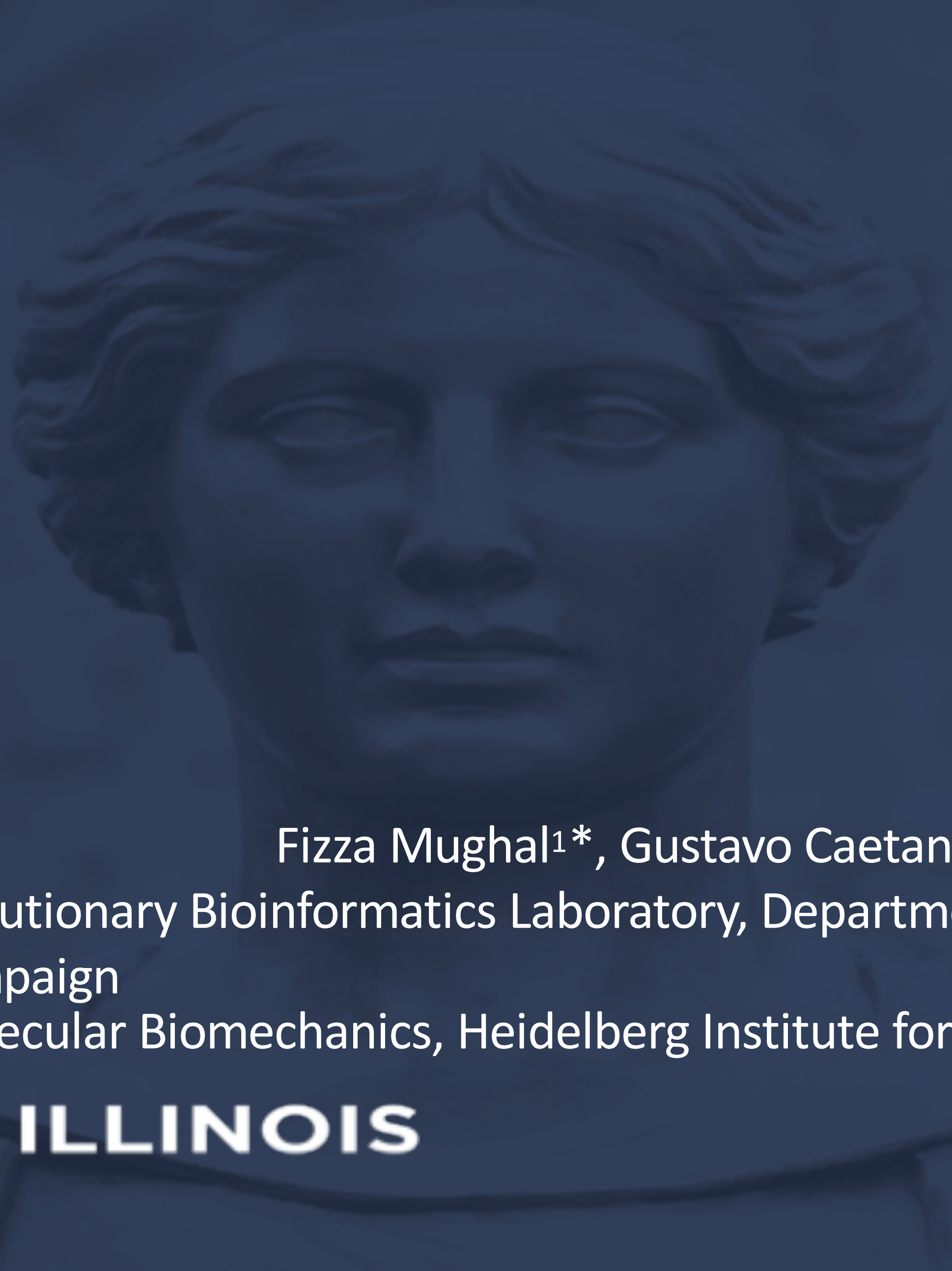

How Function Shapes Dynamics in Evolution of Proteins

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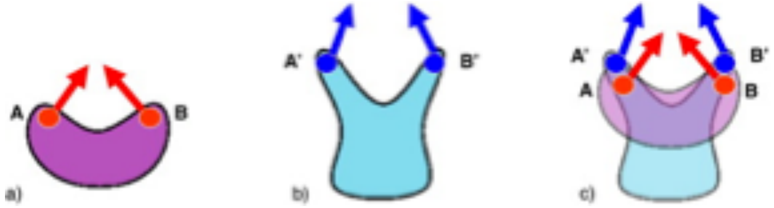
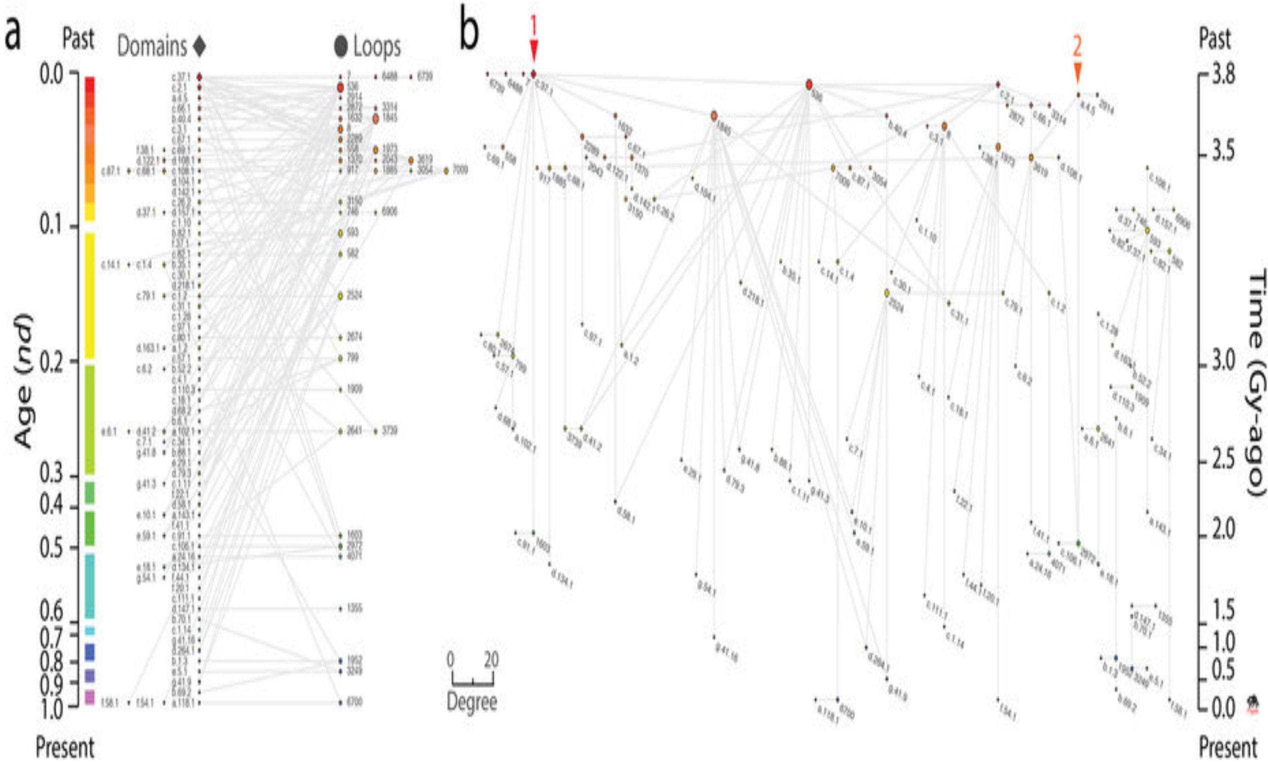
ILLINOIS

Relationship between protein dynamics and function

- Dynamics possess information that cannot be deciphered just by inspecting the structure.
- Proteins are found to be in various conformations as a dynamic ensemble (Orozco *et. al*, 2011).
- Evolution seems to constrain dynamics and flexibility (Micheleti, 2013), possibly to preserve function
  - Similar fluctuation in dynamics of Rossmann-like fold proteins (Keskin et al., 2000; Pang *et al*., 2005).
  - Common dynamics shared among members of the same protein family and superfamilies in comparison with unrelated/distant proteins (Maguid *et.al,* 2006; Maguid *et.al* 2008).
  - Common dynamics properties can be detected in proteins with different structure but common function (Ramanathan & Agarwal, 2011).



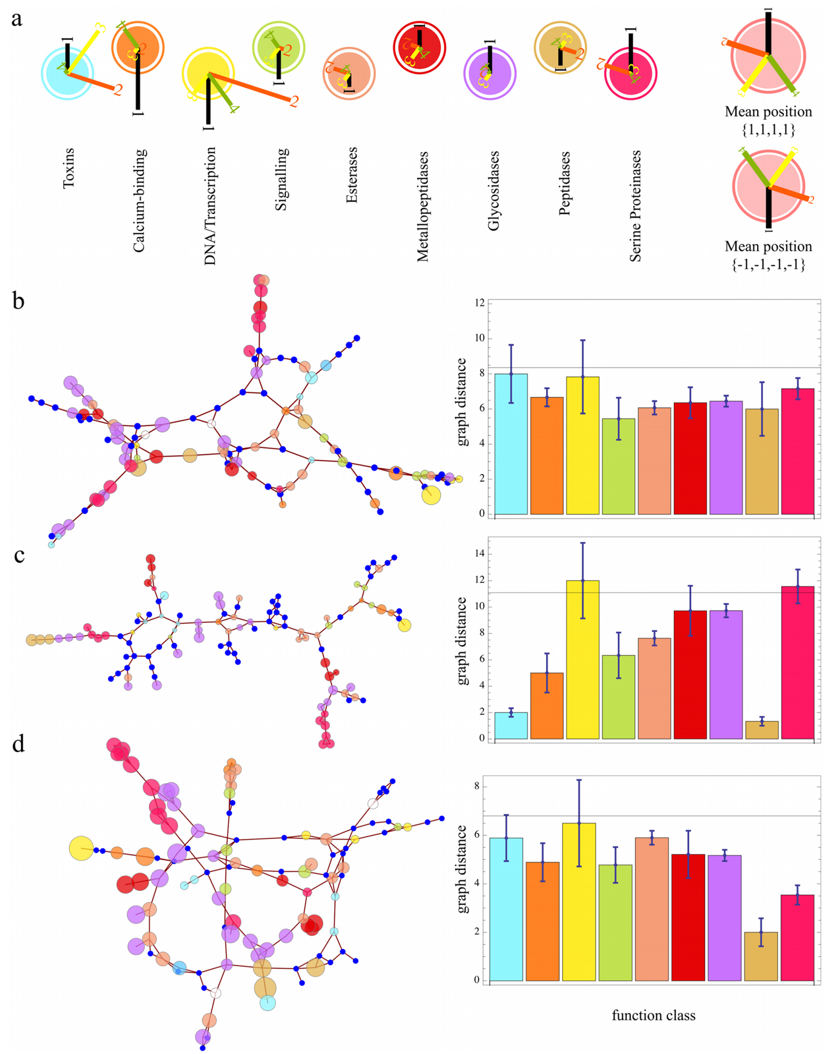
Micheletti, C. *Physics of life reviews* 10.1 (2013): 1-26.



Aziz, M. F. *et al*. (2016). *Sci. Rep.* **6**, 25058.

Constructing the Dynasome

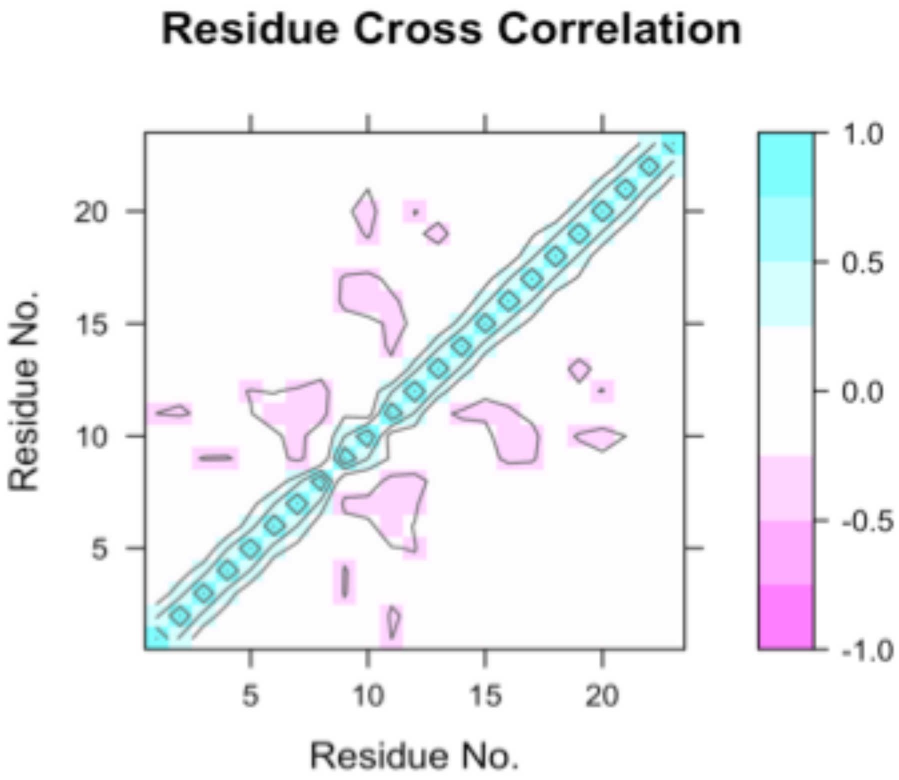
- Construction of a dynamics space based on MD data
- Functionally similar proteins tend to cluster together.
- Dynamics space is continuous.
- Combining structure and dynamics information for prediction of function yielded better results than using either of the two alone.
- Experimental overview:
  - 87 ArchDB Classifications
  - 116 GO Molecular Functions
  - 18 SCOP Fold Families
  - 10 ns NPT production runs in NAMD 2.9 with CHARMM36

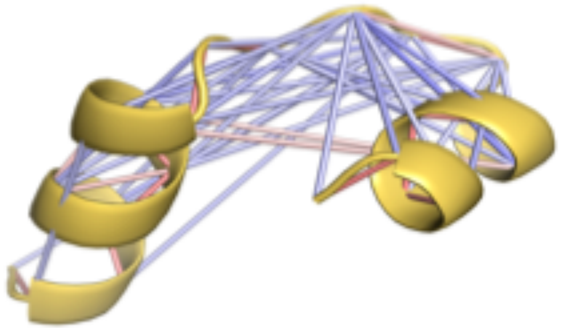


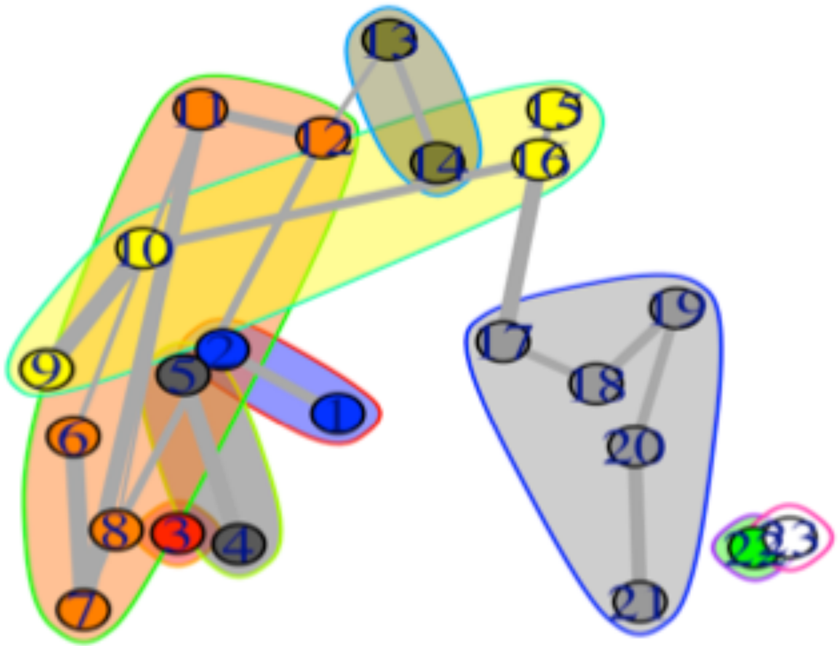
Hensen U, Meyer T, Haas J, Rex R, Vriend G, Grubmüller H (2012). PLoS ONE 7(5): e33931.

Phenyl tRNA Synthetase (1B7Y_B_408)

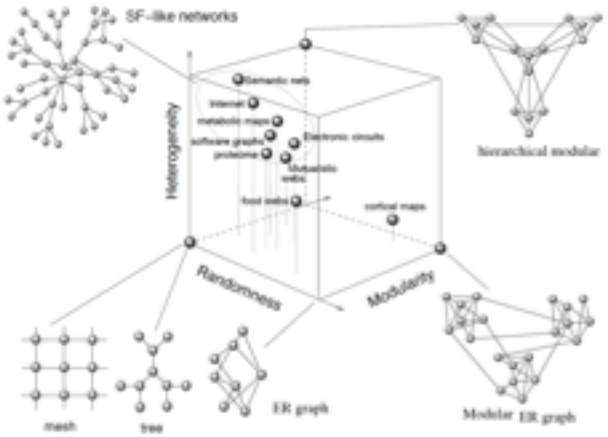
GO:0000049	tRNA binding
GO:0000287	magnesium ion binding
GO:0004826	phenylalanine-tRNA ligase activity



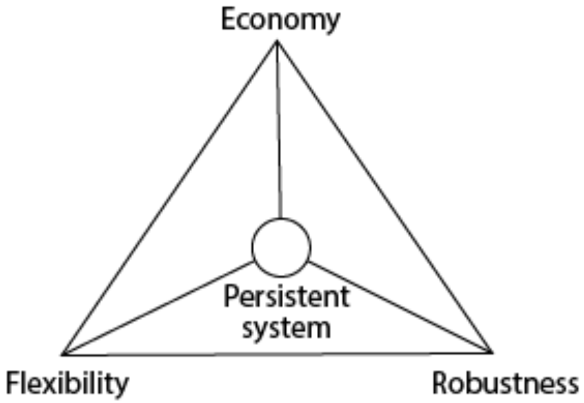




Visualizing the design space of dynamics community networks



Solé, R., & Valverde, S. (2004). *Complex networks*, 189-207.



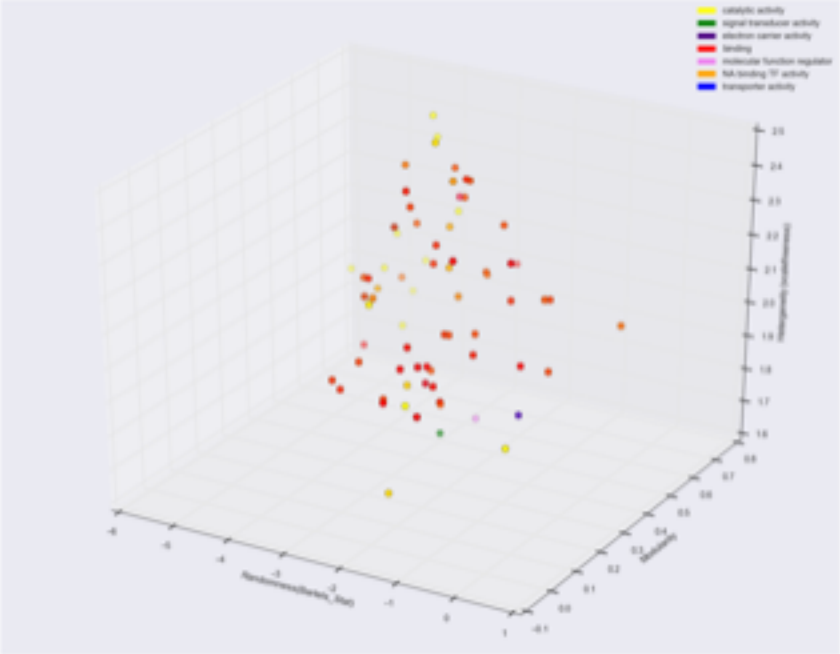
Economy

Persistent system

Flexibility

Robustness

General



Future Directions

- Clustering of all simulations based on the dynasome variables
- Devising methods for classifying community structure patterns
- Construct a “structure-evolution” space to complement the dynamics space
- Uniformly sampling more protein loops representative of all protein function classification.
- Longer timescale simulations are pertinent in capturing “slower” dynamics.