Bridging Sequence Evolution and Structural Dynamics - Evol
sequence >structure >dynamics function
sequence of the second of the
1) Sequence encodes structure
2) Each structure has a unique dynamics 3) Dynamics is functional
? Did sequences evolve to enable functional dynamics
Query Protein
Pfam PDB
Obtain MSA Obtain structure
Find corresponding sequence in MSA
MSA refinement GNM calculation
MSA refinement GNM calculation
Entropy/MI calculation
(conservation) (Mobility)
(co-evolution)
pairs of ashums Comparison MSF: Mean Square Fluctuation co-evolve
low frequency modes (soft modes/global modes) => dominant role in defining the most cooperative events
Less consolved - make thexinge
co-evolving residues: not conserved; change in regulated way
mointain function.

requere there	py: less ←>	conserved residue	
co-explution pa	ttems -> predict	structures	
co-evolution pa $hy? \Rightarrow co$ -evolving 1	residues are int	teracting I	
Information ex	vtropy (Shannon	1951)	
S(i) =	= E P(xi) log	P(xi)	for correlated mutation (CMA)
Mutual Inf	formation (MI)		
		yi) log P(xi, yi) P(xi) P(yi)	
Mobility incre	eases with seq	uence entropy	
		uence entropy y conserved e-to-high exposure	to environment)
Hinge sites (despite	are evolutionarile e their moderate	y conserved e-to-high exposure	
Hinge sites (despite		y conserved e-to-high exposure recognition are dist	inguished by Justion propensities
Hinge sites (despite	are evolutionarile e their moderate	y conserved e-to-high exposure recognition are dist	
Hinge sites (despite AA involved	ore evolutionarile 2 their moderate in intermolecular	y conserved e-to-high exposure recognition are dist	inguished by Justion propensities
Hinge sites (despite) AA involved Types of function	are evolutionarily their moderates in intermolecular	y conserved e-to-high exposure recognition are dist co-evo high	inguished by Justion propensities
Hinge sites (despite) AA involved Types of function	are evolutionarille their moderates in intermolecular al sites ×4 Mobility in	y conserved e-to-high exposure recognition are dist	inguished by hution propensities global mobility
Hinge sites (despite AA involved Types of function Functional site	are evolutionarily their moderate in intermolecular al sites ×4 Mobility in global modes	y conserved e-to-high exposure recognition are dist co-evo high Sequence	inguished by hution propensities global mobility Dominant Feature
Hinge sites (despite AA involved Types of function Functional site Chemica	are evolutionarily their moderate in intermolecular al sites ×4 Mobility in global modes Min	y conserved e-to-high exposure recognition are dist co-evo high Sequence evolution	inguished by lution propensities global mobility Dominant Feature high fidelity; precision
Hinge sites (despite) AA involved Types of function Aunctional site	are evolutionarily their moderate in intermolecular al sites ×4 Mobility in global modes	y conserved e-to-high exposure recognition are dist co-evo high Sequence evolution Conserved	inguished by hution propensities global mobility Dominant Feature