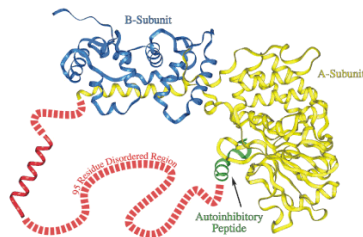


Are Protein Disordered Regions Equal to Loops?

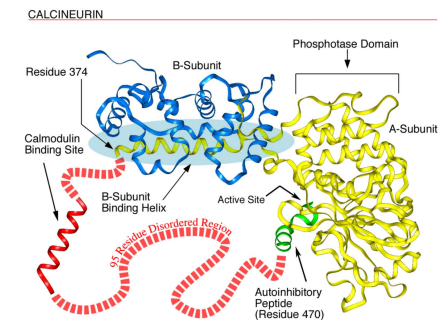
Esmeralda Vicedo

Rostlab

3 April, 2011

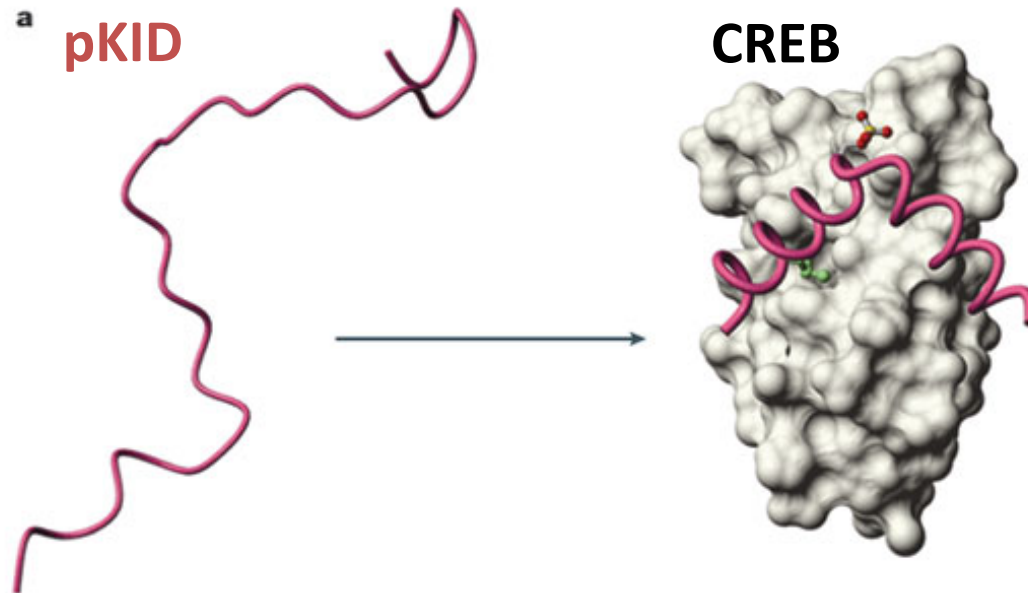


(Image adapted from: Kissinger CR, et al. 1995. "Crystal structures of human calcineurin and the human FKBP12-FK506-calcineurin complex." Nature 378:641-4.)



1. What are disorders in Proteins?

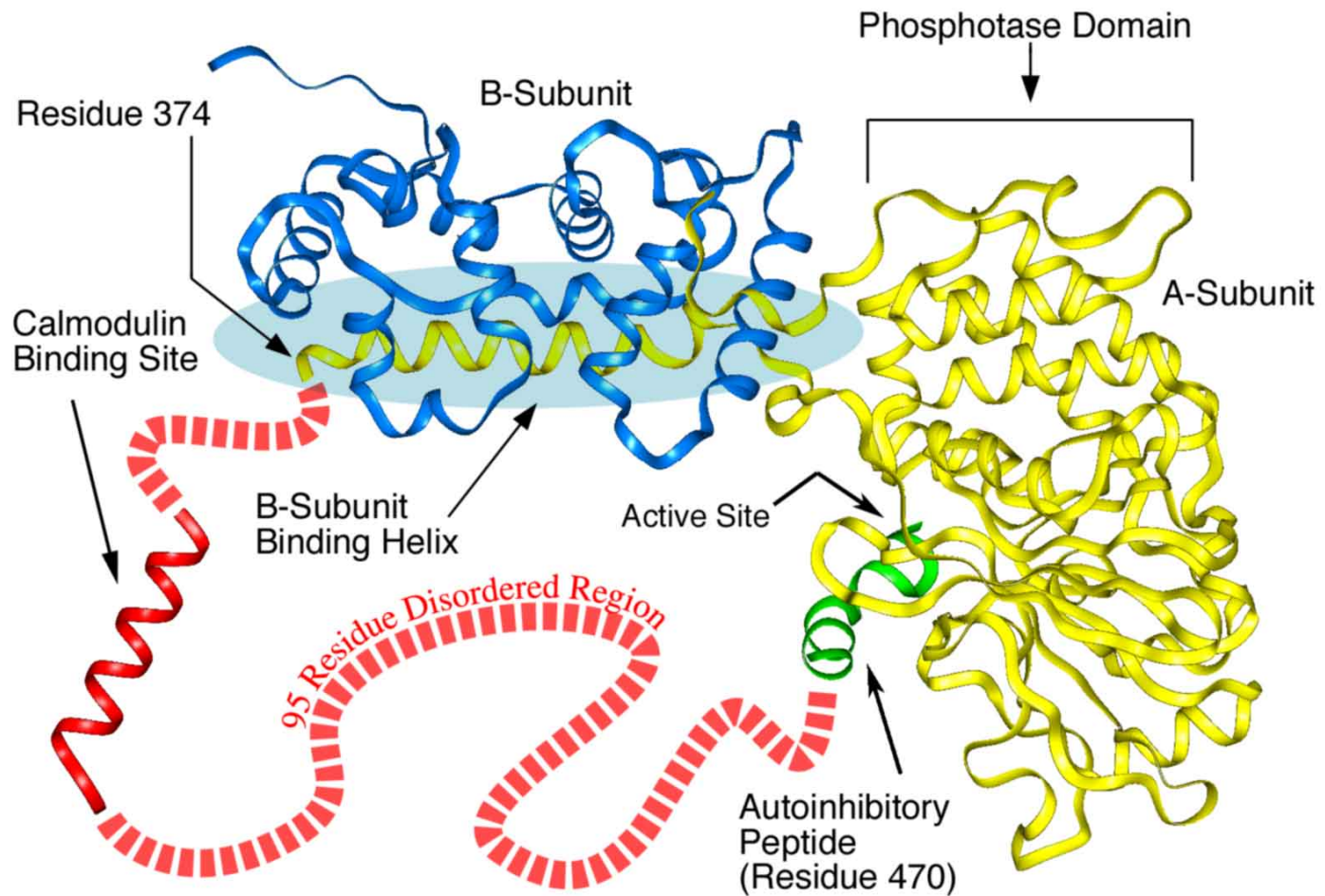
- Definition: Protein or protein regions that do not adopt a regular defined, stable three-Dimensional (3D) structures in isolation.



Dyson H & Wright P (2005) Intrinsically unstructured proteins and their functions, Nat Rev Mol Cell Biol

- Assignment of disordered regions Problematic: Different “flavors”

CALCINEURIN

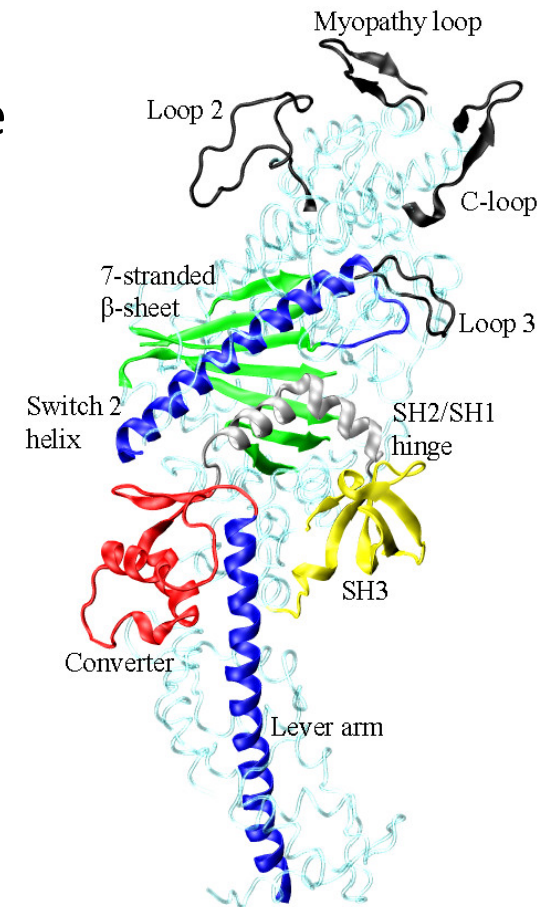


http://www.ornl.gov/sci/techresources/Human_Genome/publicat/hgn/v12n1/13trinity.shtml

2. Could we predict disordered regions?

➤ Different Predictors capture different properties of the disordered regions:

- missing coordinates in X- ray structure
- total pairwise interresidue interaction
- **unstructured Loops -> NORSnet**
- and others more



3. Analysis of the Data I

- UNIPROT DB (release March 2011)¹:
 - 2298 completely sequenced organisms -> > 4 mill. proteins

- prediction of secondary structure and disorder
 - PROFsec² : H=helix, E=extended (sheet), L=loop
... HHHLLLLLEEEE ...

 - NORSnet³ : D=disorder, blank = order
... DDDDDDD----- ...

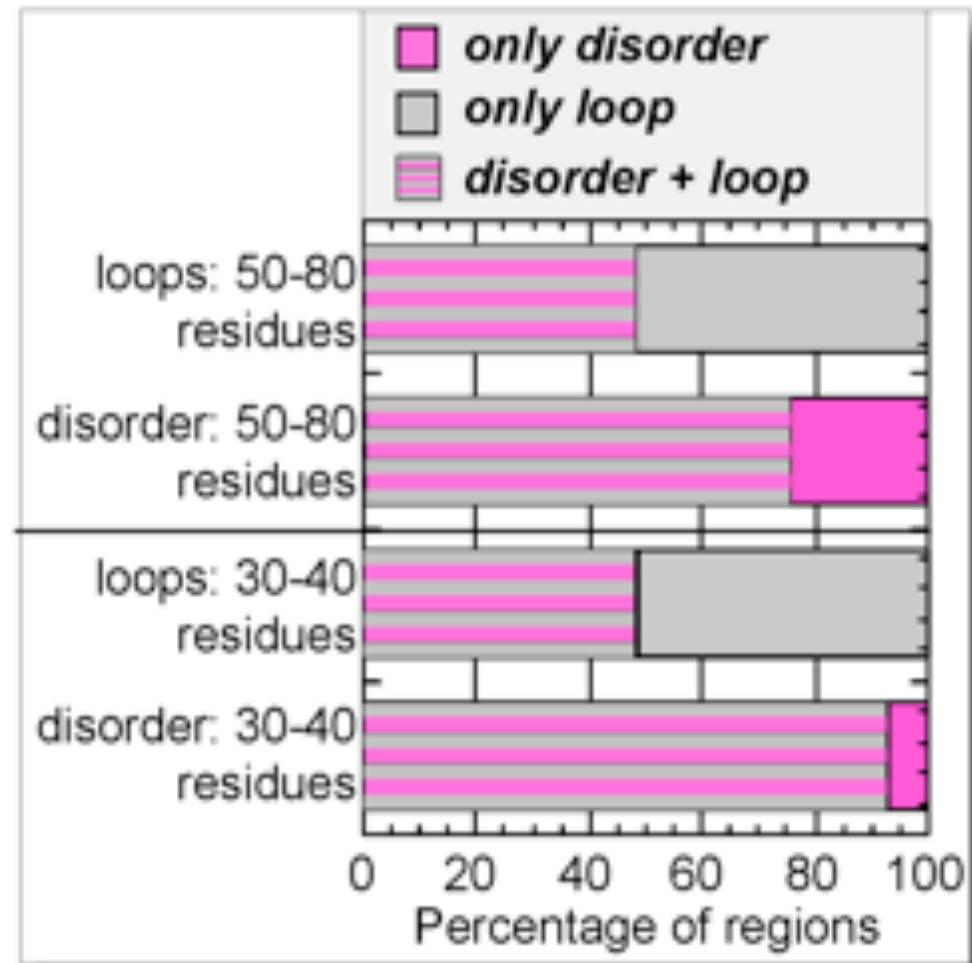
1. The UniProt Consortium (2011), Ongoing and future developments at the Universal Protein Resource Nucleic Acids Res. 39

2. Rost B, Sander C. (1994). Combining evolutionary information and neural networks to predict protein secondary structure. Proteins.

3. Schlessinger A, Jinfeng L, Rost B (2007) Natively Unstructured Loops Differ from Other Loops. PLoS Comput Biol 3(7):e140

4. Interpreting the Results

For few entirely sequenced organisms of different kingdoms



Schlessinger A, Rost B & al. 2011, Protein disorder – breakthrough invention of evolution?, Current Opinion in Structural Biology.

*Are Protein Disordered Regions
Equal to Loops?*

NO ! THEY ARE NOT EQUAL

5. Next Steps

- Analyze proteins of entire available organisms (2298).
- Compare results with other predictors based on other properties of the disordered regions in proteins (IUPred, metadisorder, VLS2...).



- Are disordered regions more conserved than ordered regions in proteins. ?

THANKS FOR YOUR ATTENTION!