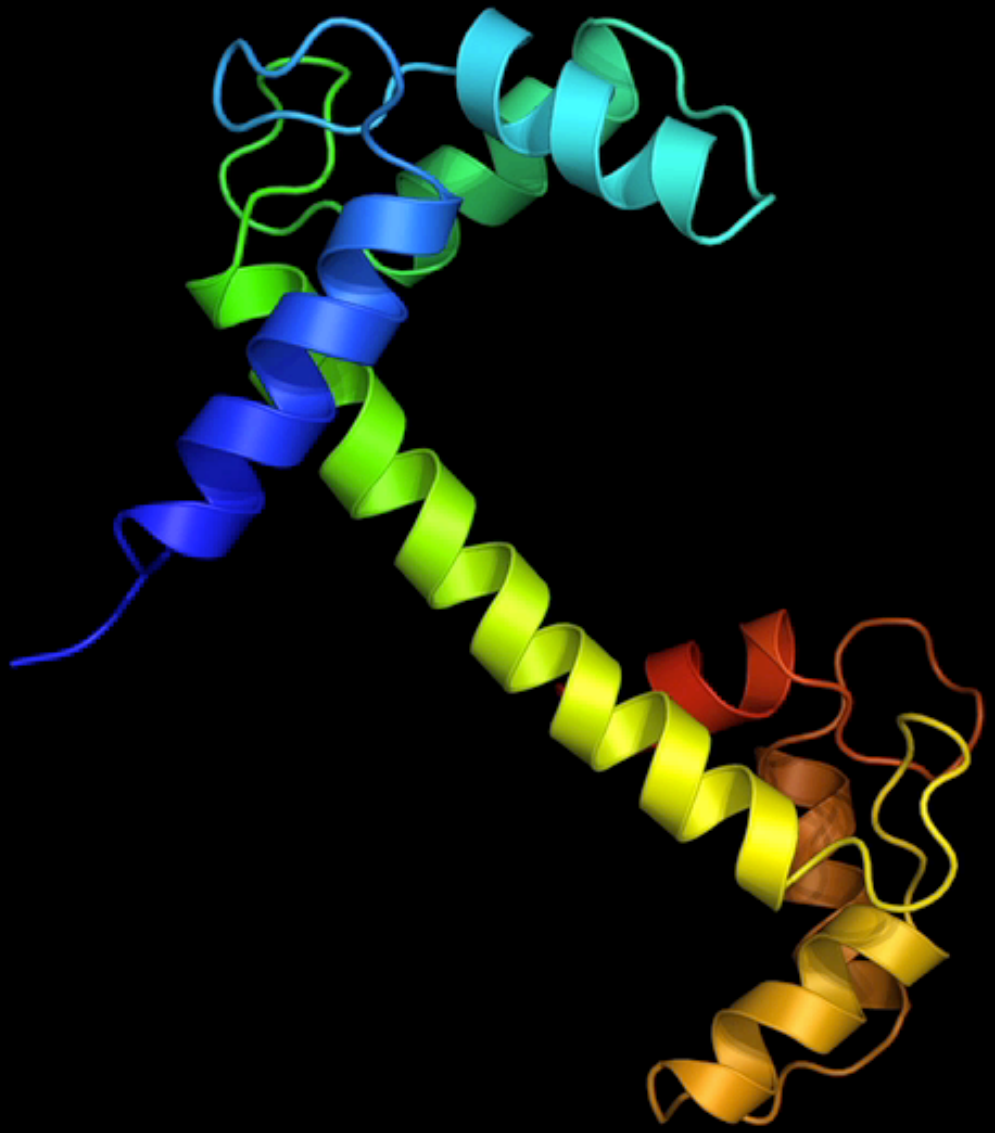
Exploring the protein dynamics space:

Structure / dynamics / function relationship



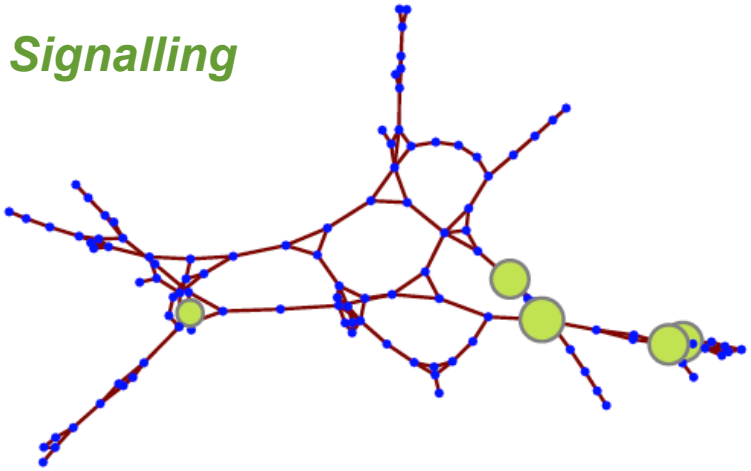
Ulf Hensen, Tim Meyer,
Jürgen Haas, René Rex,
Collaboration: Gert Vriend

Pang A, Arinaminpathy Y, Sansom M, Biggin P (2005) Proteins 61: 809–822.
Meyer T, de la Cruz X, Orozco M (2009) Structure 17: 88–95.
Jonsson AL, Scott KA, Daggett V (2009) Biophysical Journal 97: 2958–2966.

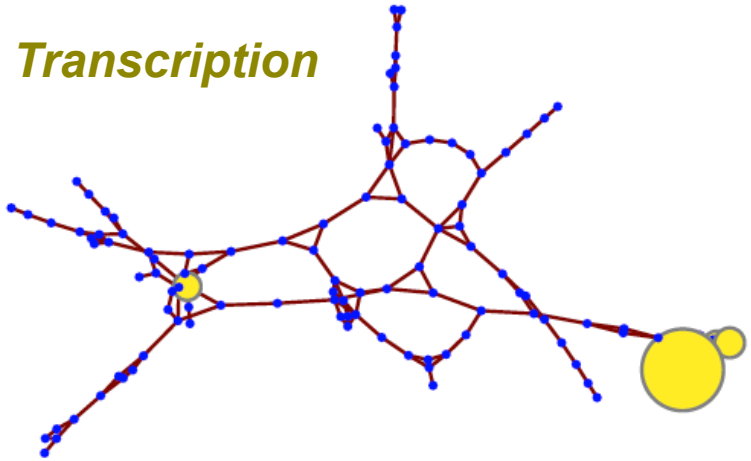


Dynamics correlates with function!

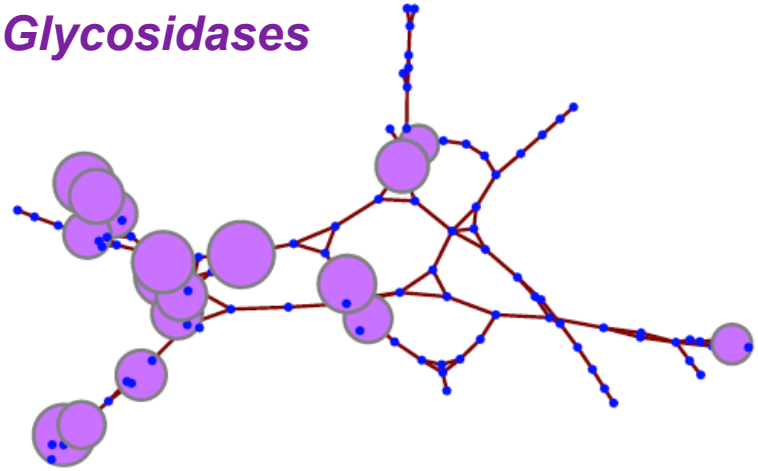
Signalling



Transcription



Glycosidases



Proteinases