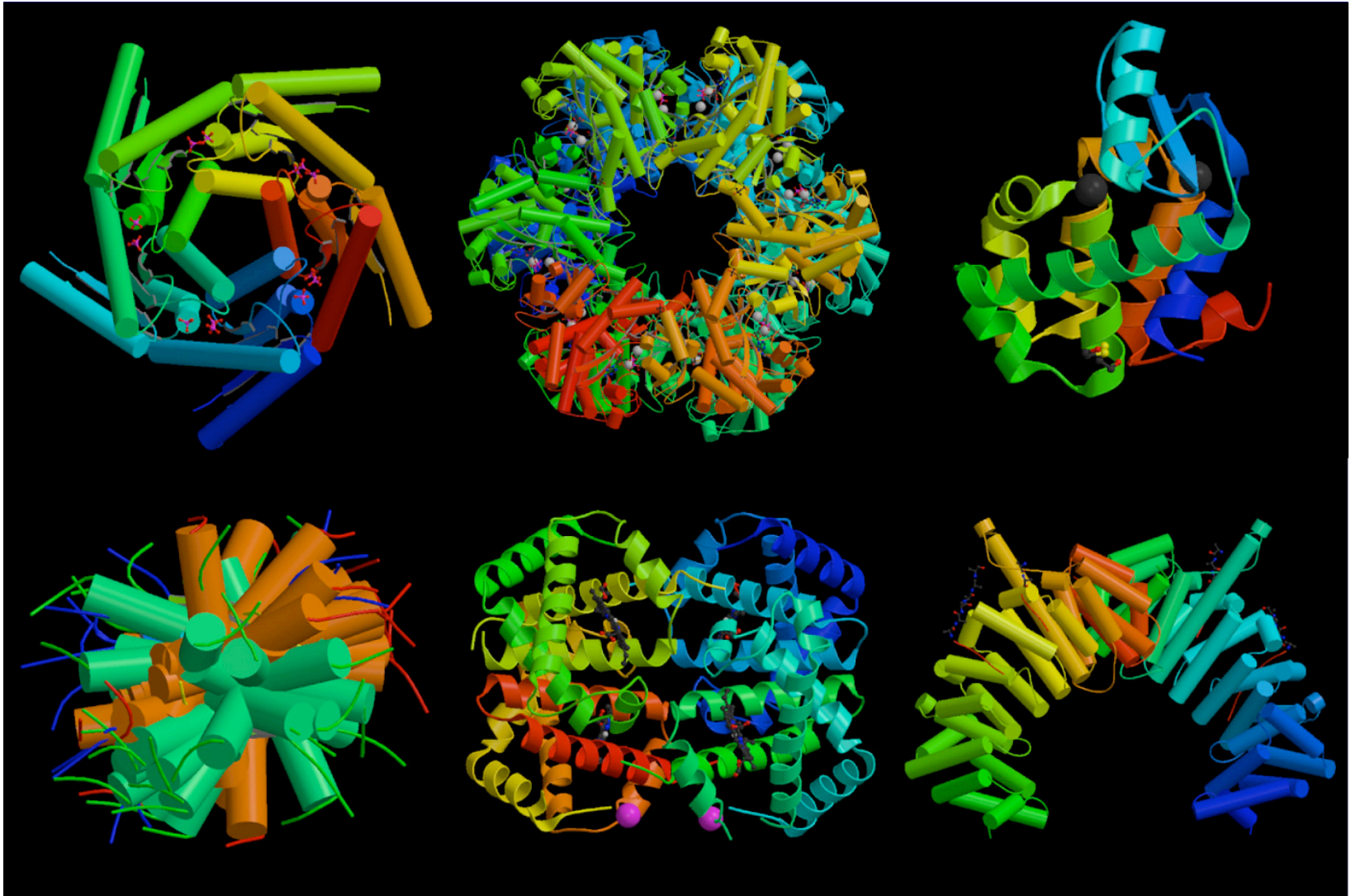



Structural Bioinformatics




Paradigms

 **Sequence \Rightarrow 3D structure**

 **Chaperones/Fold as complex/Environment**

 **3D structure \Rightarrow function**

 **Disordered proteins/Different solutions/
Tough task**

Progress

 *"Nothing happened over last 10 years..."*

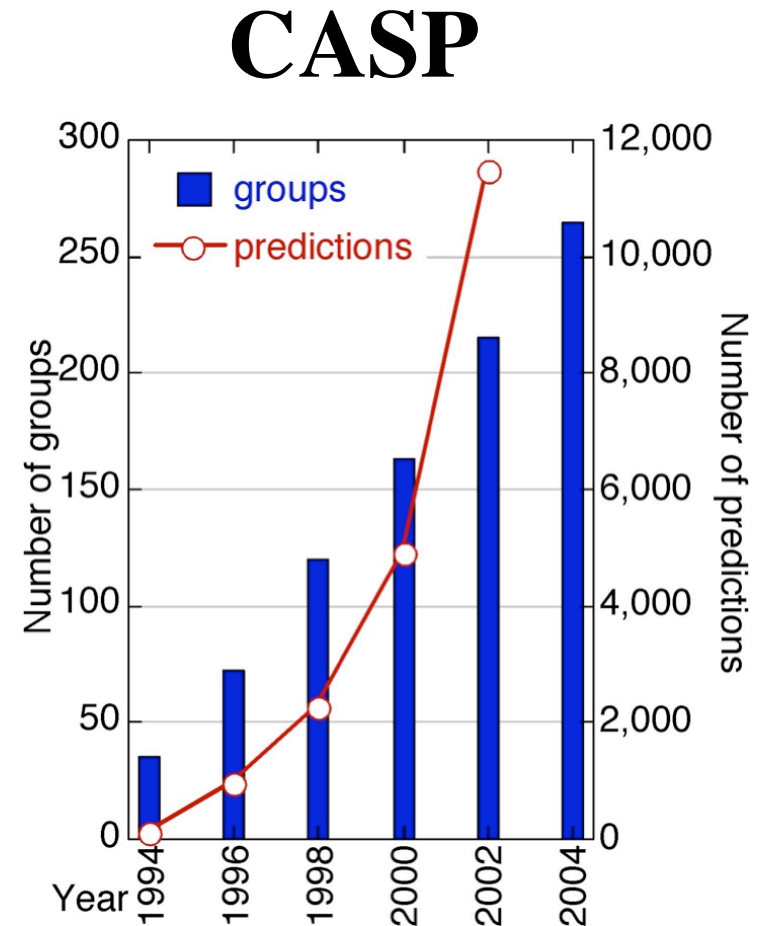
Edgardo Ferran & Reinhard Schneider

 **... except for what we hear today ...**

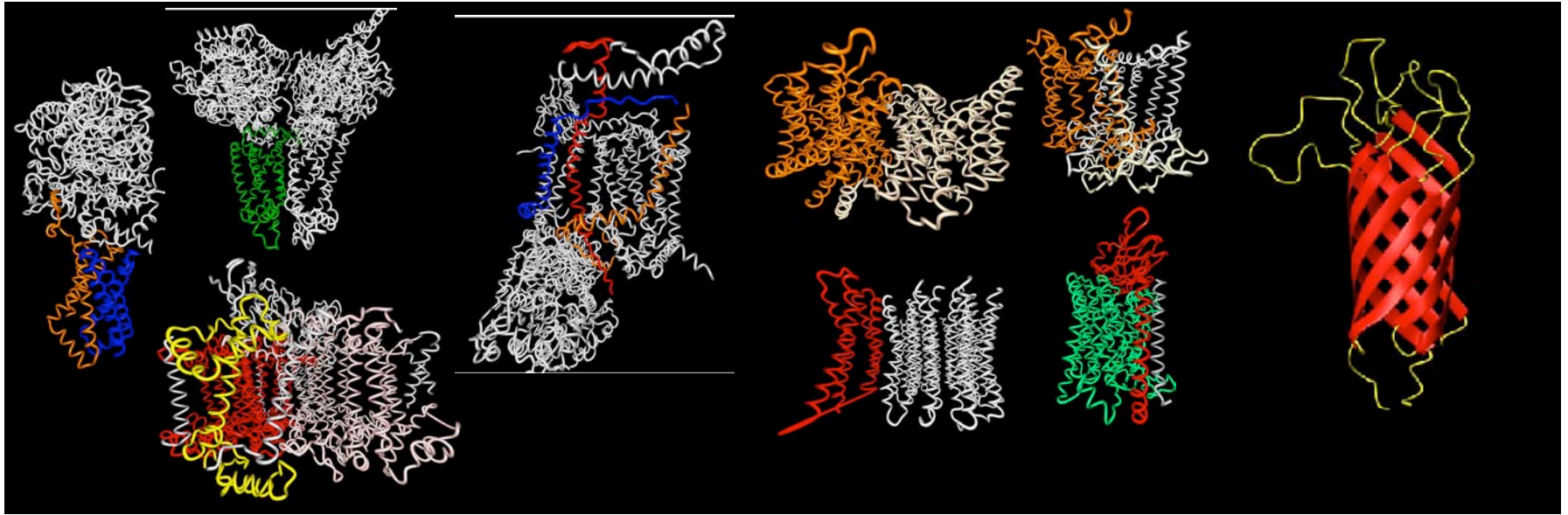
 **... and of what all those at the meeting did!**

Protein Structure Prediction

- Only homology modelling good
- No general prediction of 3D from sequence, yet
- Important improvements in many fields!



Membrane proteins

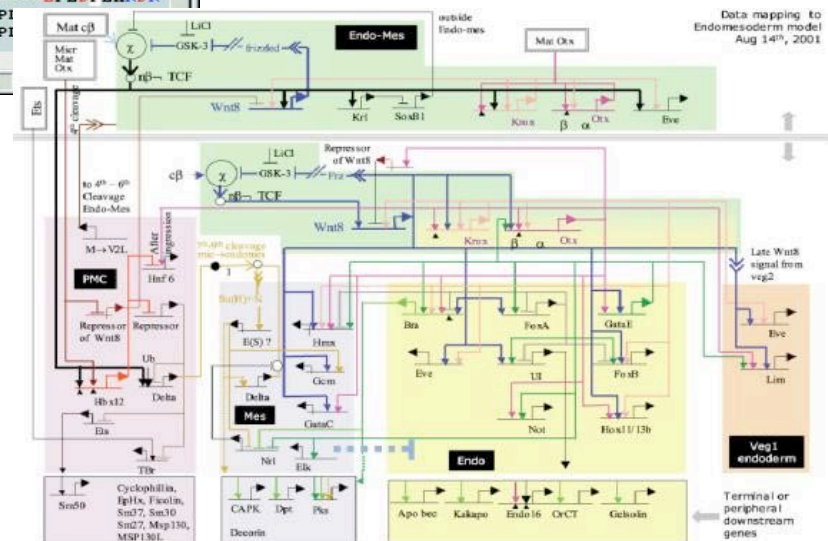
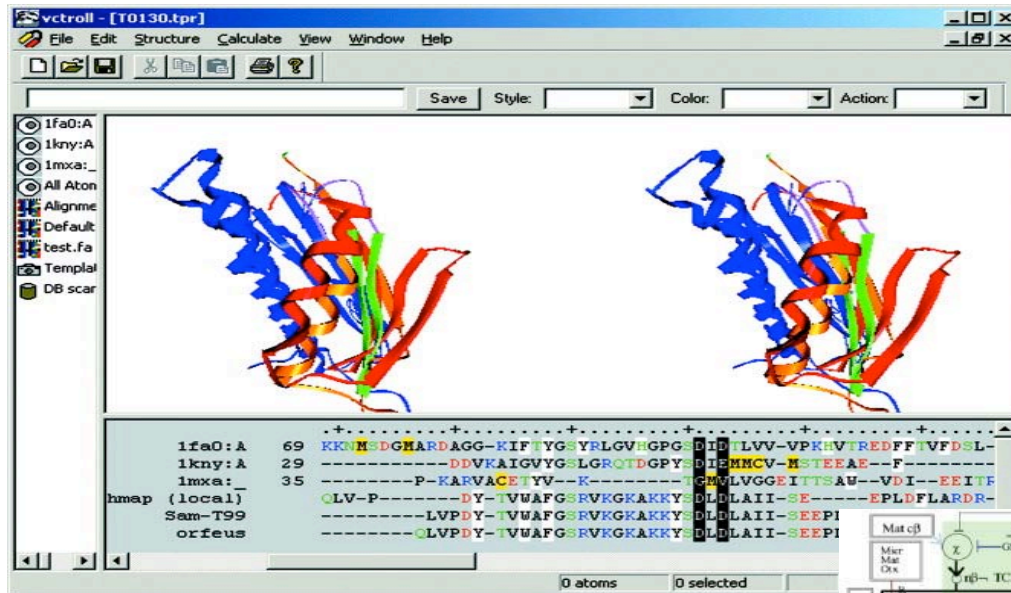


14:20-14:50

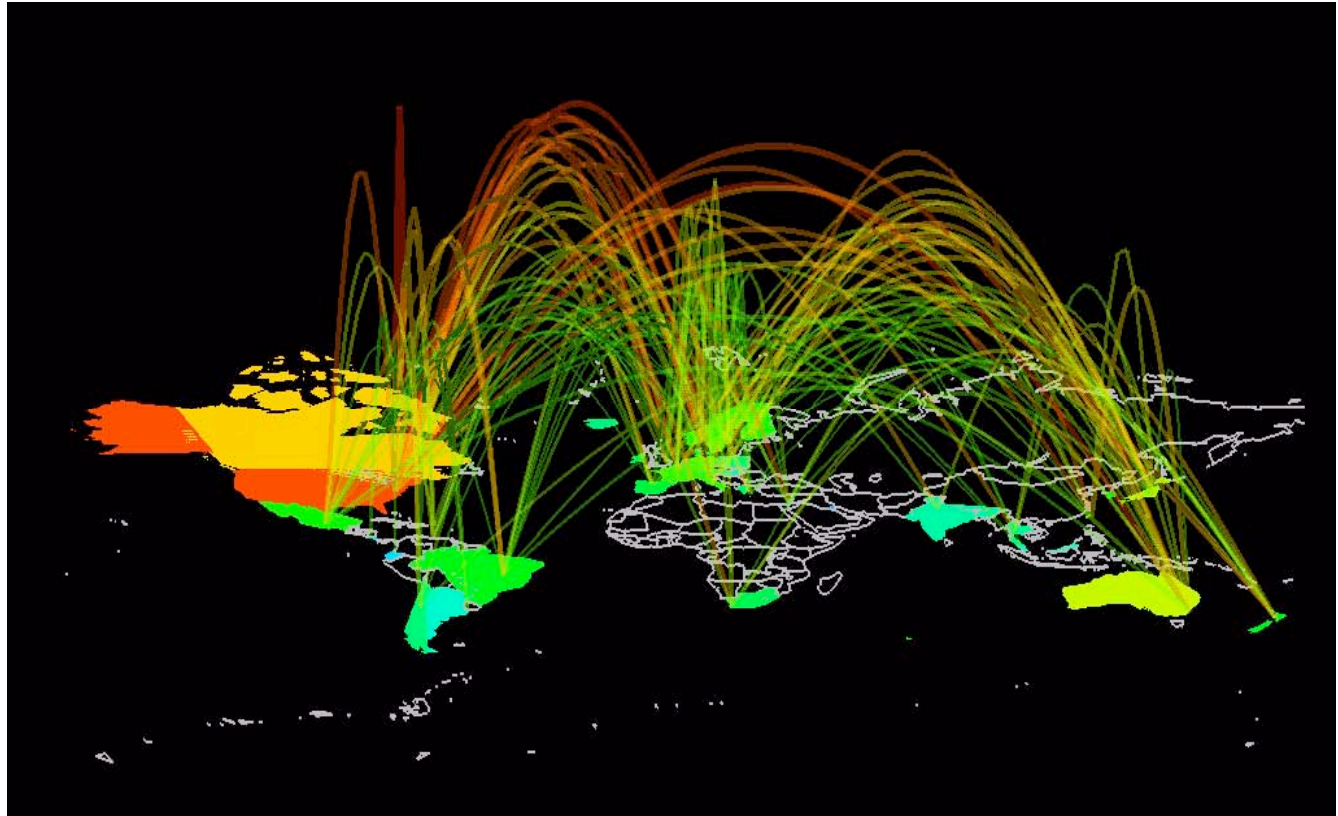
Assigning transmembrane segments to helices in intermediate-resolution structures

A Enosh, S Fleishman, **N Ben-Tal**, D Halperin
- Tel Aviv University

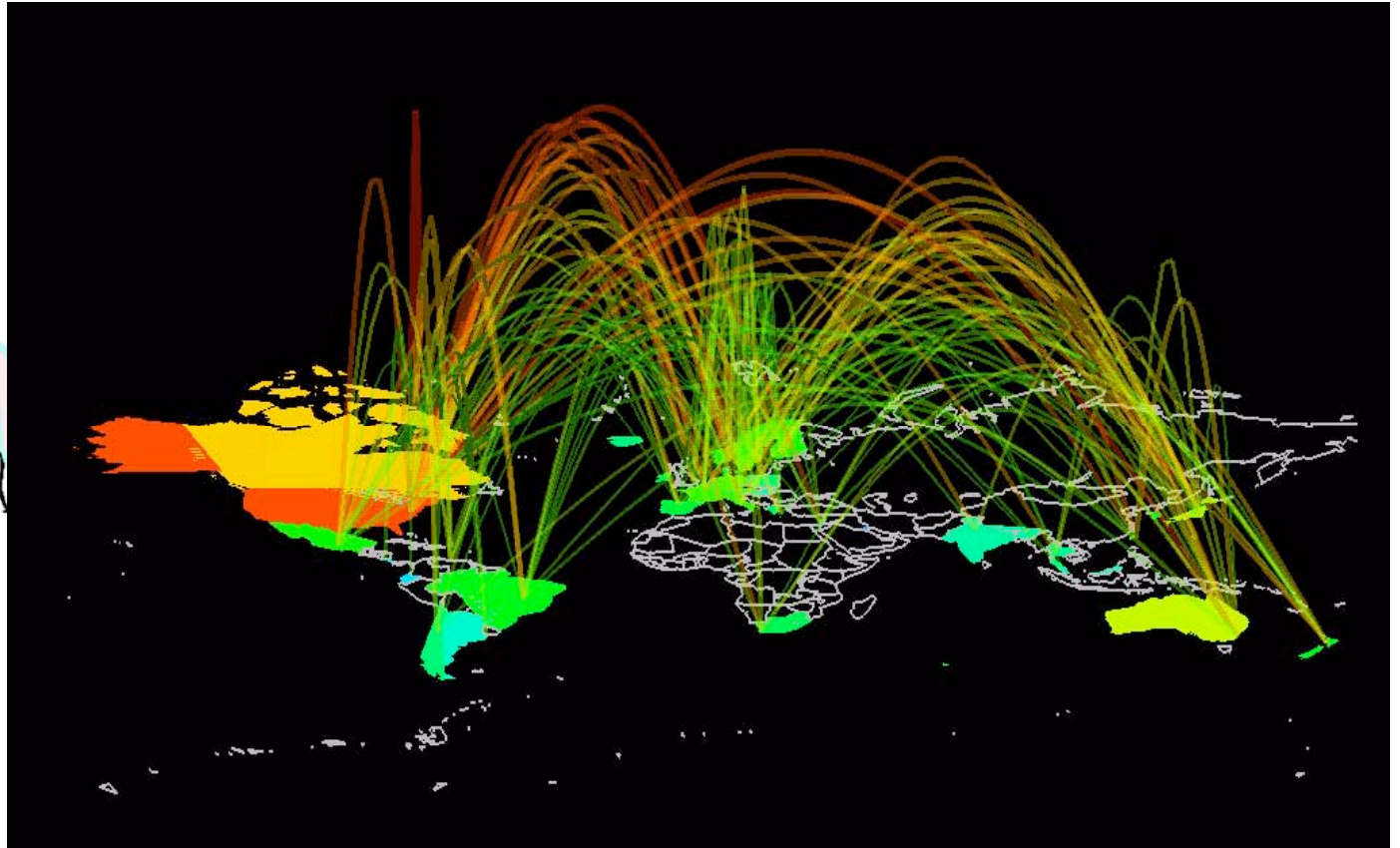
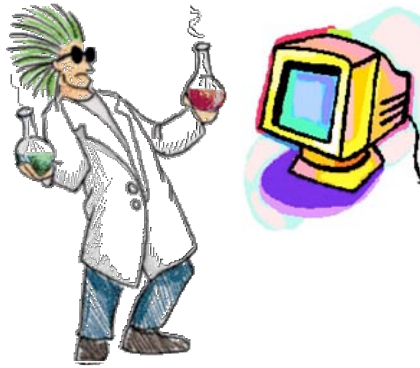
Structure prediction servers impacted biology



Servers, Meta-servers, Meta-meta ...



The real thing: clever humans WITH machines!



Breakthrough not proportional to resources!

● Problem may be too hard ...

● ... still: we need solutions

Experimental Structural Genomics
alone not getting there!

● Change of focus:

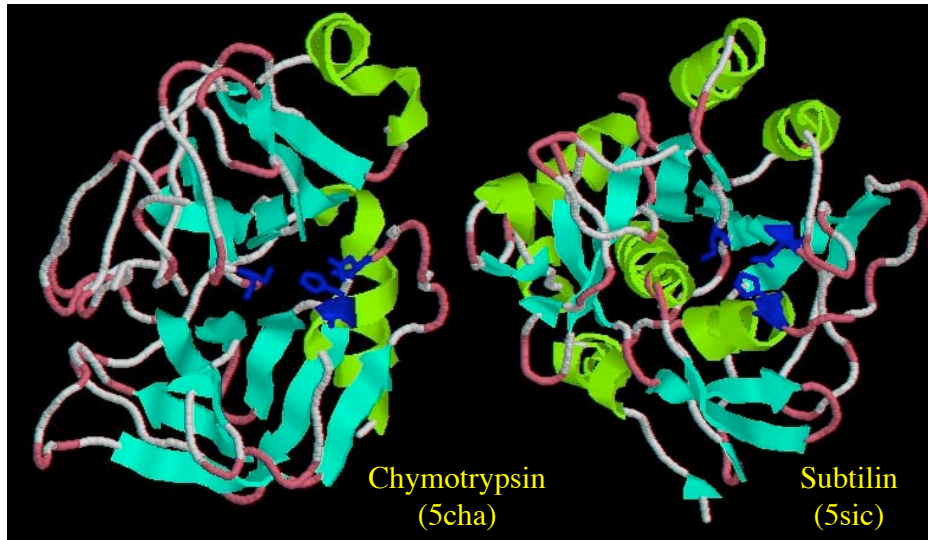
3D structure / structure prediction
-> predict **protein function?**

POSTSCRIPT

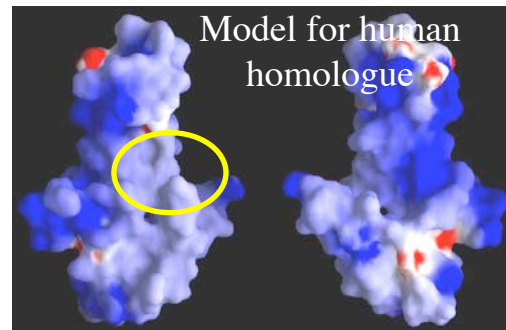
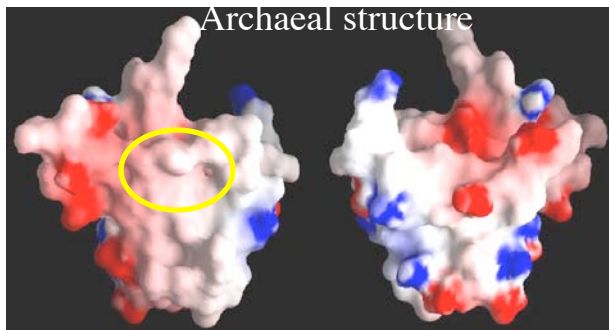
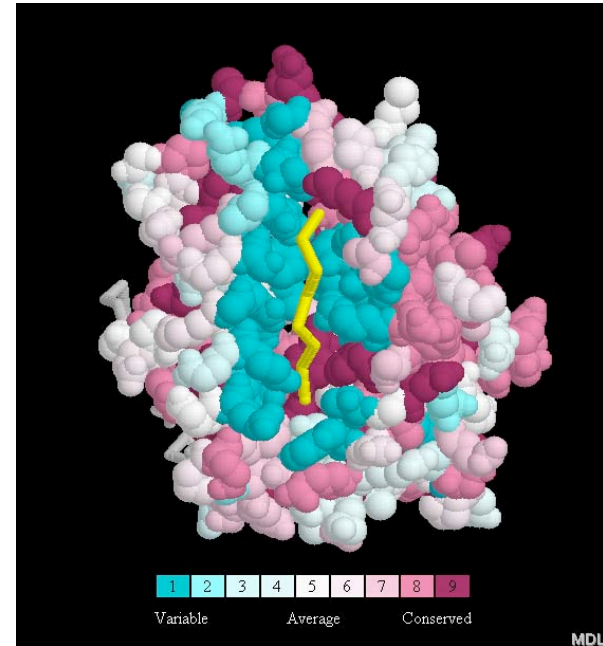


**the following 3
slides were used to
briefly introduce
speakers in the
morning**

Using structure to predict function



ConSurf



Using predicted structure to predict function

- alanine scan for

V1 domain of CD4/gp120

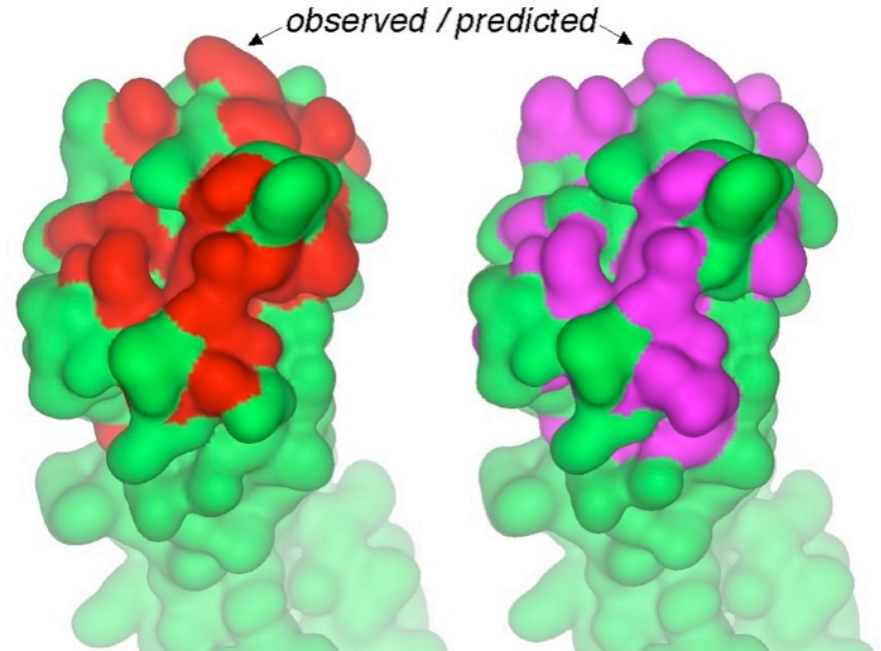
A Ashkenazi et al. & DJ Capon (1990) *PNAS* **87**, 7150

- structure:

PD Kwong et al. & WA Hendrickson (2000) *Structure* **8**, 1329-1339.




red: observed
purple: predicted

KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQ	observed to strongly impact binding
GSFLTKGPSKLNDRADSRRLWDQGNFPLIIKNLKIEDSD	sequence
TYICEVEDQKEEVQ	predicted



Y Ofran & B Rost (2004) *submitted*

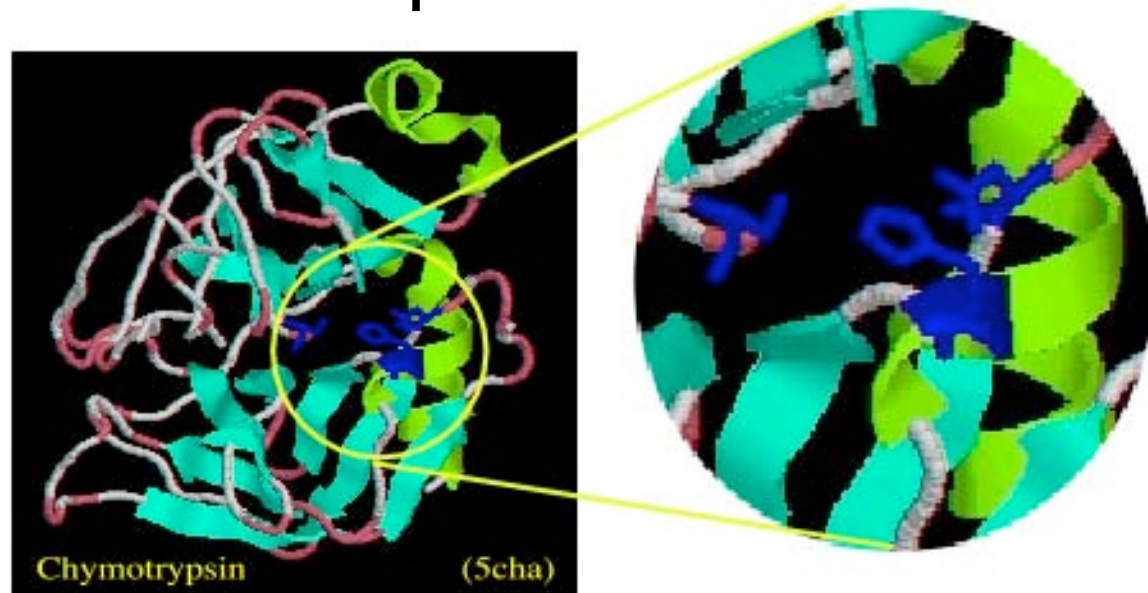
Conclusions: automated methods in structural bioinformatics

-  **Progress in structure prediction, but slow**
-  **Servers have impacted biology and the impact is increasing**
-  **Function from experimental or predicted structure now cool**

Structural motifs and protein function

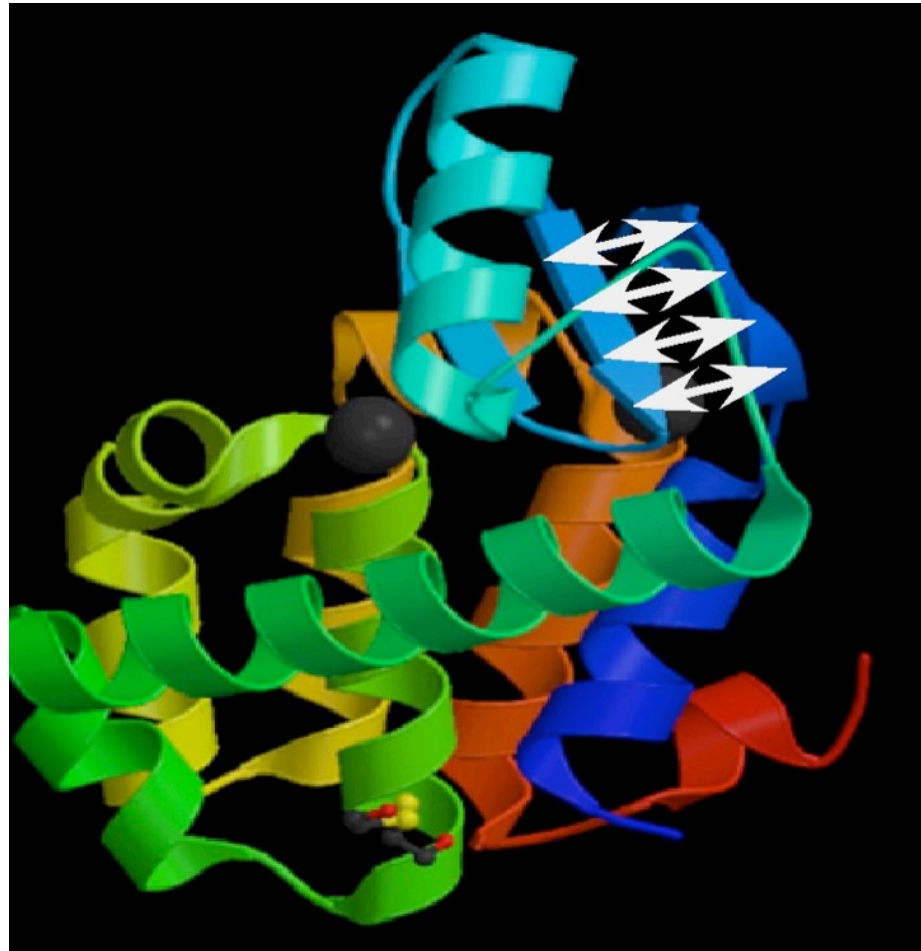
10:10-10:40 Mining .. Patterns .. [in] .. proteases
S-C Chen & I Bahar - Pittsburgh

11:40-12:10 SCOPEC: ... catalytic domains
R George, G Spriggs, J Thornton & B Al-Lazikani
- EBI & Inpharmatica

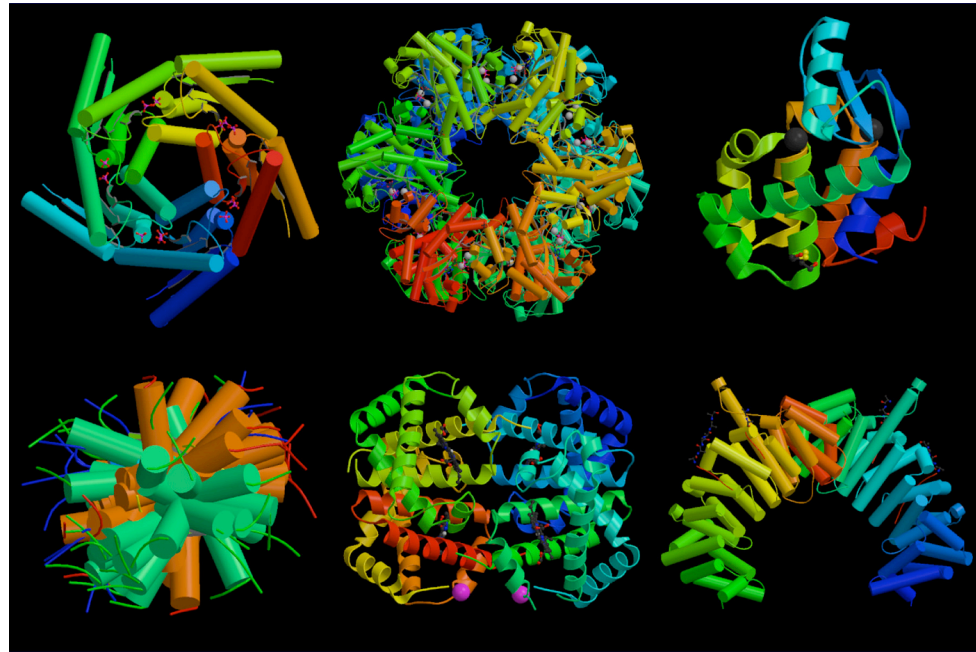


Protein contact prediction

11:10-11:40 Striped Sheets ... Prediction
Robert MacCallum - Stockholm



Effects of single residue changes



9:40-10:10

A Neural Network-Based Method for Predicting
Protein Stability Changes upon Single Point
Mutation

E Capriotti, P Fariselli & R Casadio - Bologna