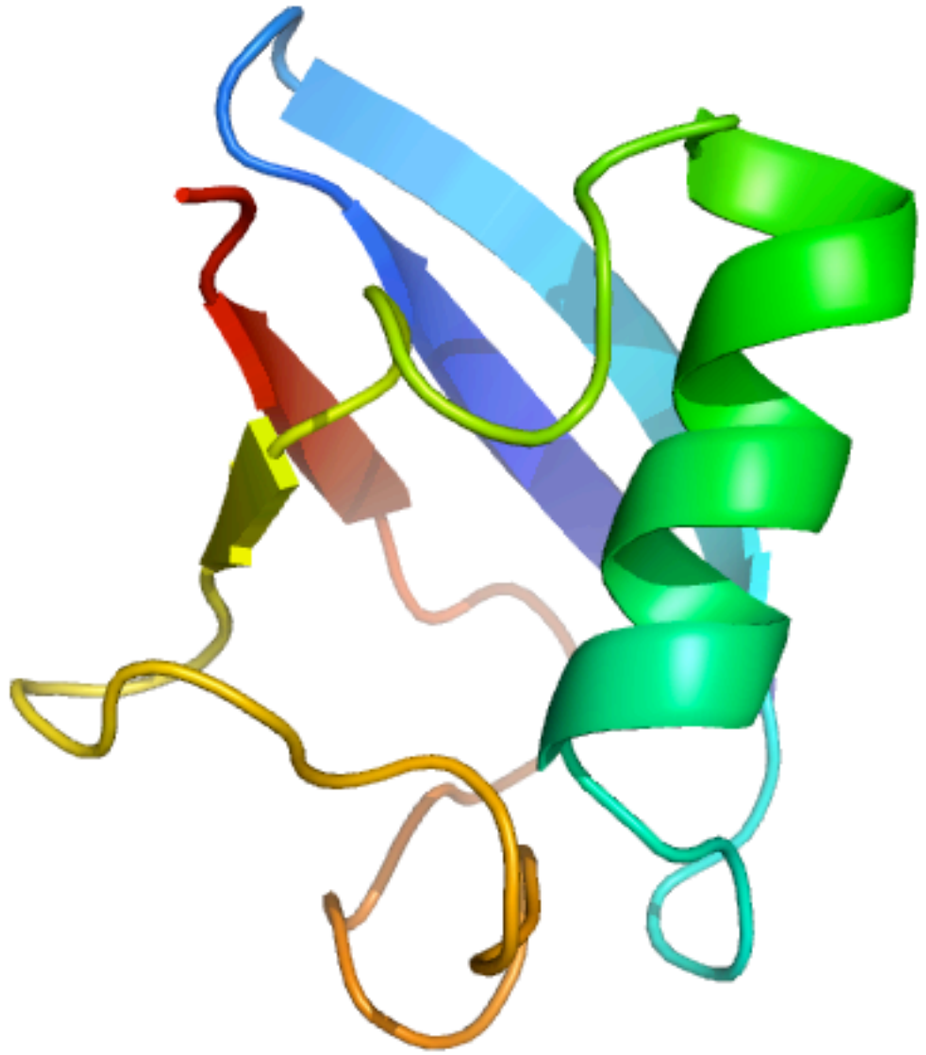
Markov State Models

Gregory R. Bowman
Miller Fellow
University of California, Berkeley

Defining “The Protein Folding Problem”



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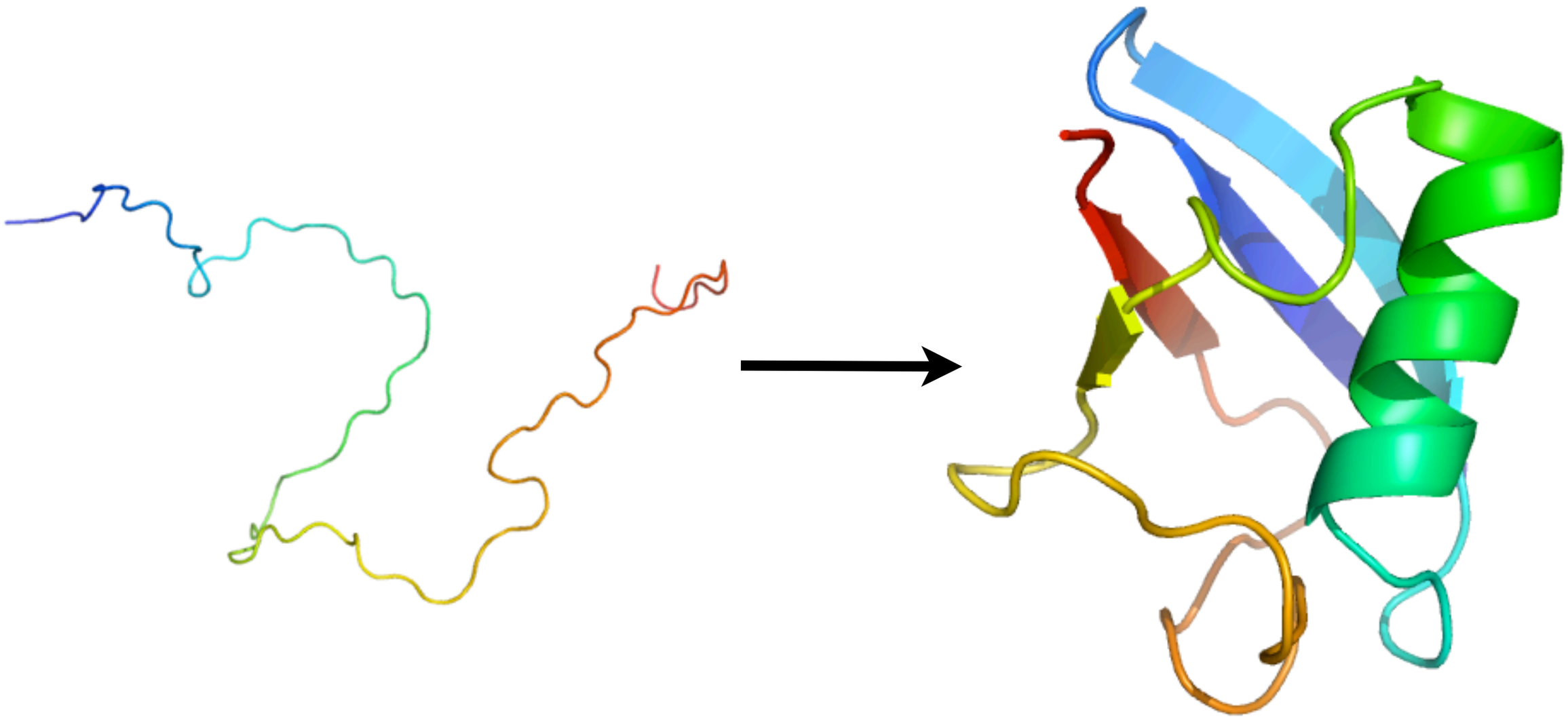

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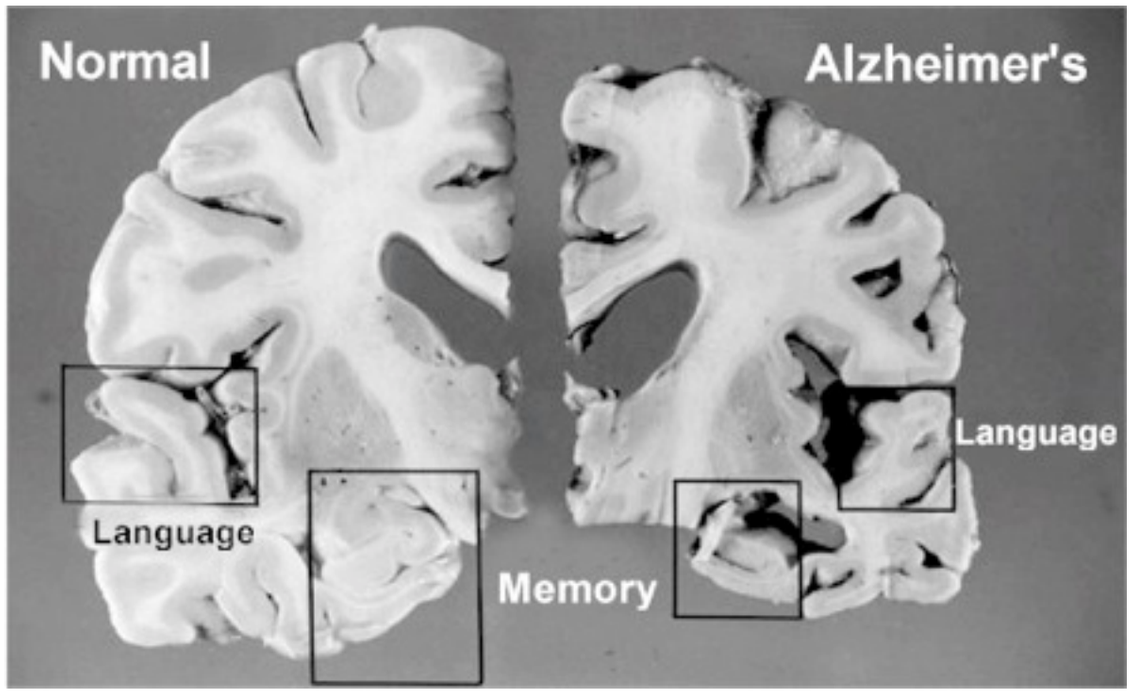

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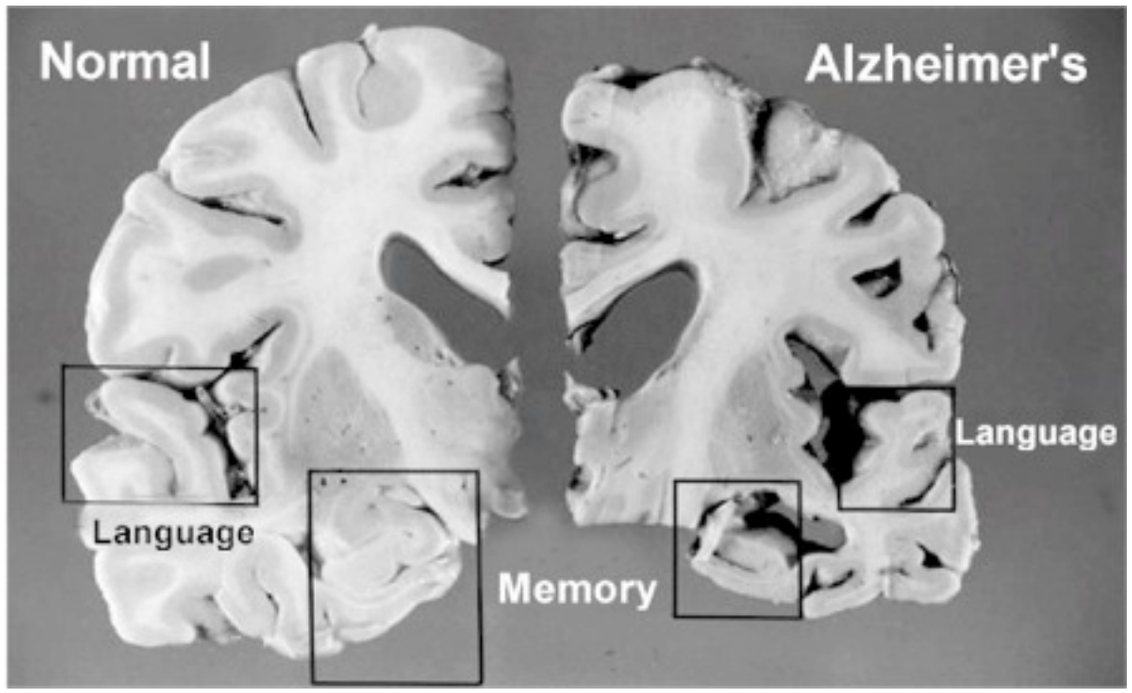
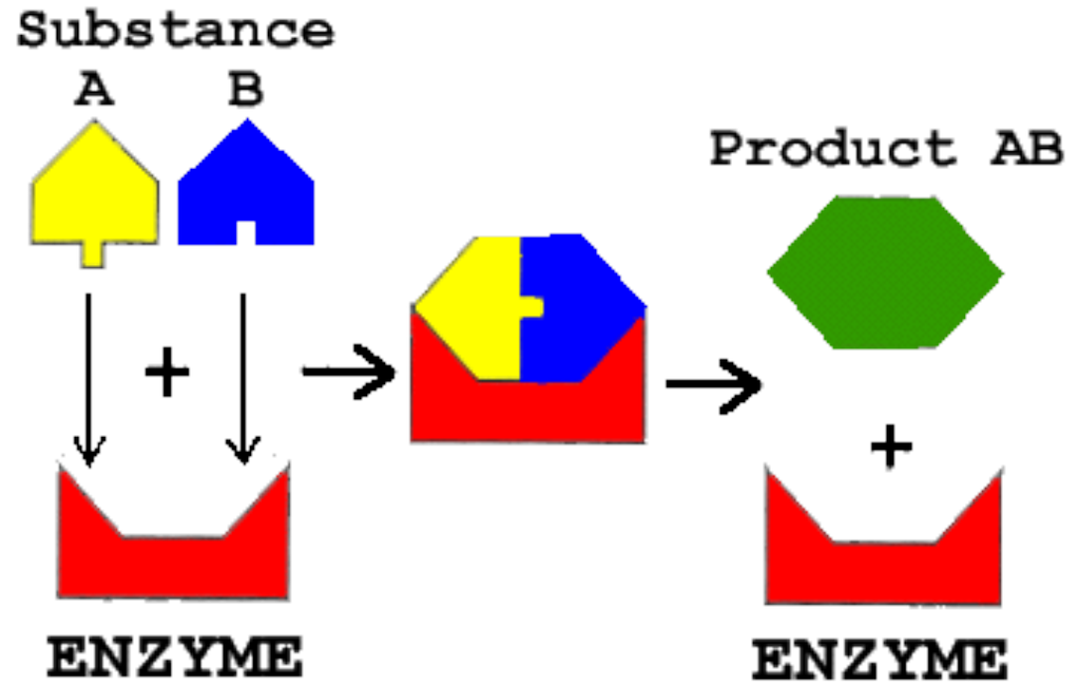
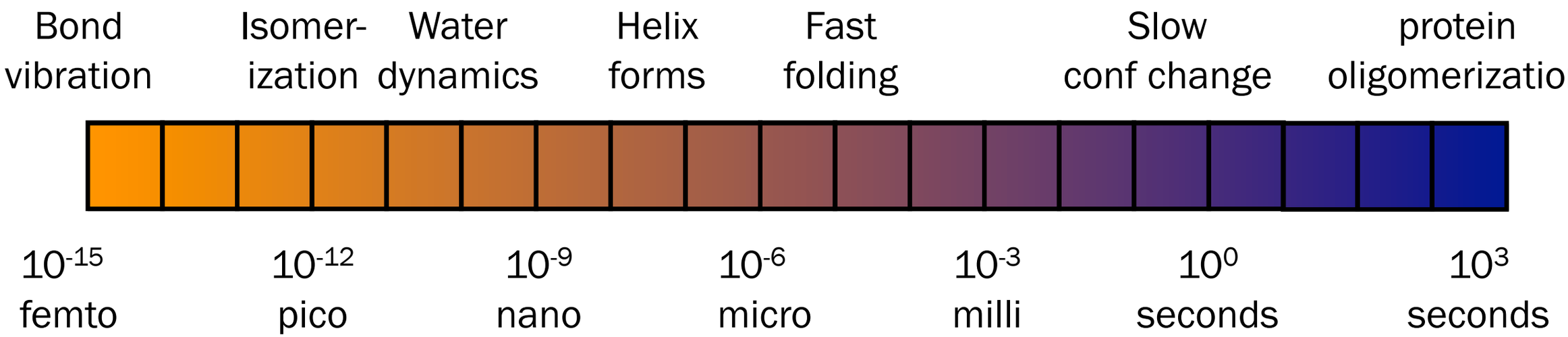


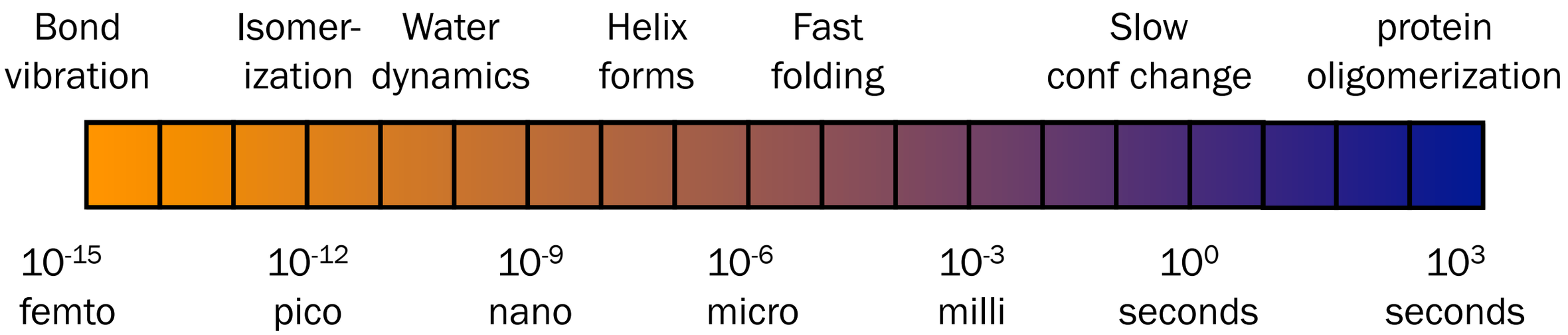


The Sampling Challenge



MD step

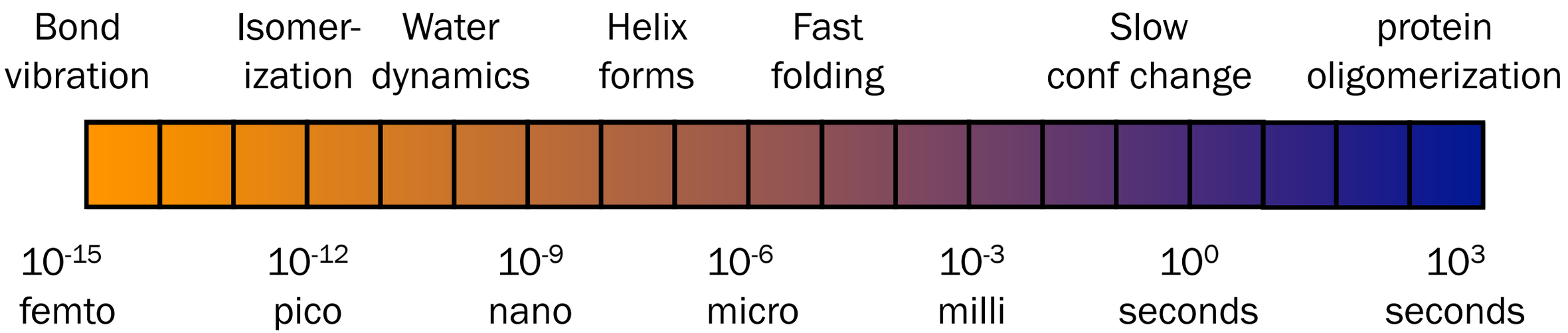
The Sampling Challenge



MD step

where we'd love to be

The Sampling Challenge



MD step

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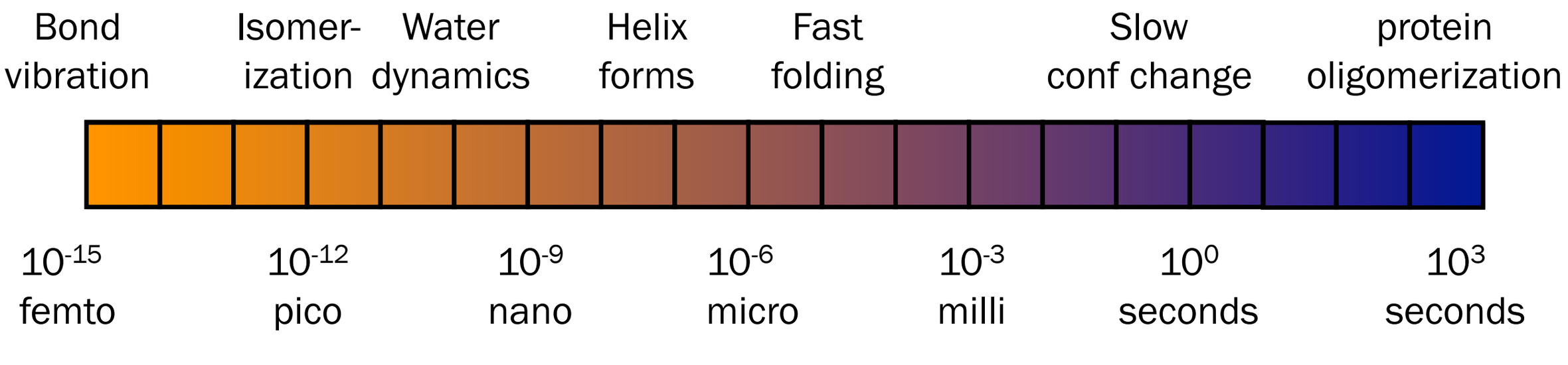

MD step

long MD run

where we'd love to be

Tuesday, August 16, 2011

Markov State Models (MSMs)

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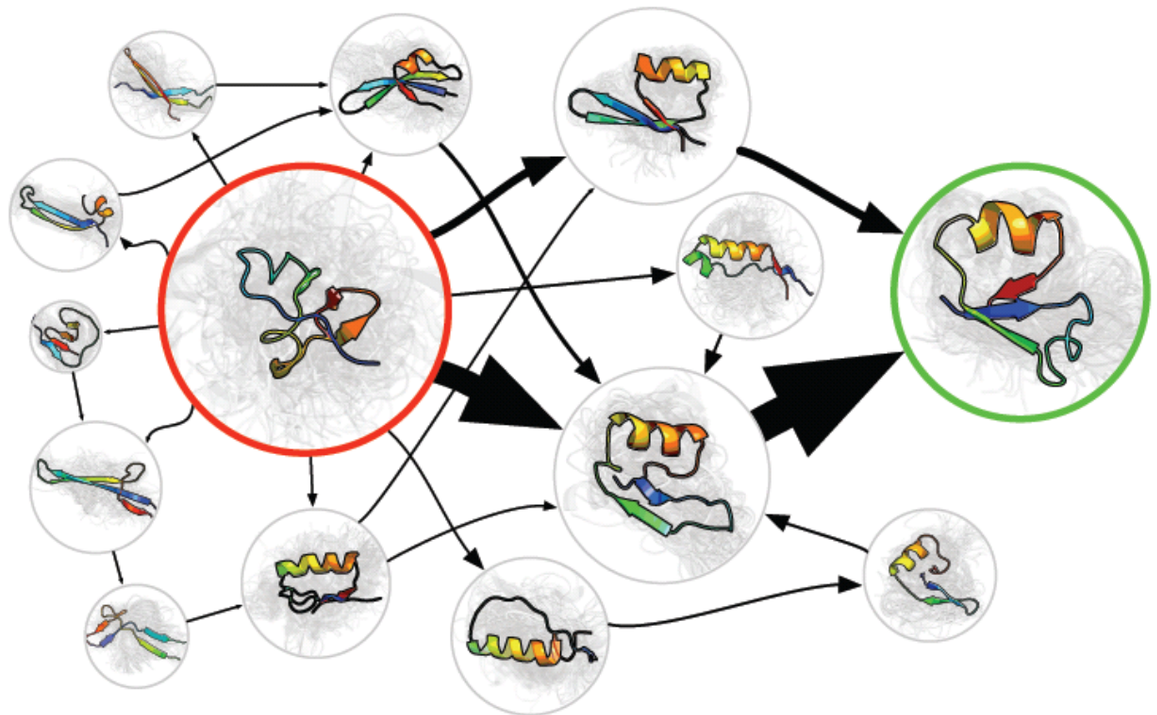
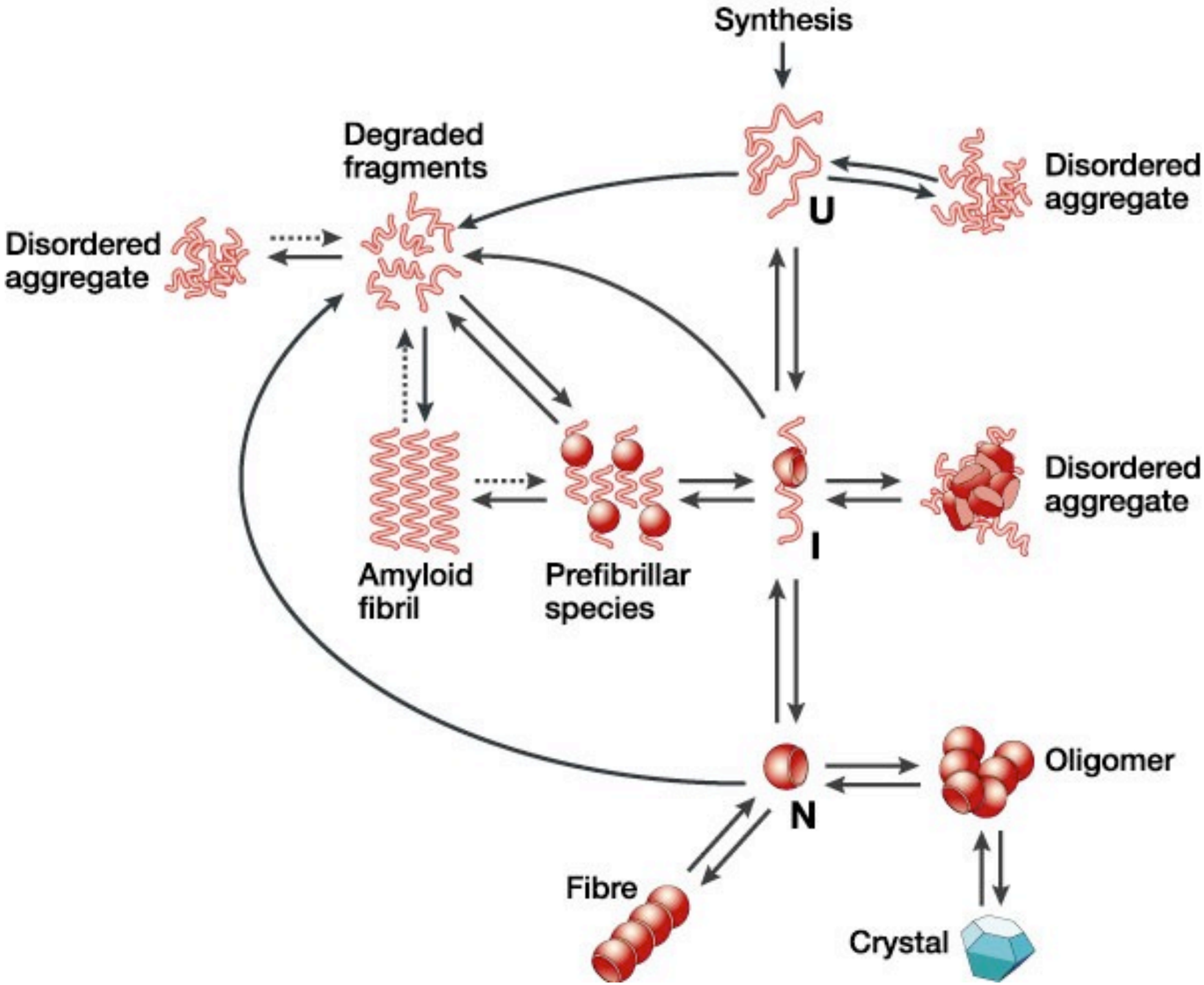


How to Build an MSM



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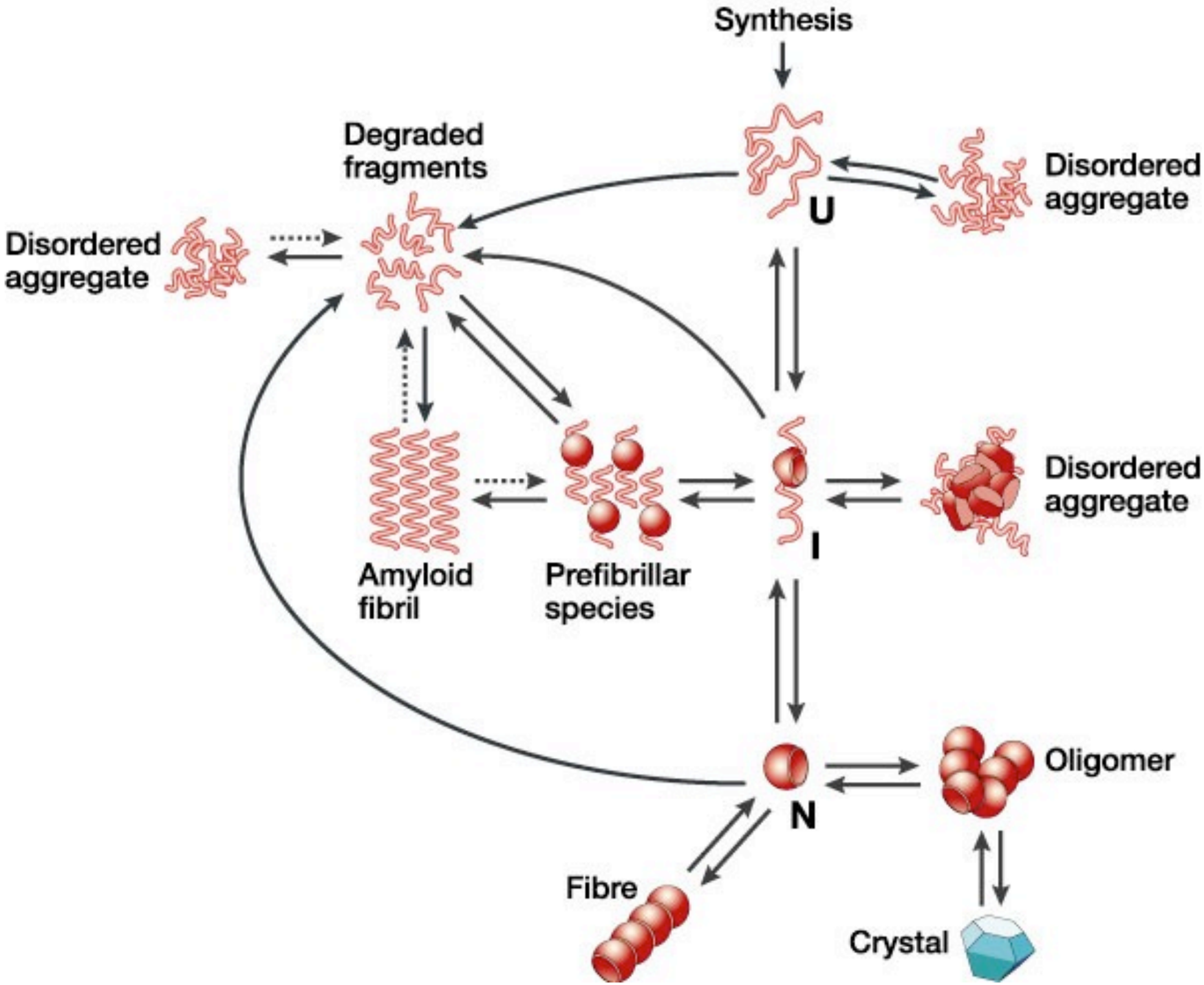
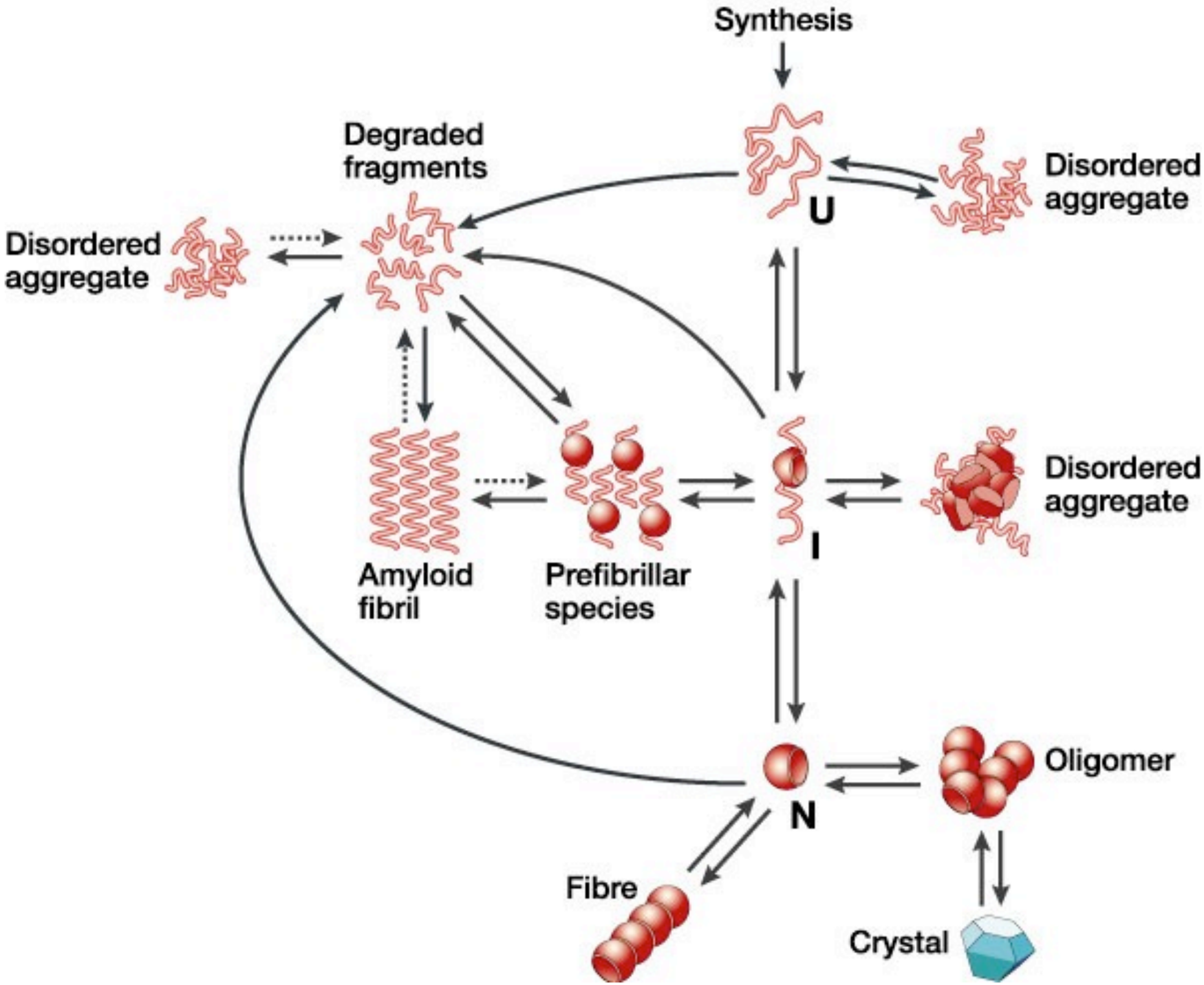
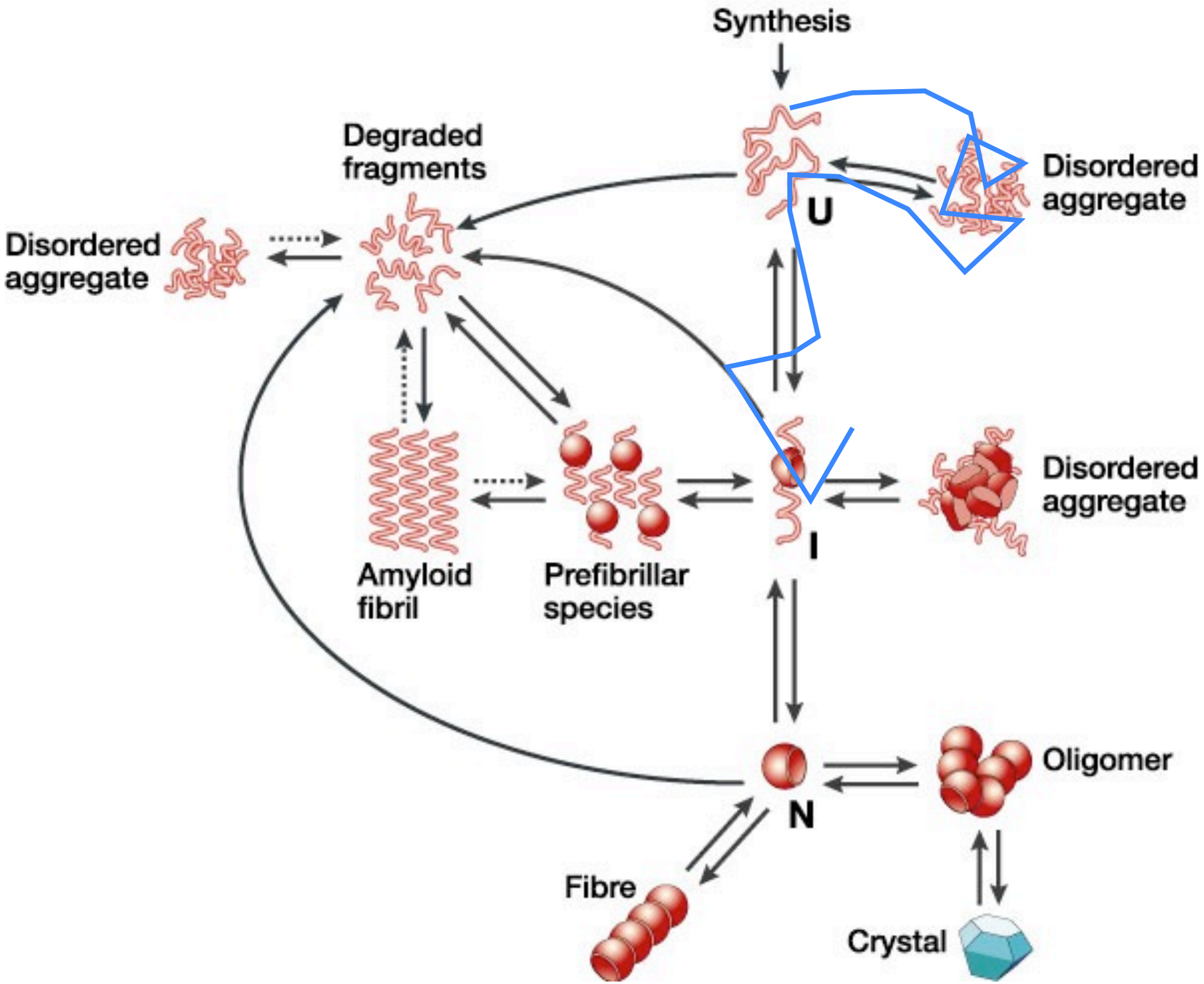


Sample


Synthesis
Degraded fragments
Disordered aggregate
U
Disordered aggregate
Amyloid fibril
Prefibrillar species
I
Disordered aggregate
N
Oligomer
Fibre
Crystal

Sample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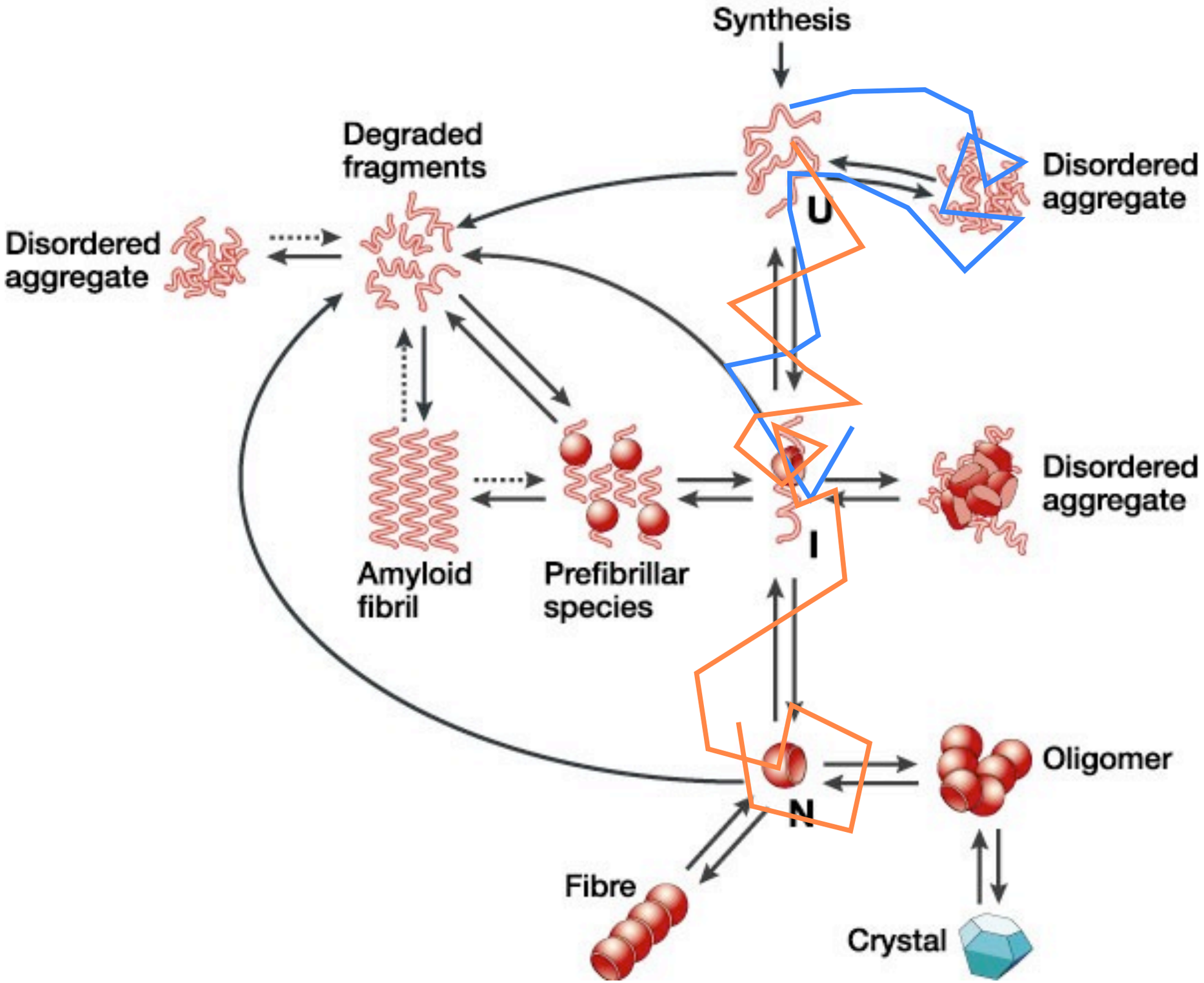
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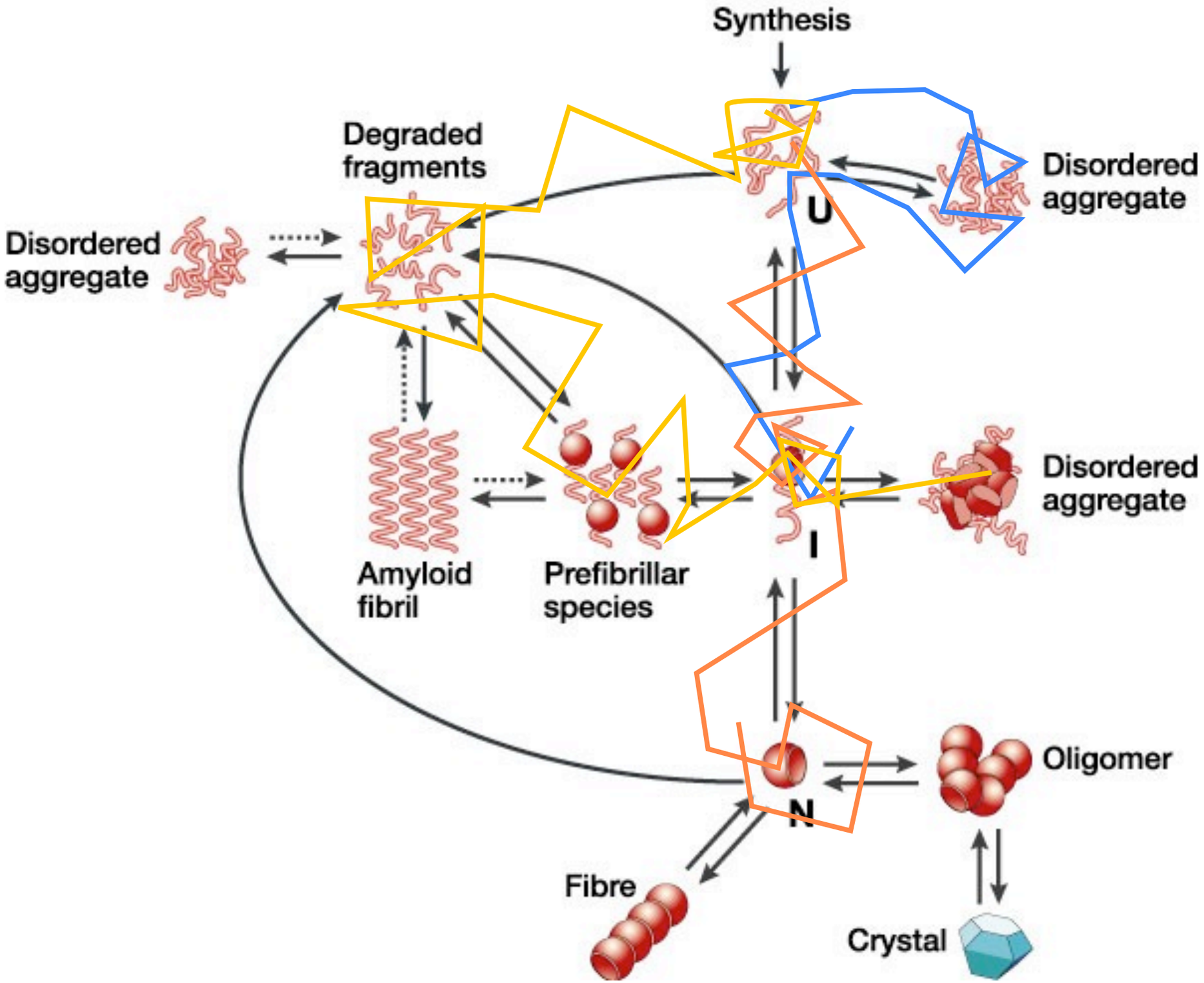
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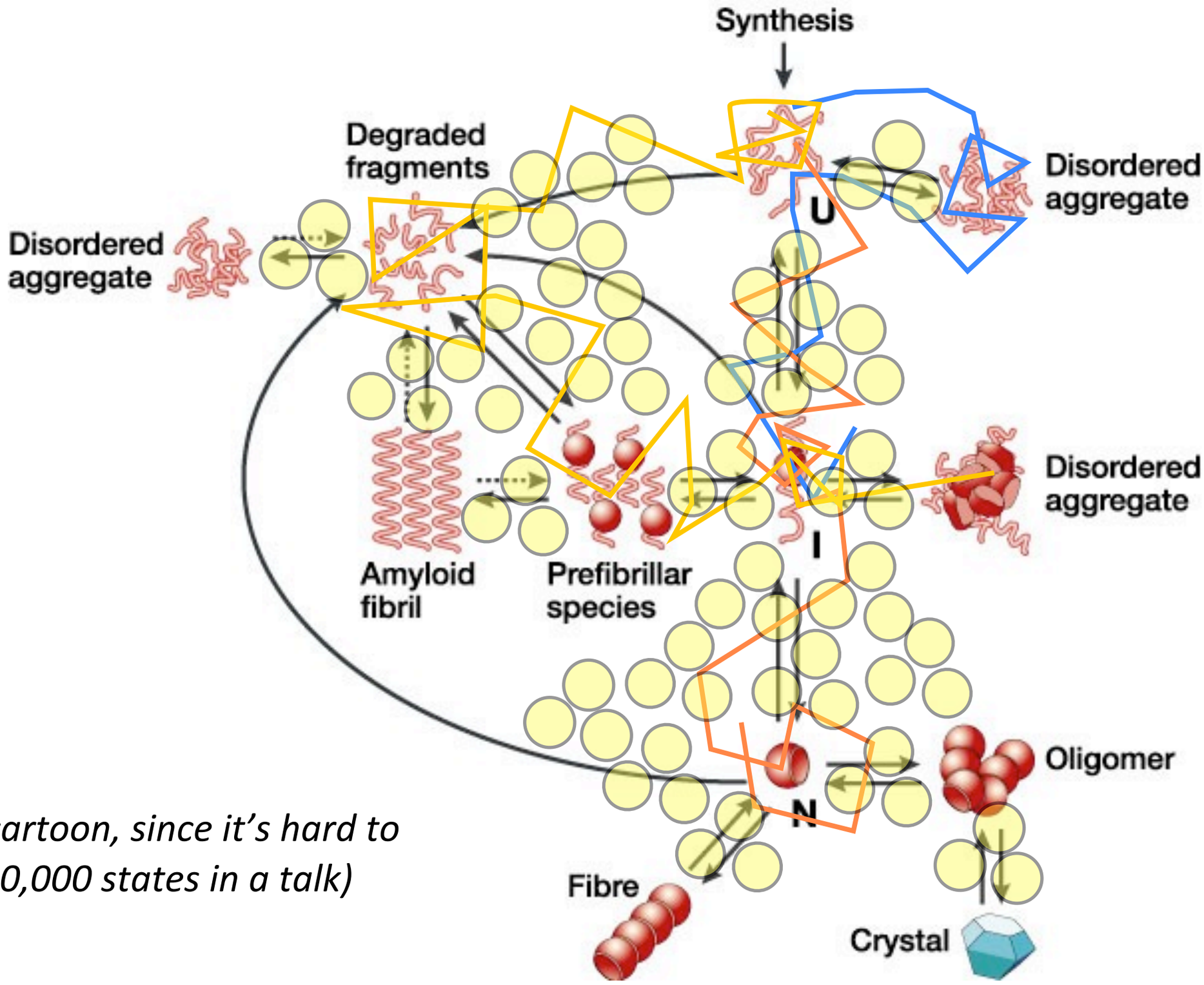
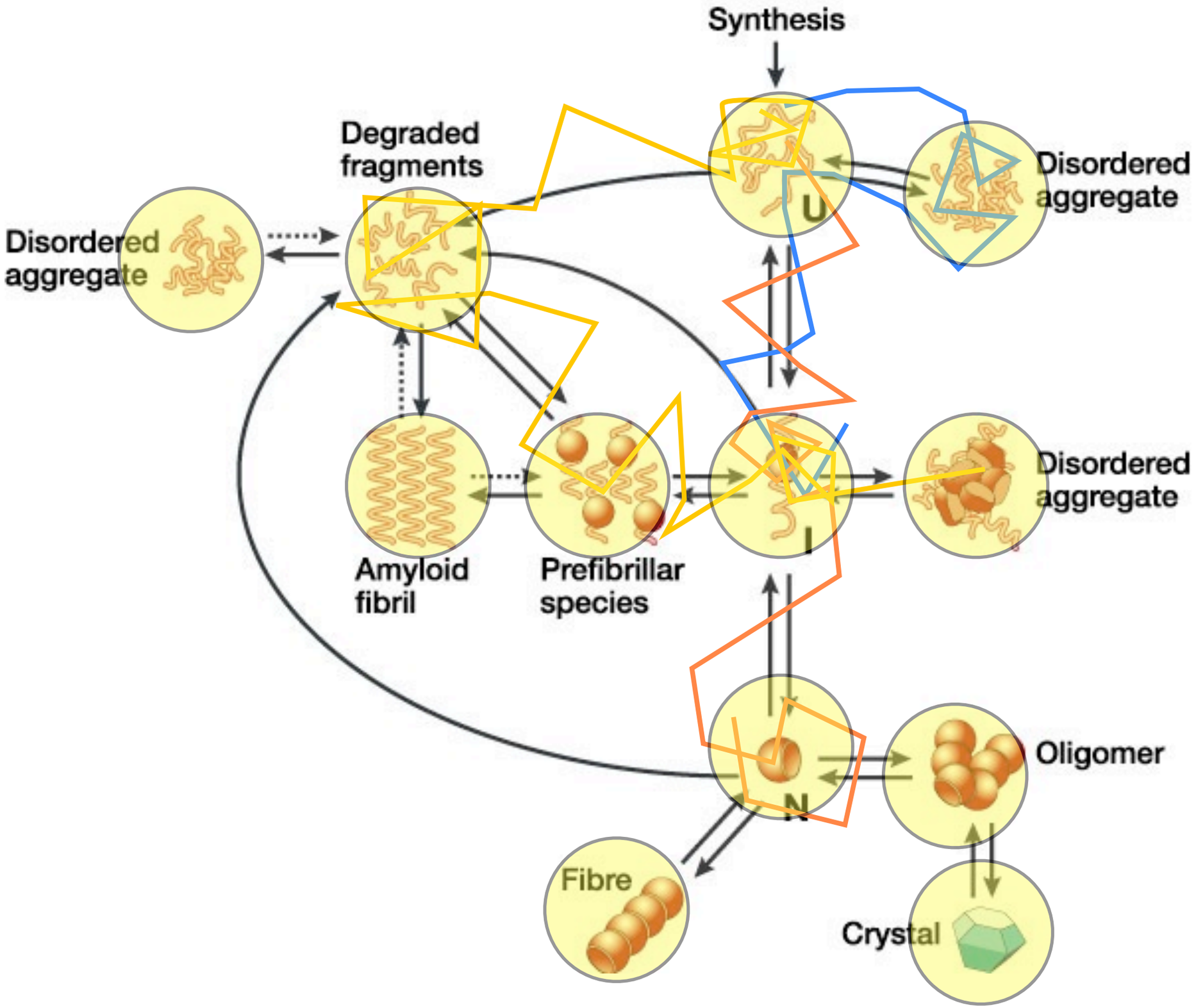
Clustering Gives a High-resolution Model



(this is a cartoon, since it's hard to draw 10,000 states in a talk)

Lumping Provides Human Intuition

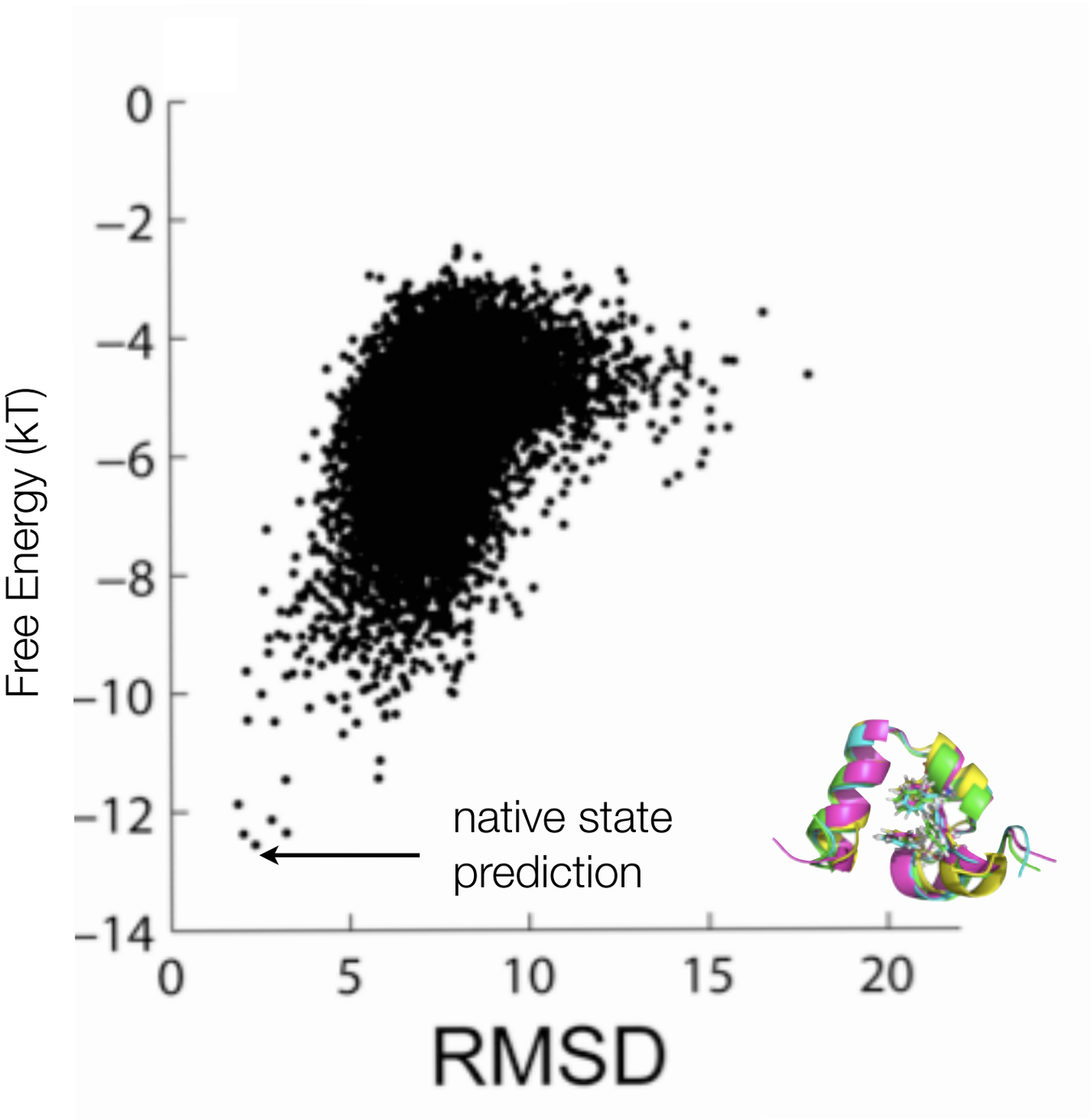


Under the Hood

$$T(\Delta t) = \begin{pmatrix} 0.8 & 0.05 & 0.1 & \dots \\ 0.1 & 0.6 & 0.1 & \dots \\ 0 & 0.02 & 0.9 & \dots \\ \dots & \dots & \dots & \dots \end{pmatrix}$$

$$p(t+\Delta t) = T(\Delta t)p(t)$$

Modeling Experiments



Bowman, Beauchamp, Boxer, and Pande. JCP 2009.
Bowman, Voelz, and Pande. JACS 2011.

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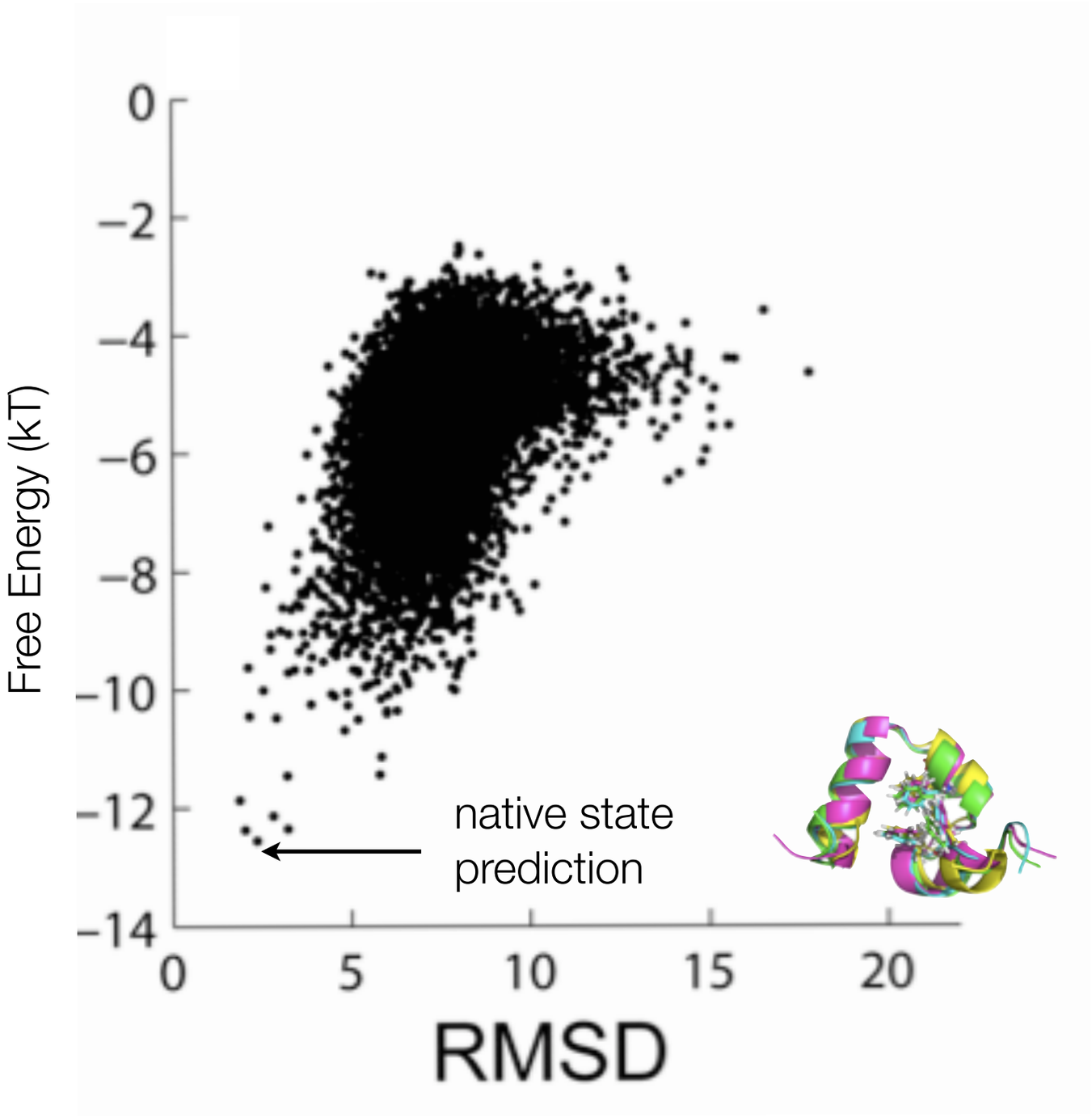

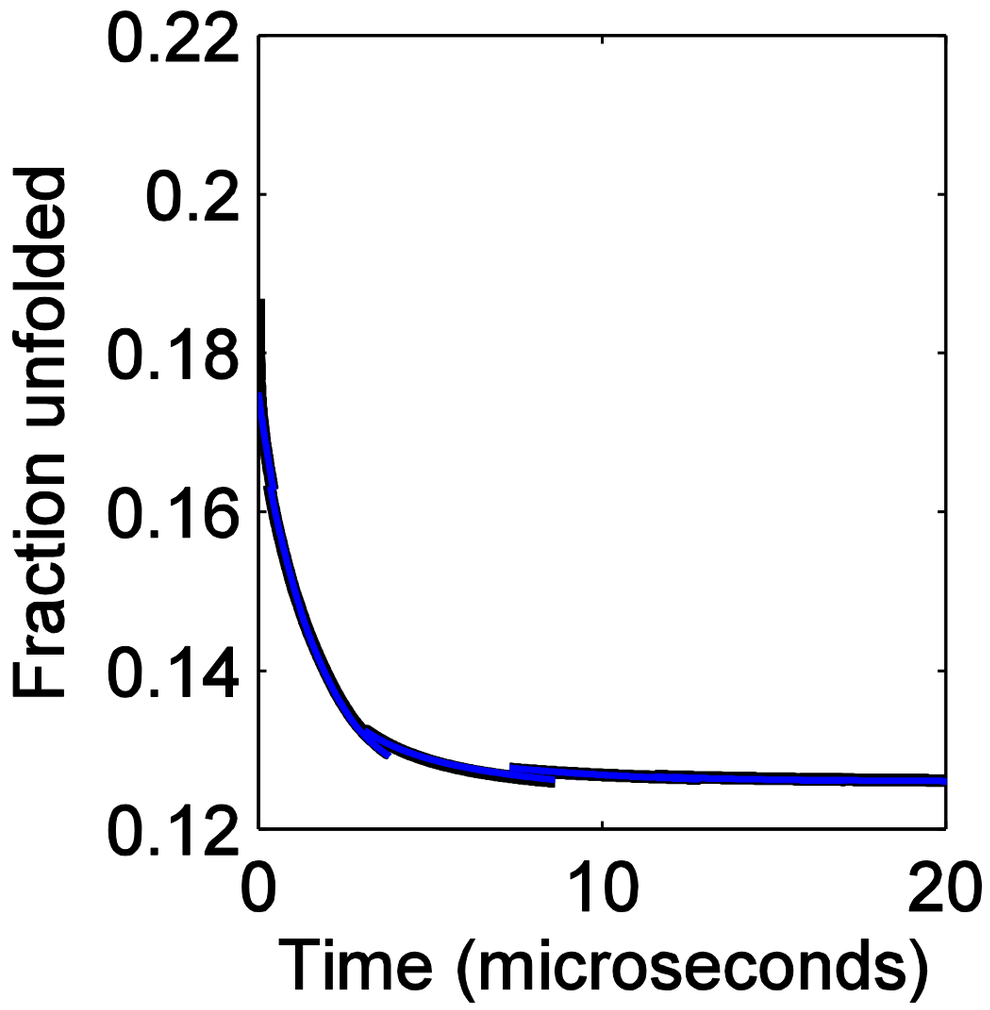

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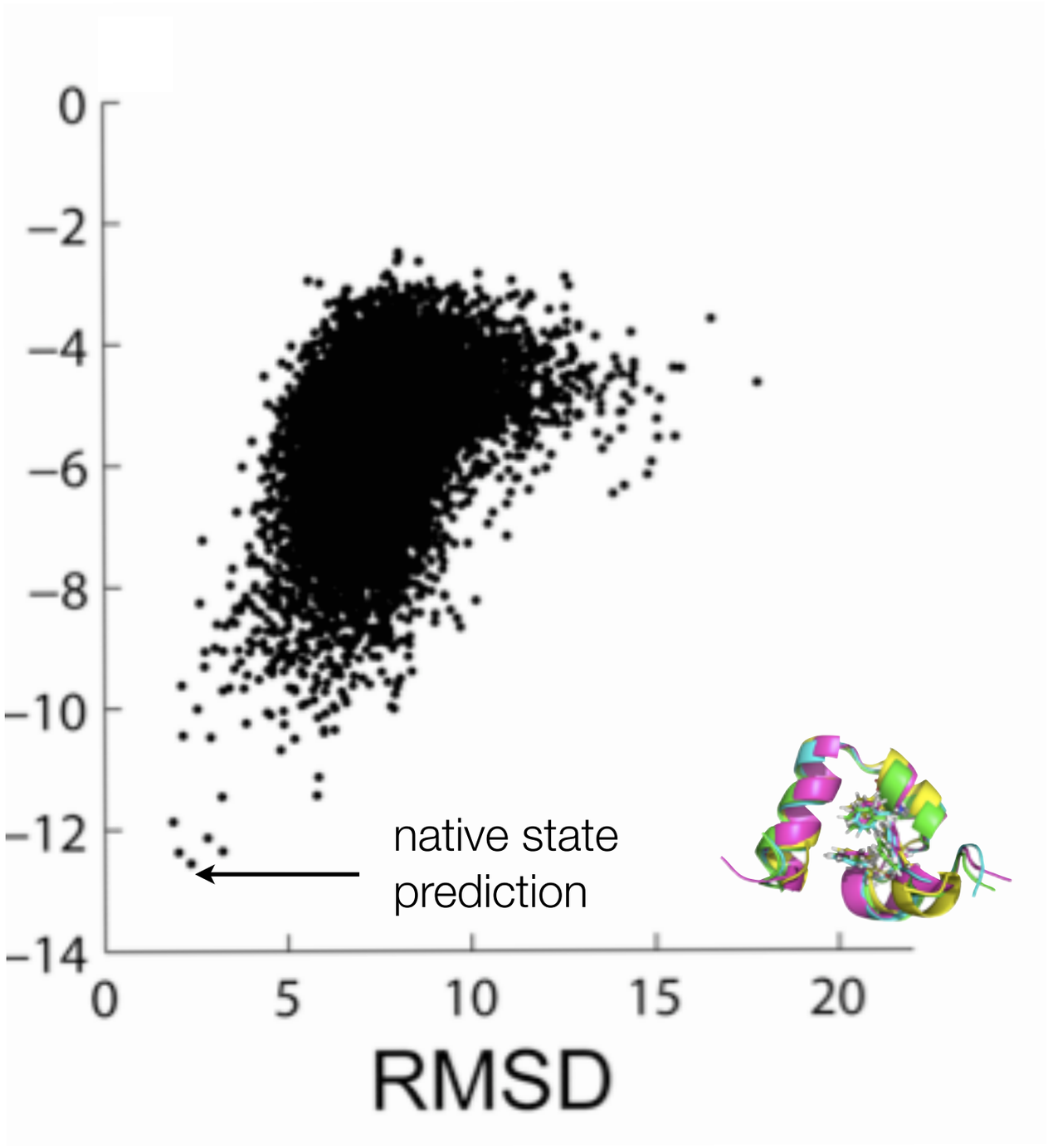

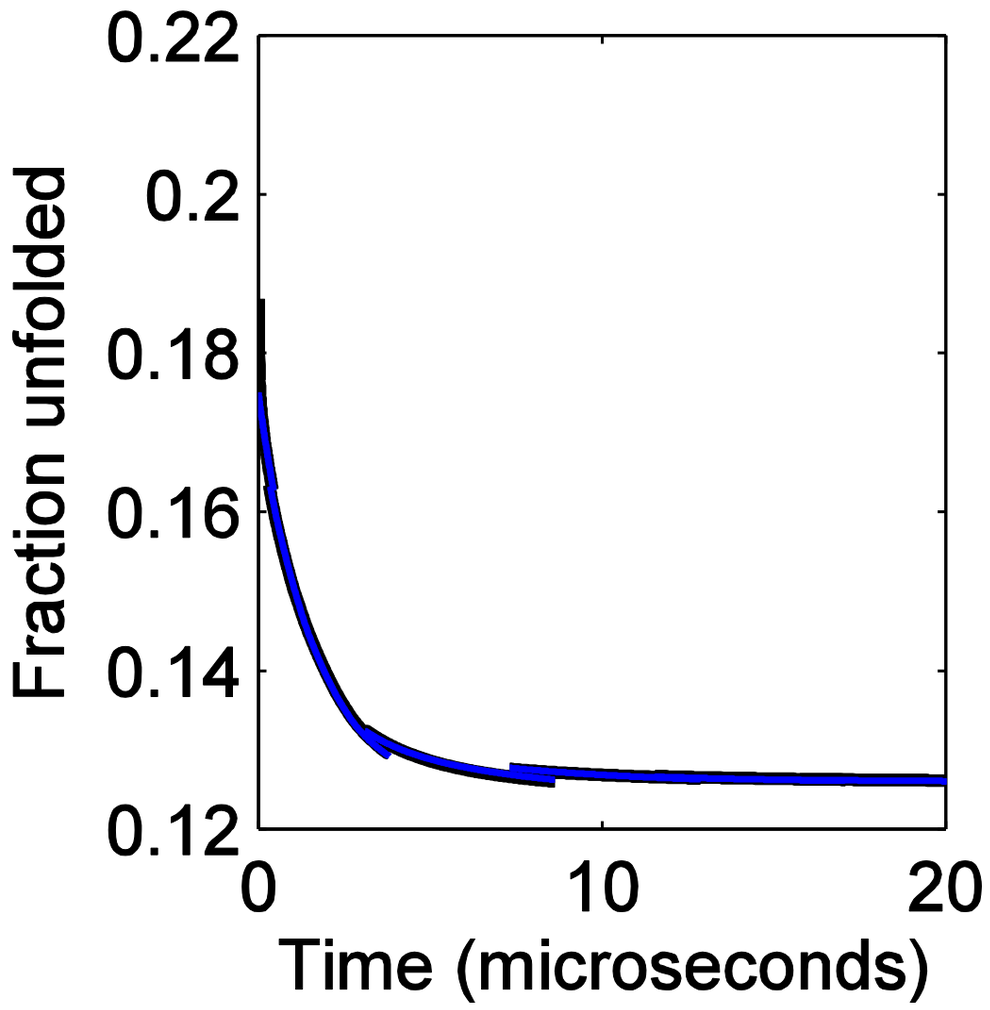

$p(t+\Delta t) = T(\Delta t)p(t)$

$Obs(t) = p(t) \bullet Obs$

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One Area Where We Need Help…

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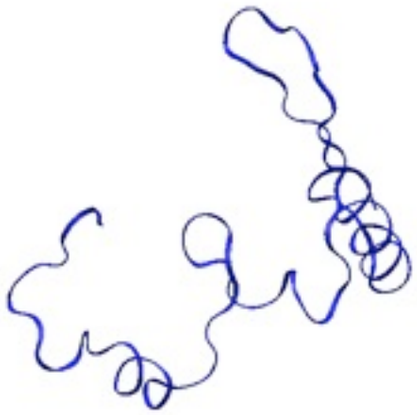
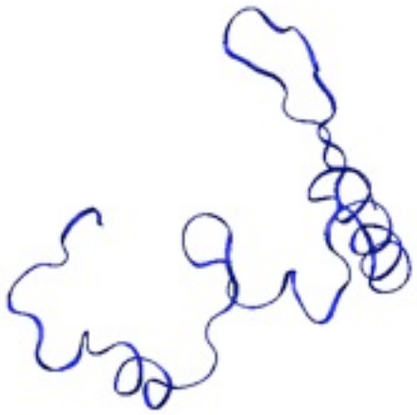


Jump-starting an MSM with Rosetta



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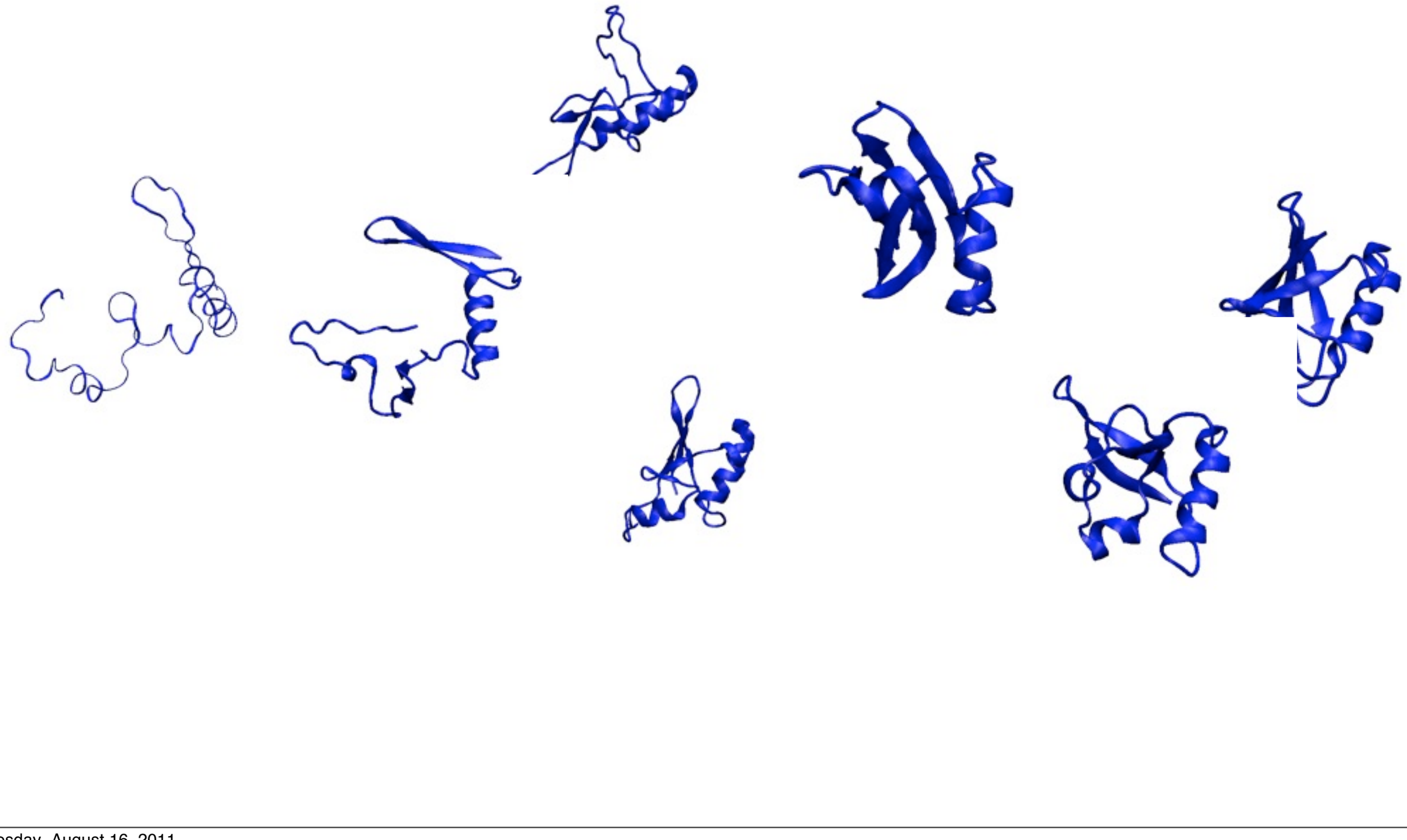

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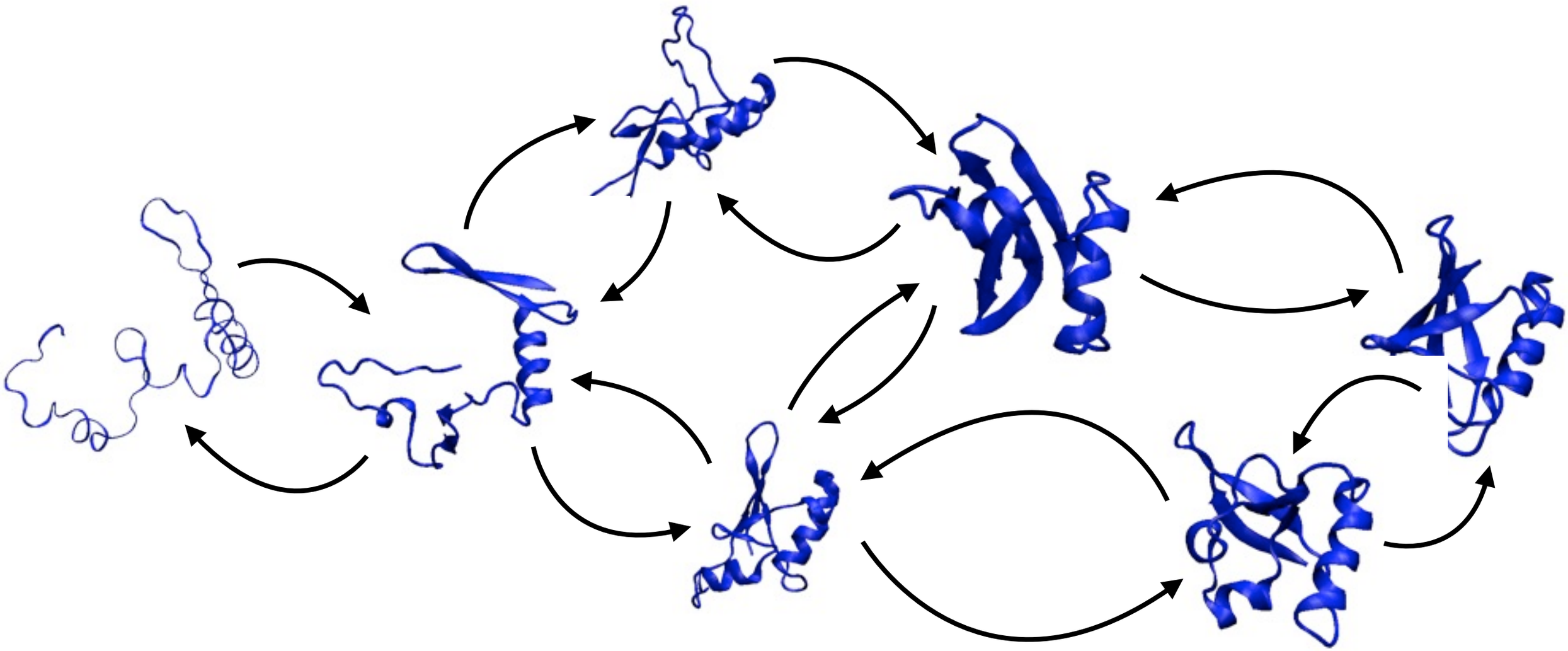

What Can We Do For You?

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Dynamics in Design

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Sampling

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Force Field Assessment

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Conclusions

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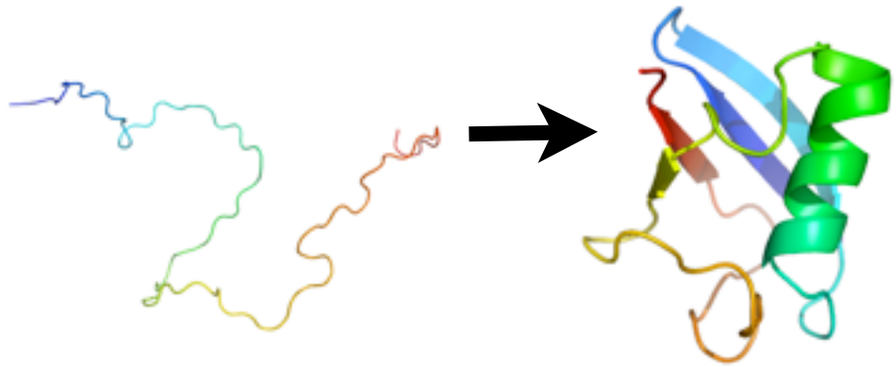
Mechanism is important



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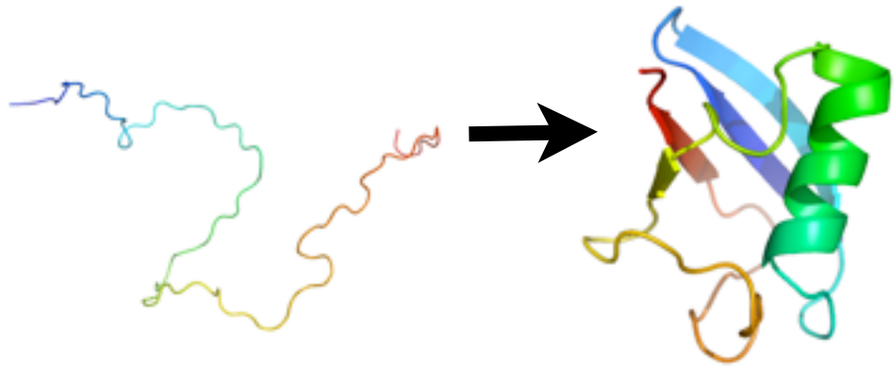

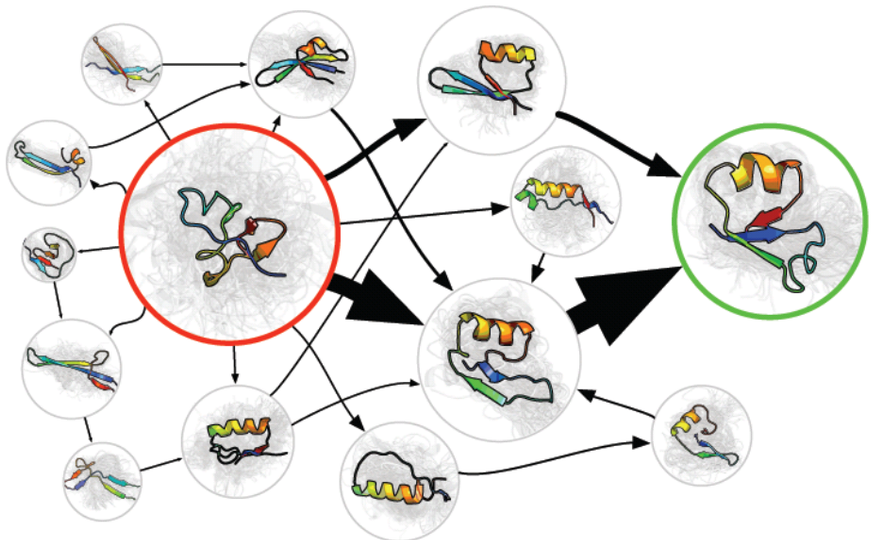

Markov state models are a powerful way of capturing the mechanisms of conformational change

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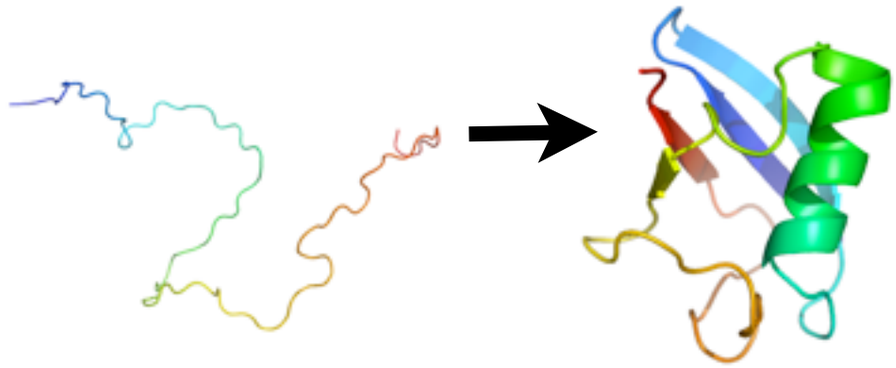

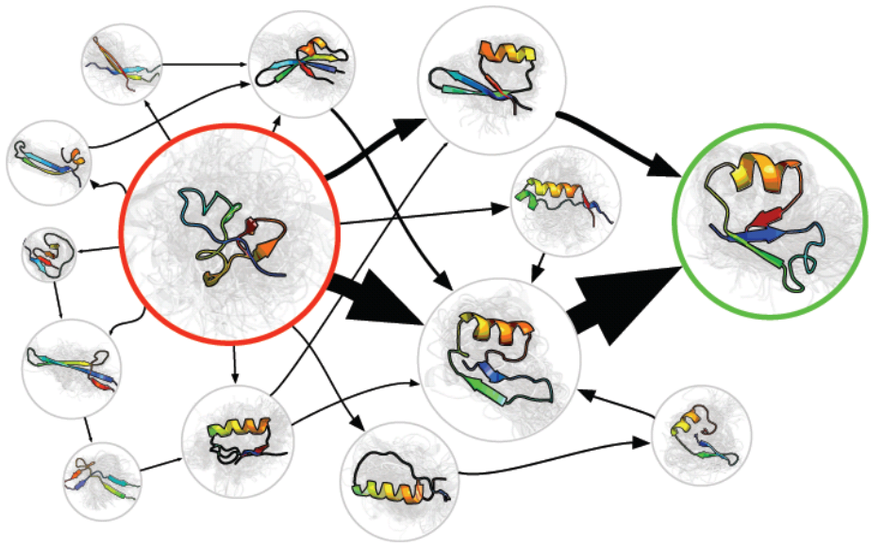

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There's lots of room for collaboration!

Thanks!

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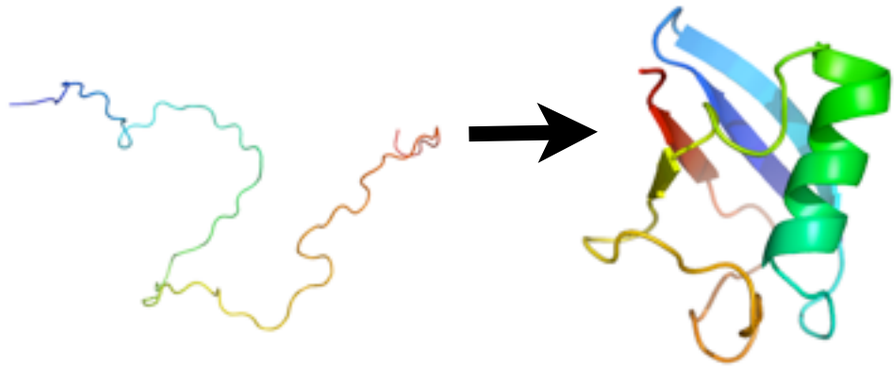

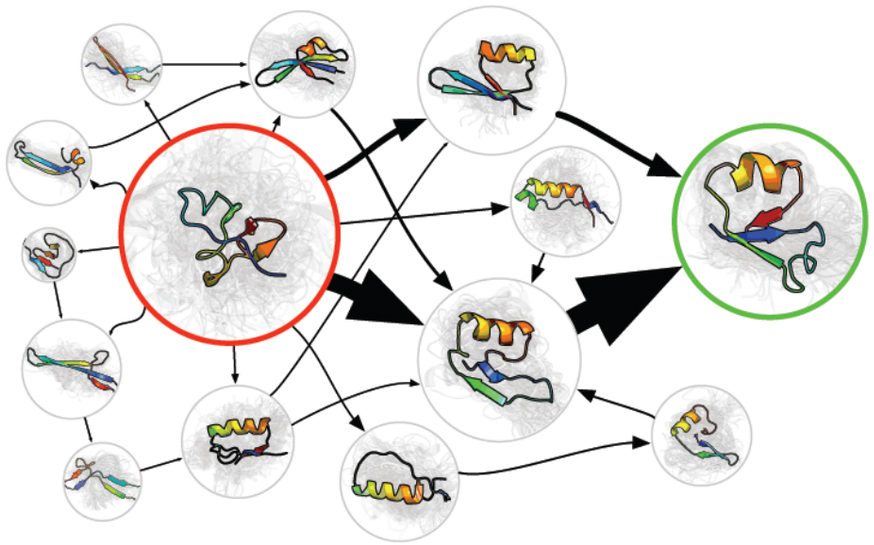

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