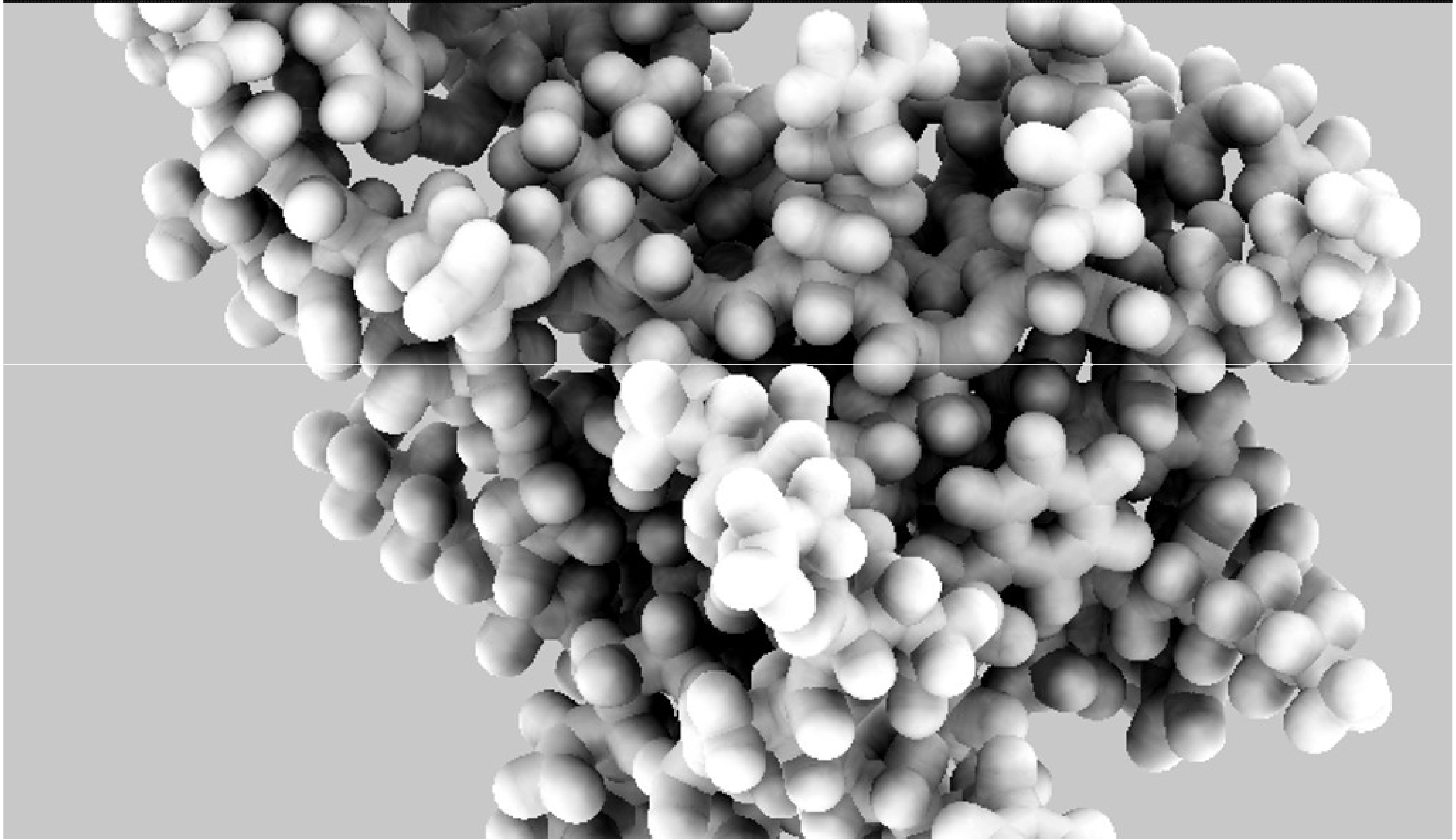
VISUALIZATION (AND ANALYSIS) OF LARGE-SCALE DYNAMIC BIOCHEMICAL STRUCTURES



HCI Laboratory | Faculty of Informatics | Masaryk University

Vilém Šustr

OUTLINE

INTRODUCTION

- Protein structure
- Motivation for protein analysis
- Channel detection

VISUALIZATION OF PROTEIN STRUCTURES

- Visualization techniques
- State of the art visualization software

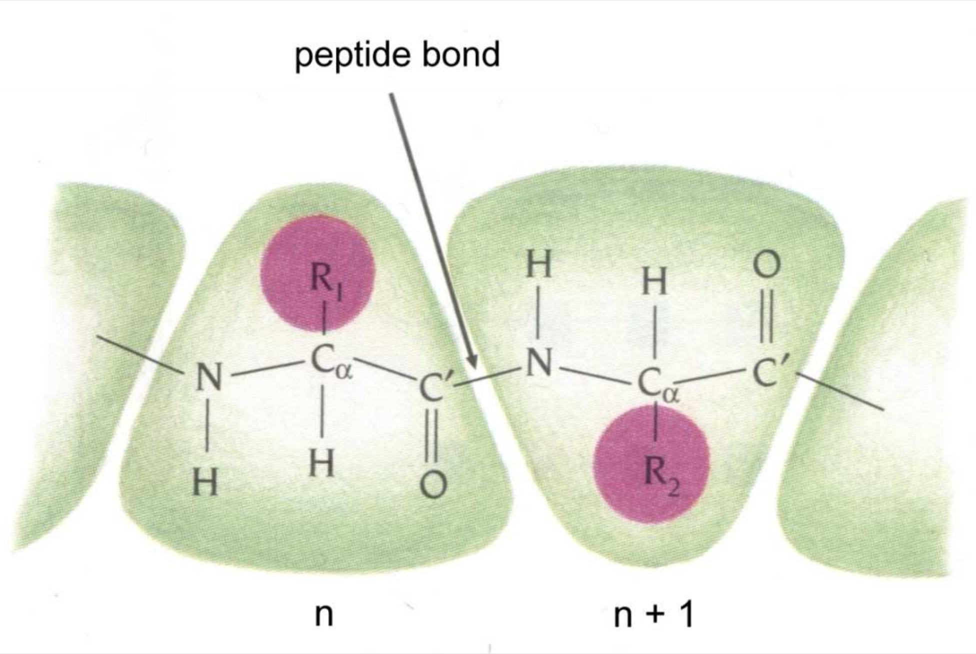
CURRENT RESULTS

- CAVER Viewer Software
- Future work

CONCLUSION

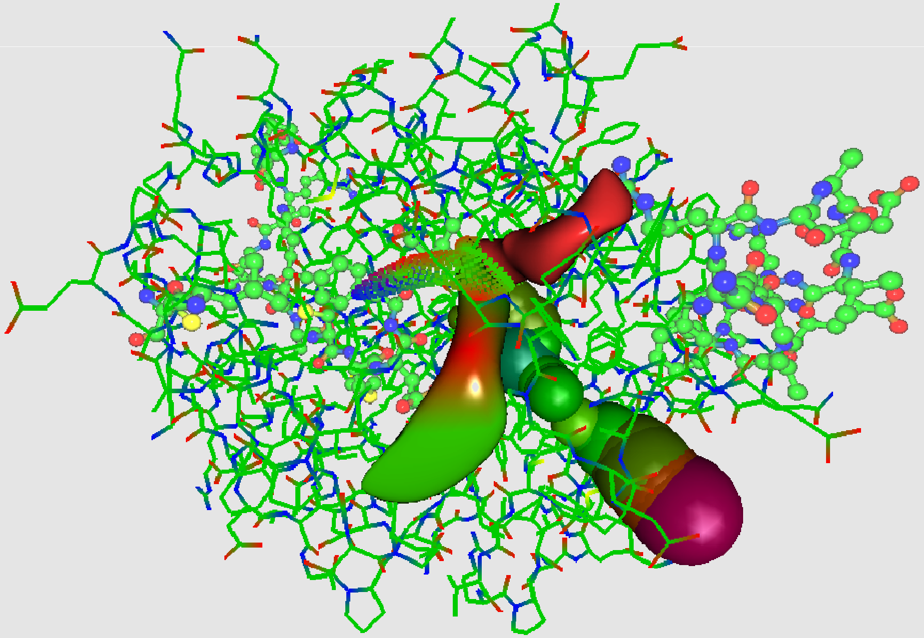
PROTEIN STRUCTURE

- Thousands to tens of thousands of atoms
- Groups of atoms forming residues, which are connected together with peptide bond
- All residues form a polypeptidic chain = single protein molecule

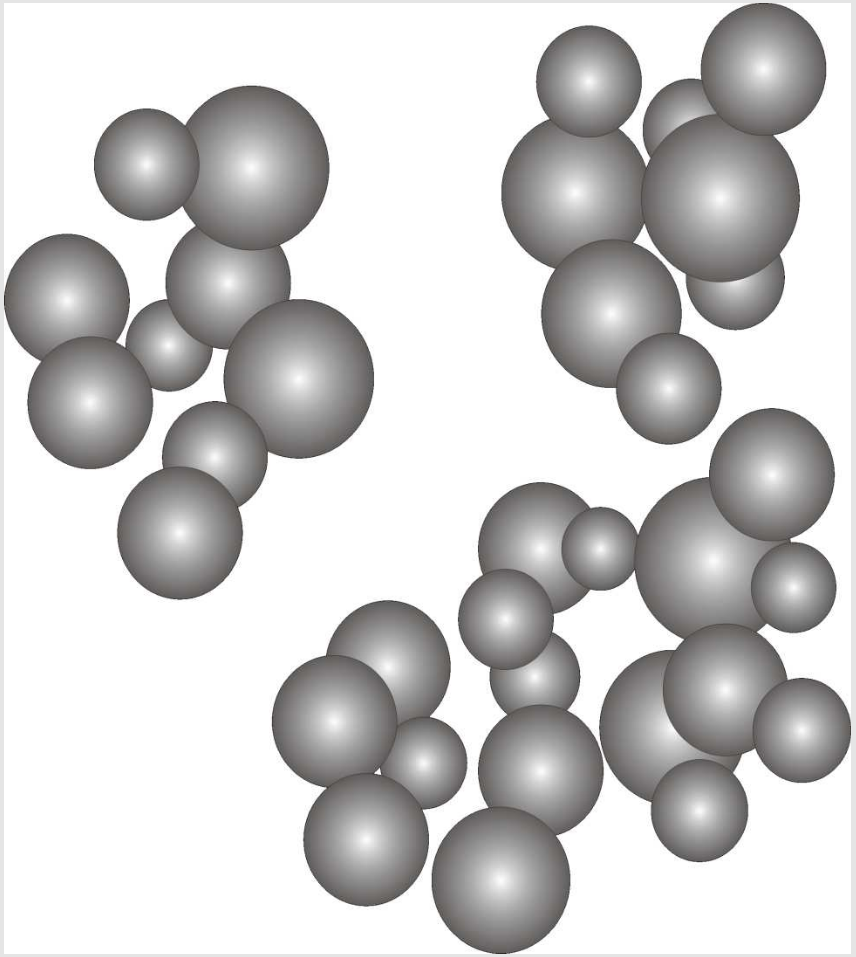


MOTIVATION

- Analysis leading to channel computation
- All chemical reactions between protein and substrate take place in the active site
- Checking the possibility of entering substrate into protein molecule
- Channels are substantial for creating new compounds, especially in drug design

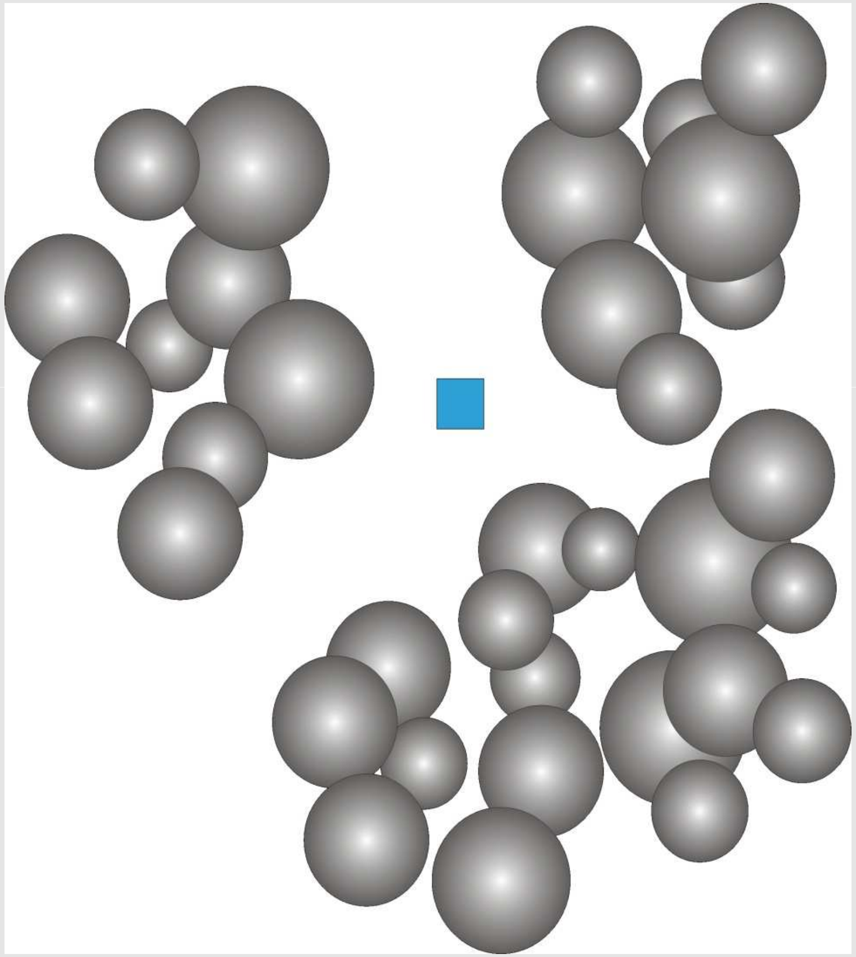


CHANNEL DETECTION



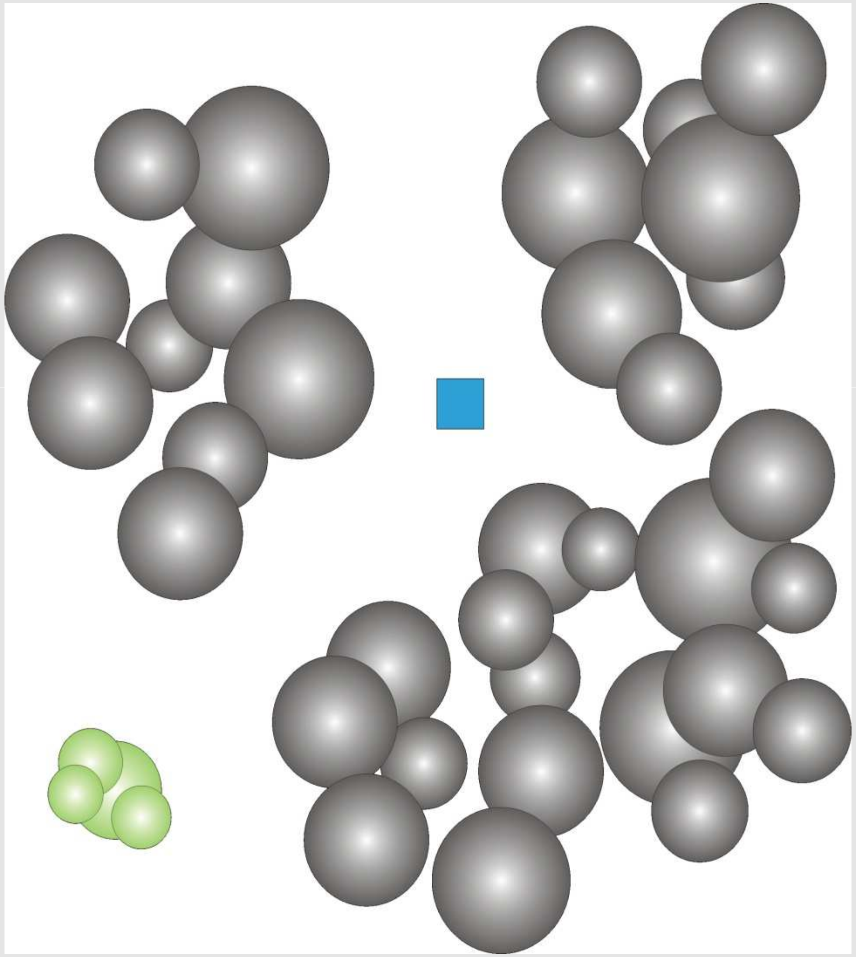
- Protein molecule

CHANNEL DETECTION



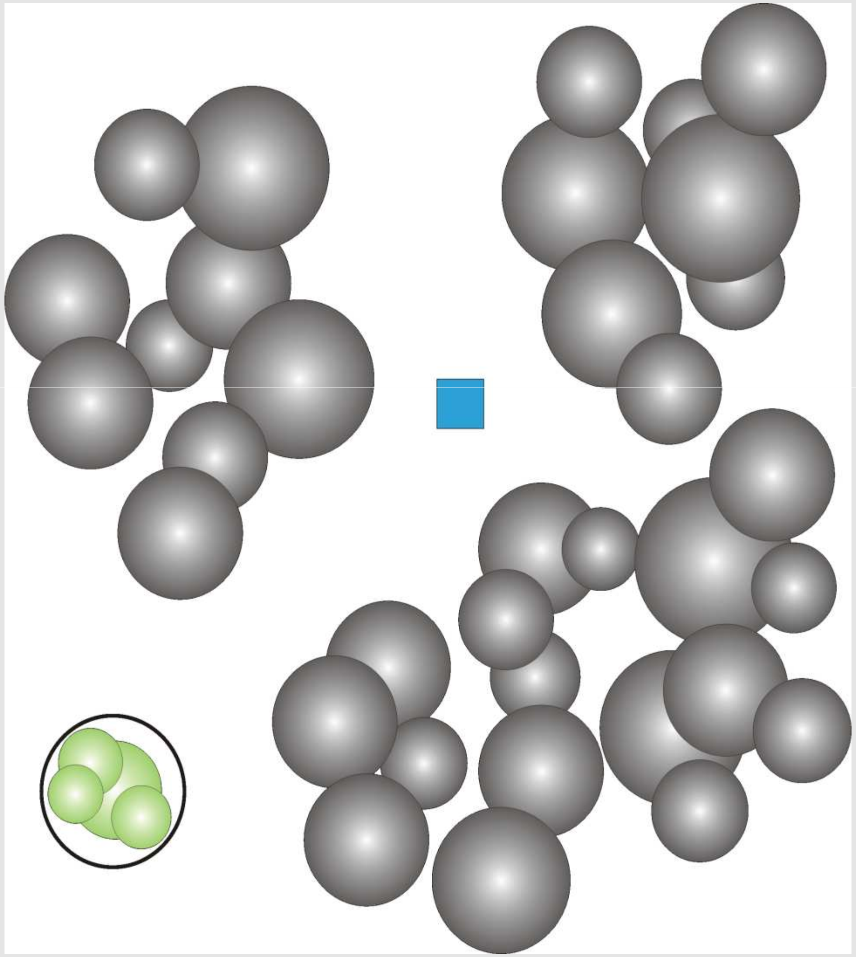
- Active site

CHANNEL DETECTION



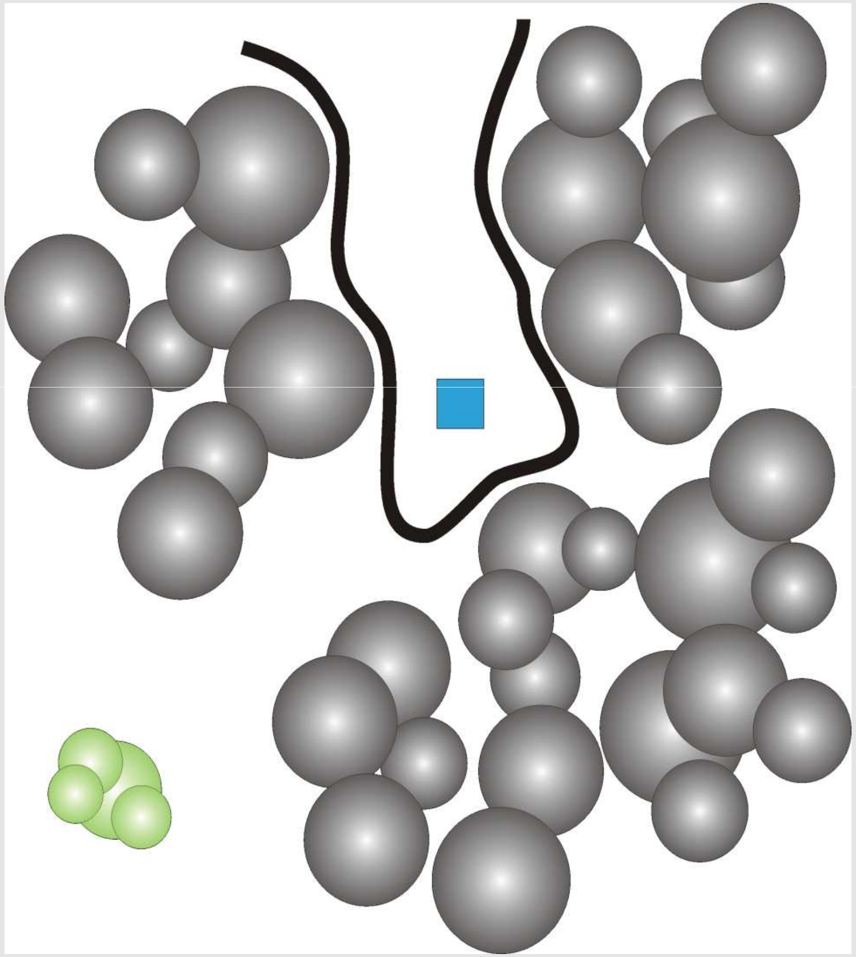
- Small molecule of substrate

CHANNEL DETECTION



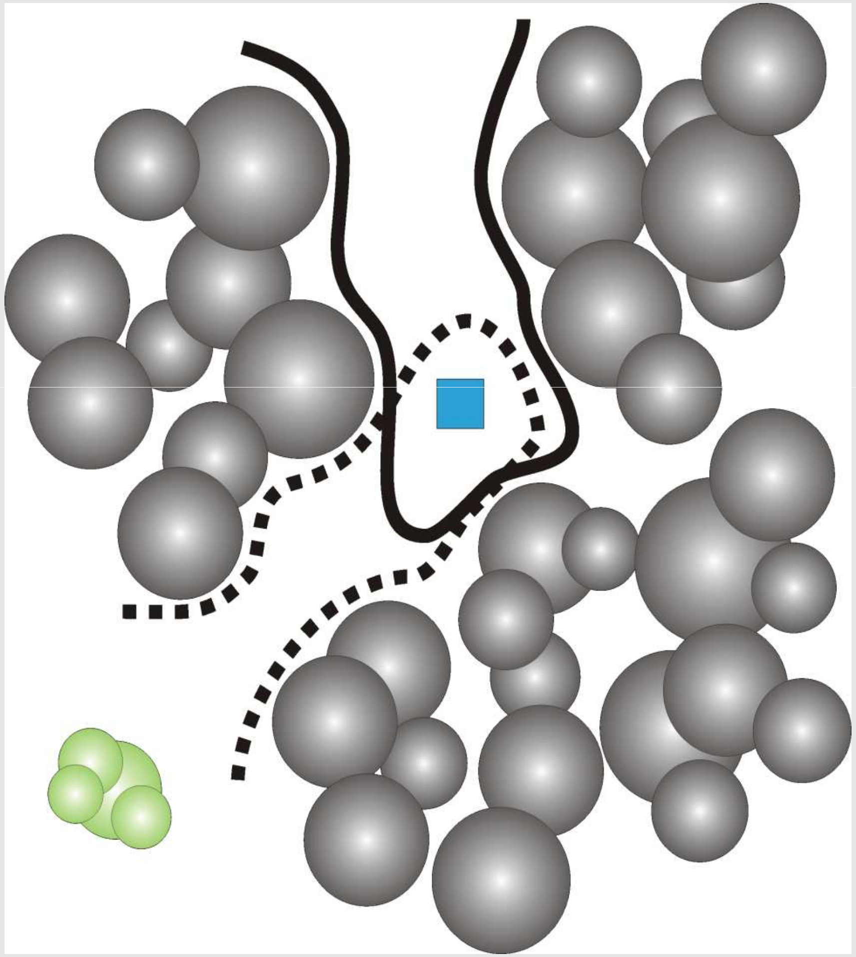
- Approximation of the substrate molecule (bounding box)

CHANNEL DETECTION



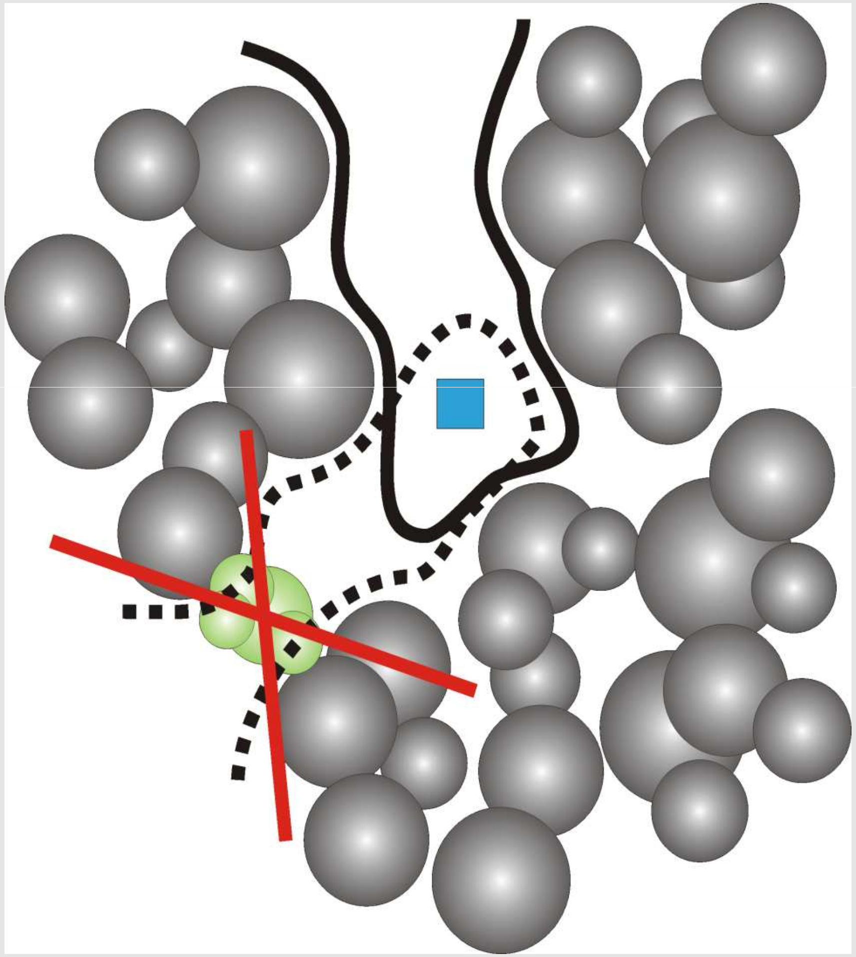
- Computed channel

CHANNEL DETECTION



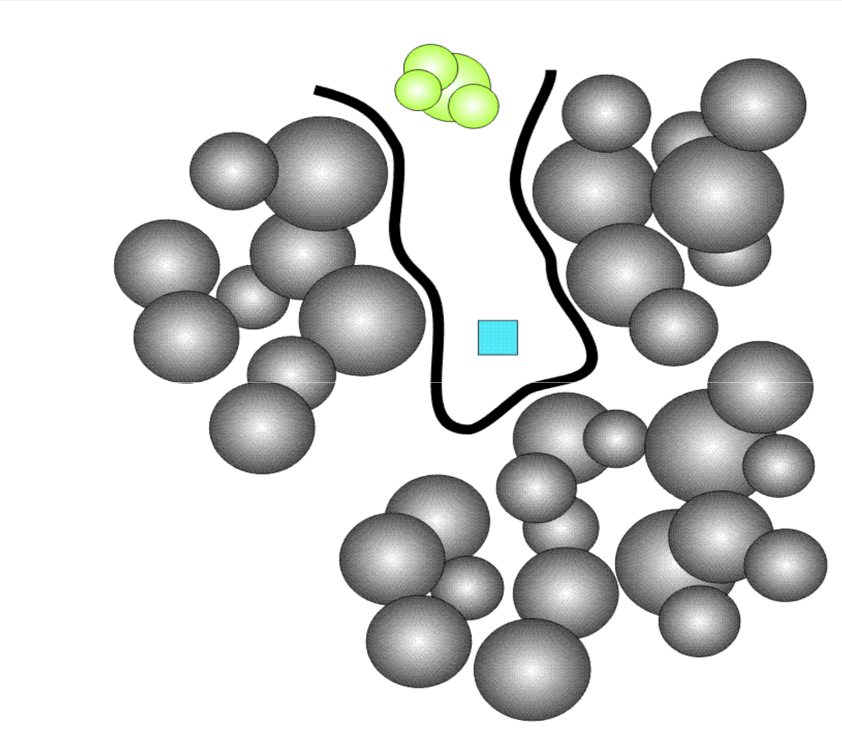
- Another posible channel

CHANNEL DETECTION



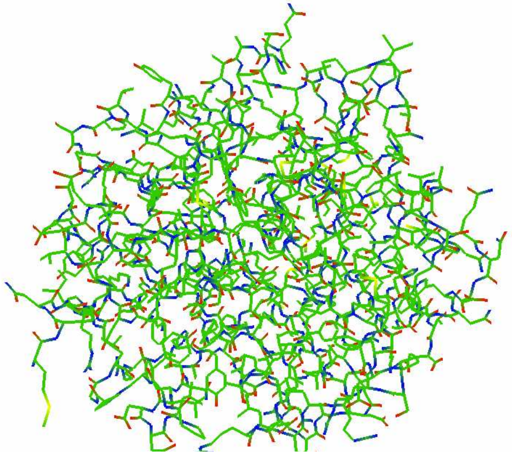
- Second channel is too narrow

CHANNEL DETECTION

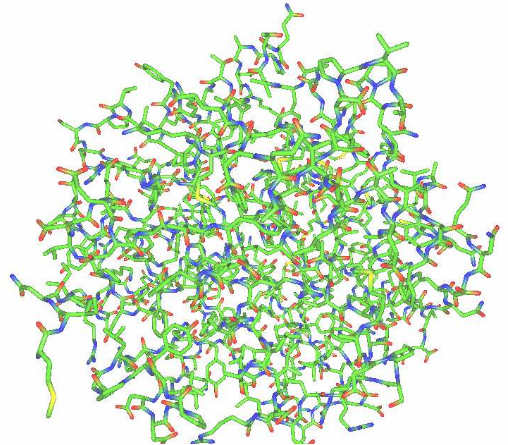


- The best possible channel

VISUALIZATION

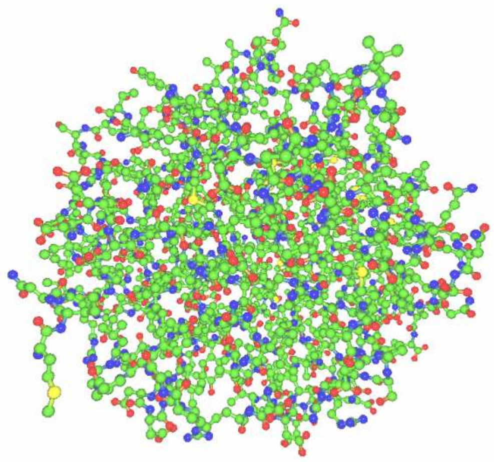


Lines

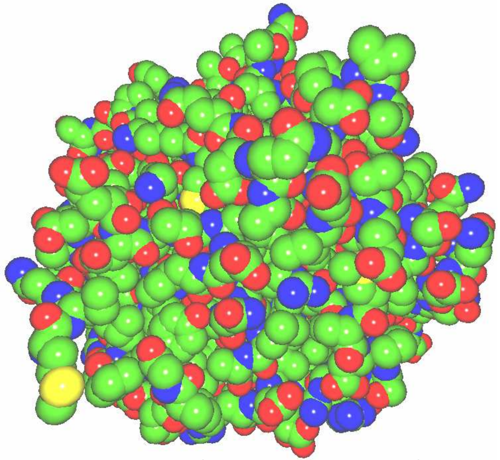


Sticks

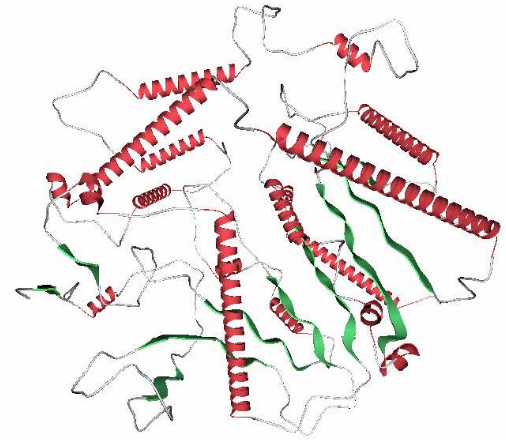
Alpha Trace



Balls and sticks

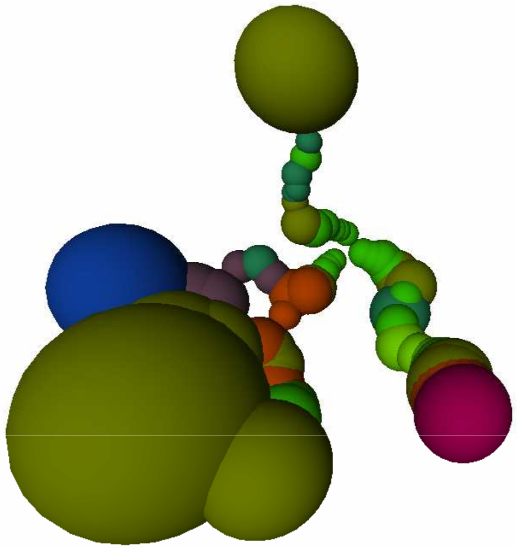


Balls (VDW Radii)

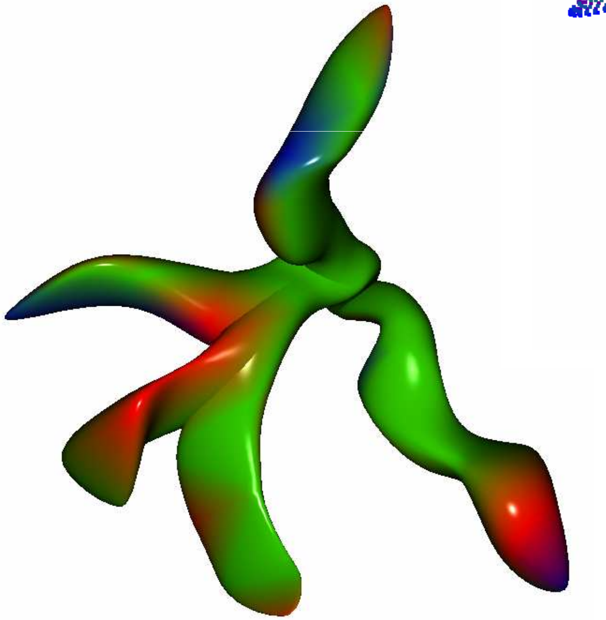


Secondary Structures

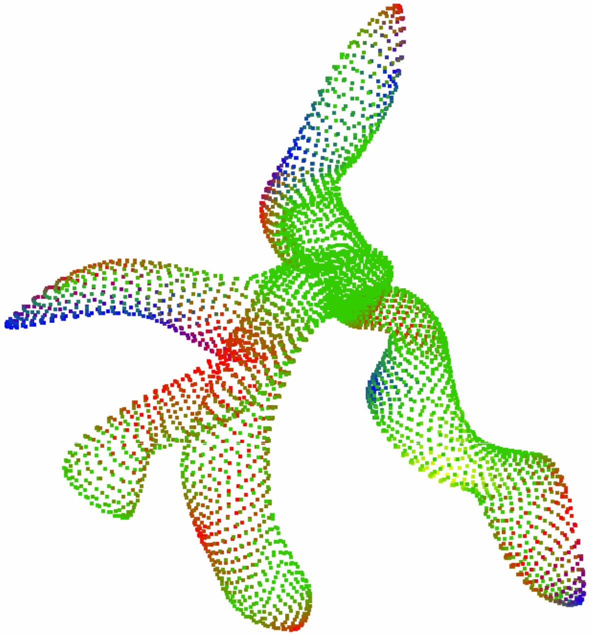
CHANNEL VISUALIZATION



Balls



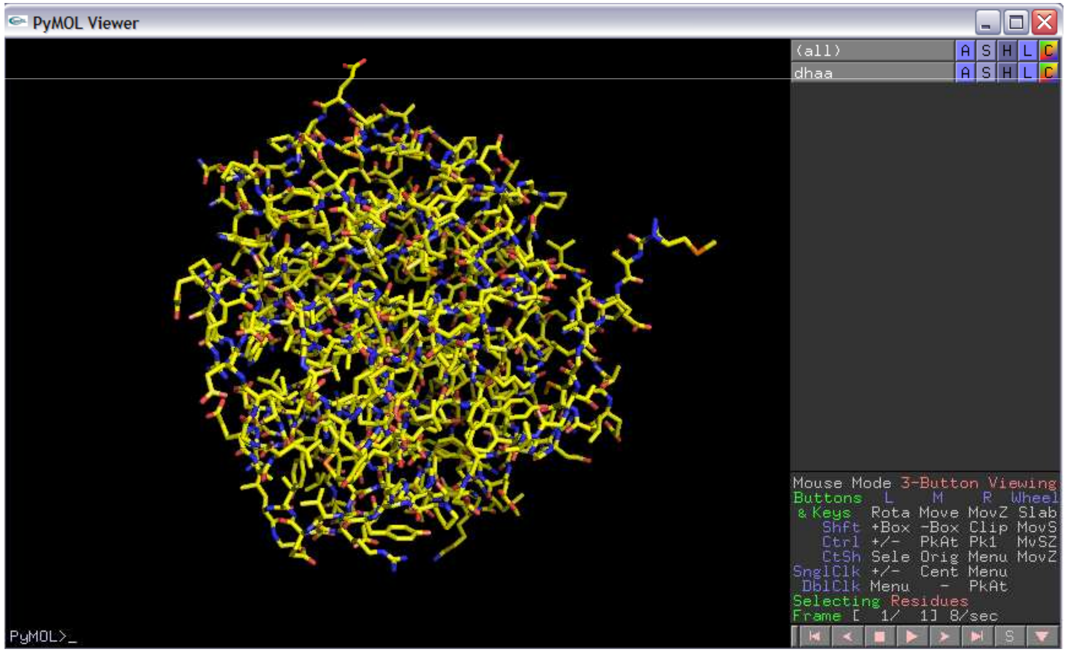
Tetrahedrons -> Surface subdivision



Points

VISUALIZATION APPLICATIONS

- Many applications developed
- Only few widely used (PyMOL, VMD…)



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Mouse Mode 3-Button Viewing
Buttons  L    M    R  Wheel
 & Keys  Rota Move MovZ Slab
   Shft  +Box -Box Clip MovS
   Ctrl  +/-  PkAt Pk1  MvSZ
   CtSh  Sele Orig Menu MovZ
SnglClk  +/-  Cent Menu
 DblClk  Menu  -   PkAt
Selecting Residues
Frame [  1/  1] 8/sec
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PyMOL>_
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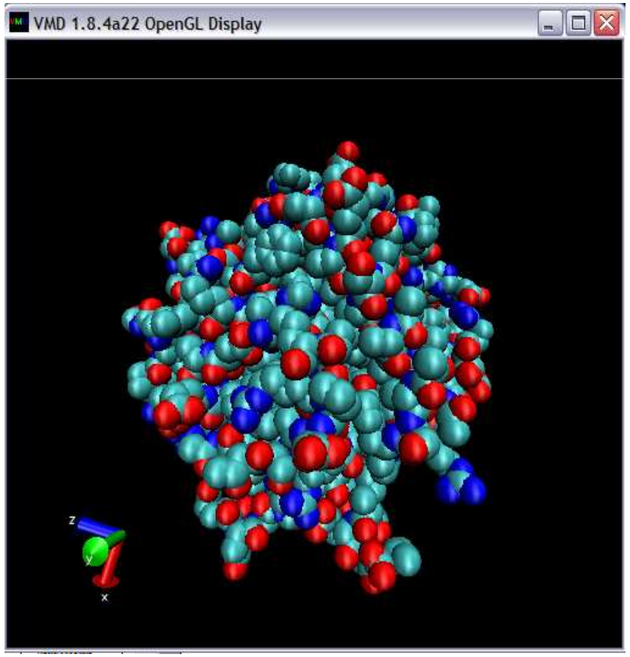
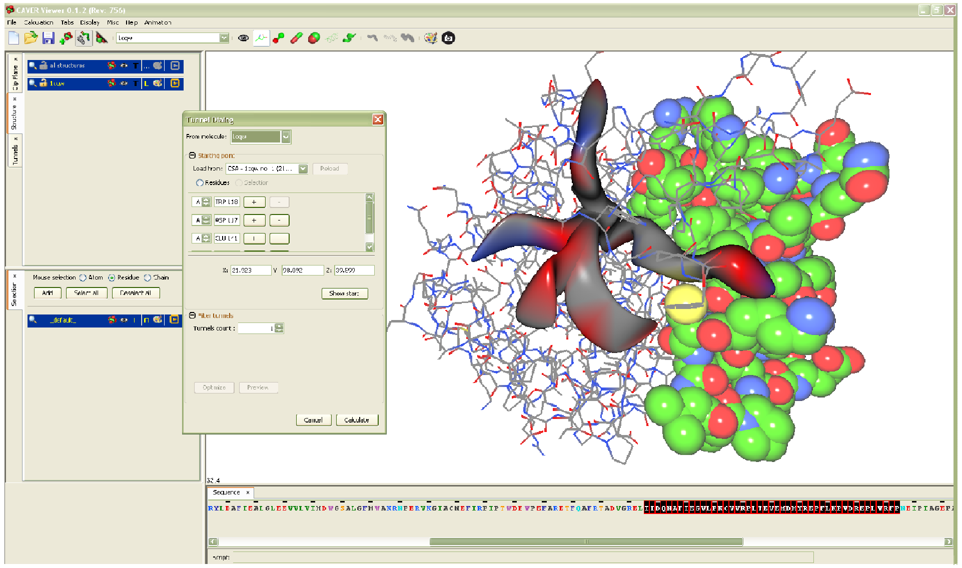
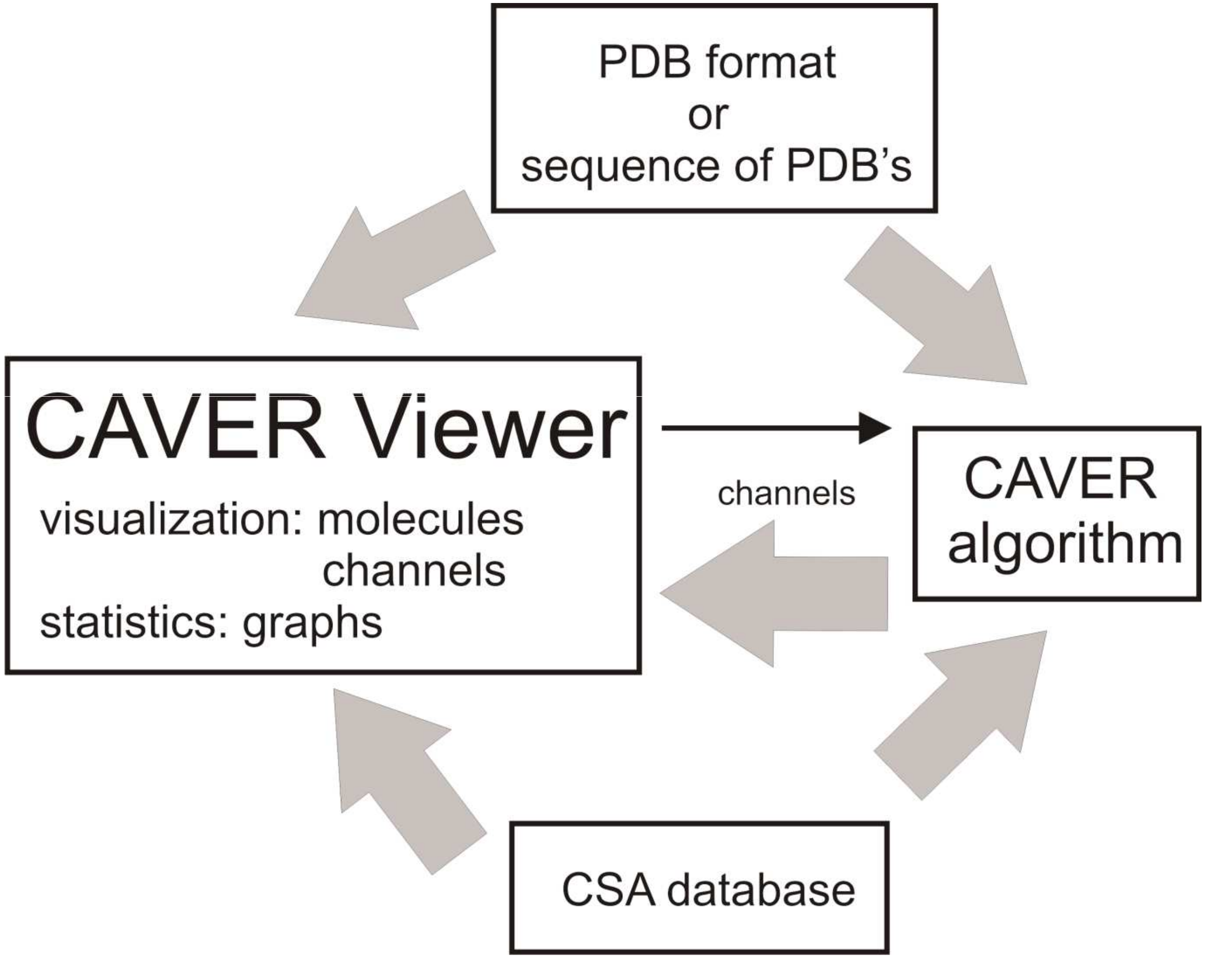


CAVER VIEWER SOFTWARE

- Software combining protein analysis and visualisation, developed in cooperation with biochemists from the Loschmidt Laboratories, Faculty of Science, MU
- 3000 users of caver viewer od pymol plugin around the world of both academic and commercial sphere
- Advanced features for further channel exploration



CAVER VIEWER SOFTWARE



PDB format
or
sequence of PDB's

CAVER Viewer

visualization: molecules
channels
statistics: graphs

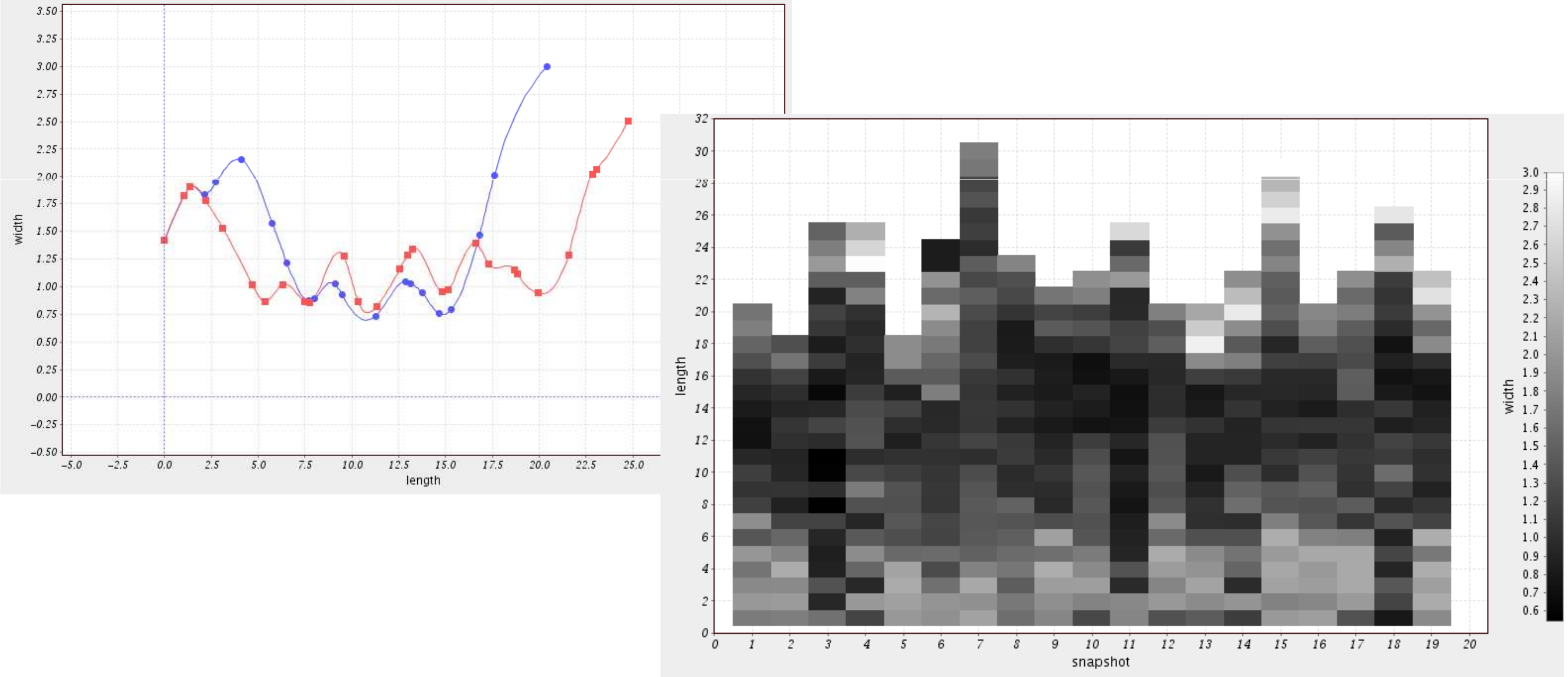
channels

CAVER
algorithm

CSA database

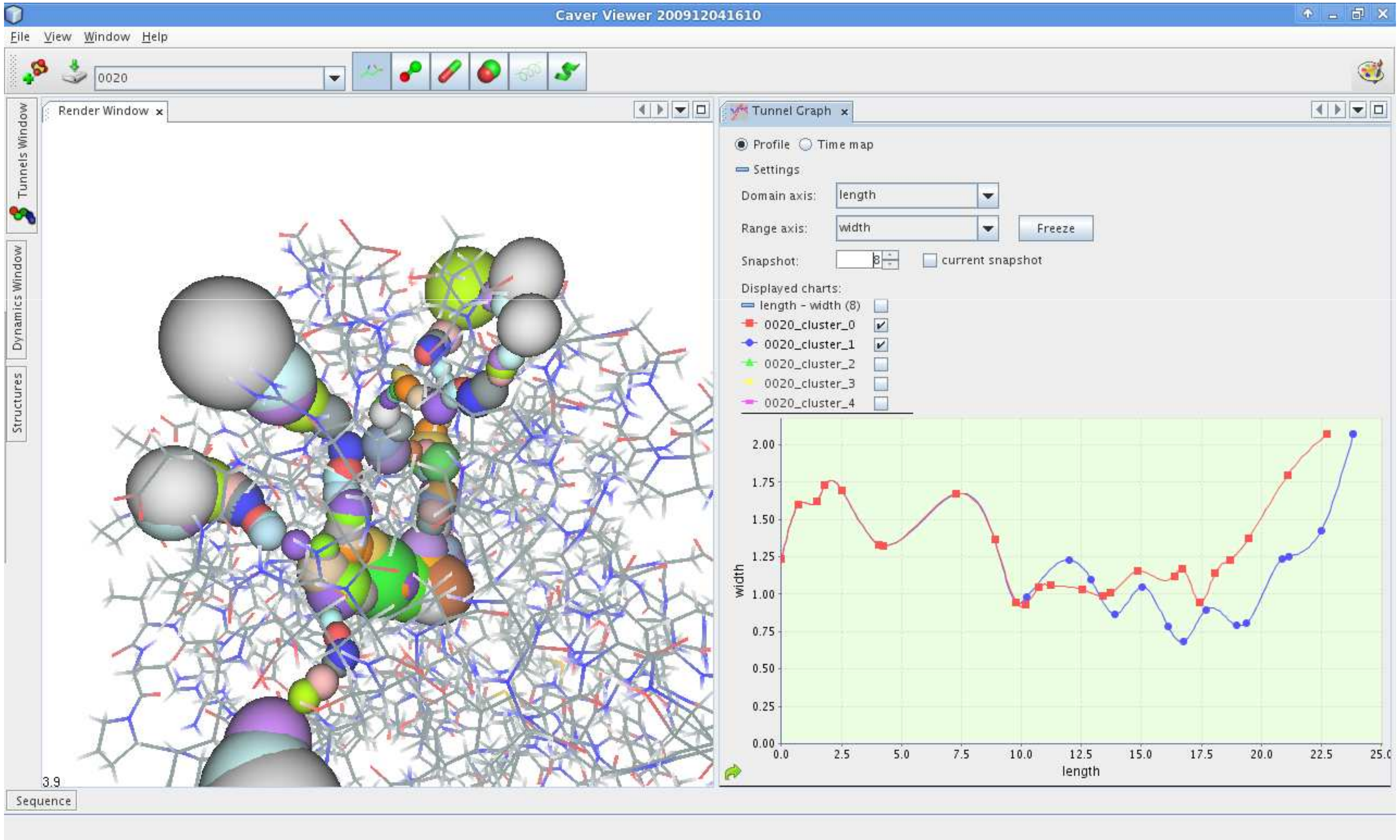
CAVER VIEWER SOFTWARE

- Properties of channels (lenghts, widths, curvature…)
- 2D and 3D graphs



CAVER VIEWER SOFTWARE

- Graph statistics



● Profile ○ Time map

Settings

Domain axis: length

Range axis: width

Freeze

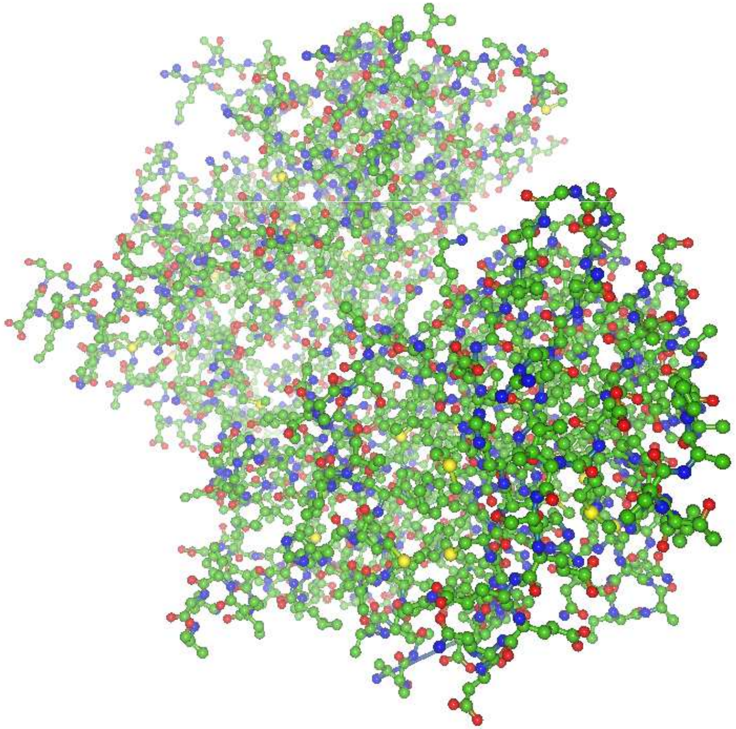
Snapshot: 8 ☐ current snapshot

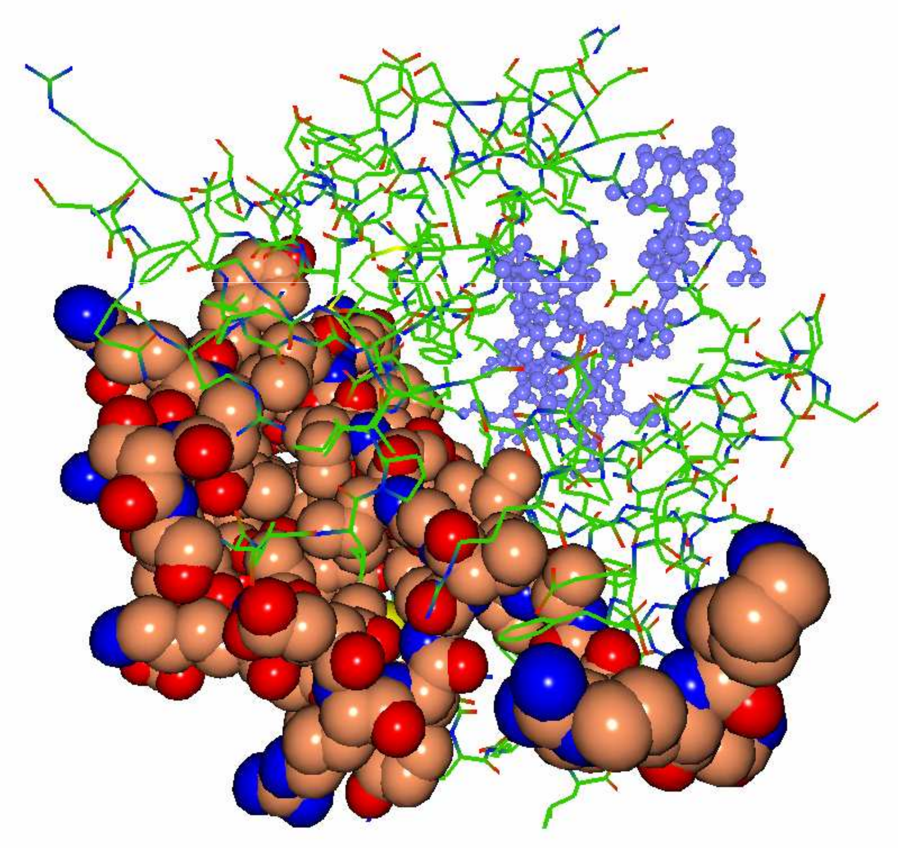
Displayed charts:

- length - width (8) ☐
- 0020_cluster_0 ☑
- 0020_cluster_1 ☑
- 0020_cluster_2 ☐
- 0020_cluster_3 ☐
- 0020_cluster_4 ☐

CAVER VIEWER SOFTWARE

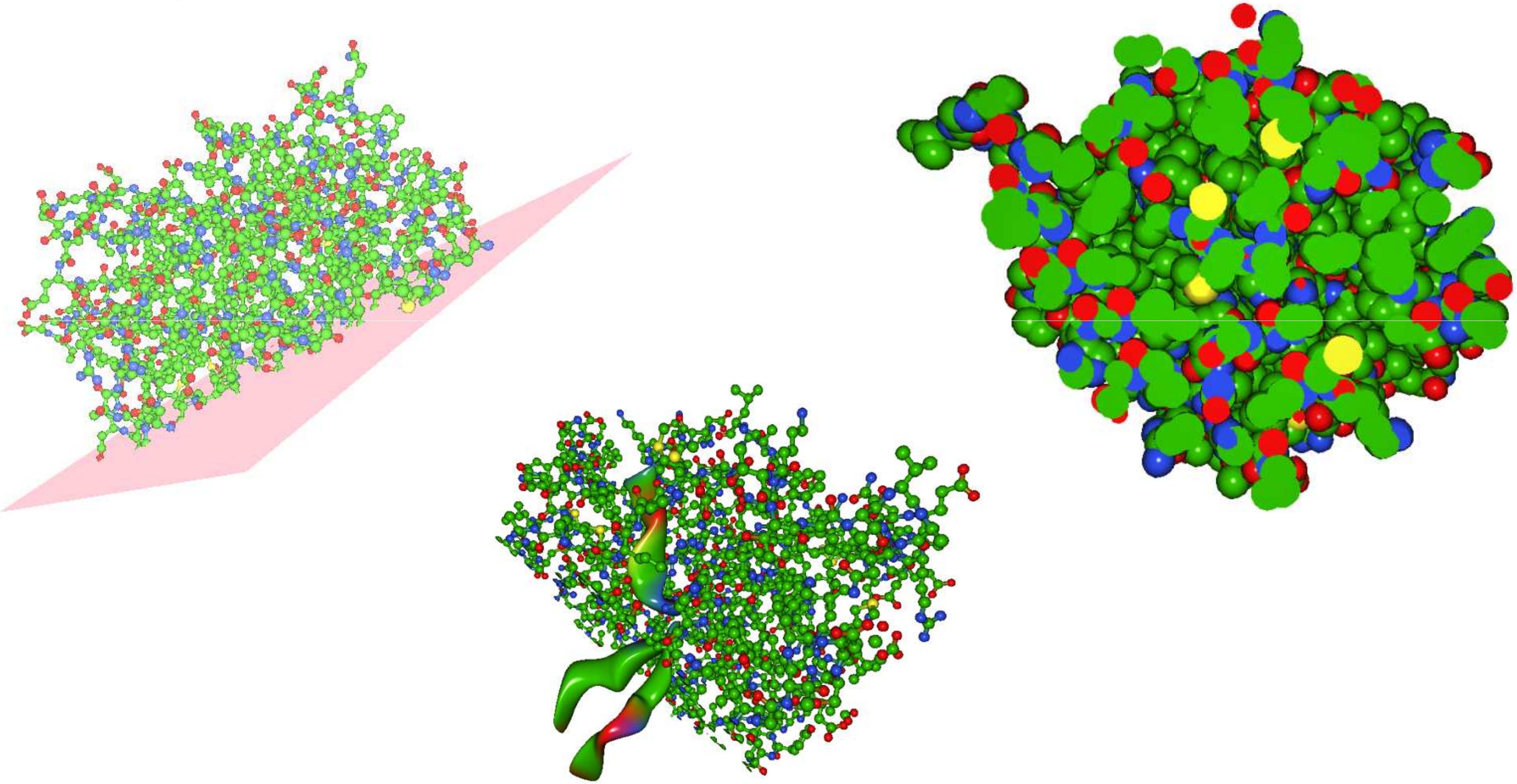
- Depth visualization
- Creating selections





CAVER VIEWER SOFTWARE

- Clipping plane

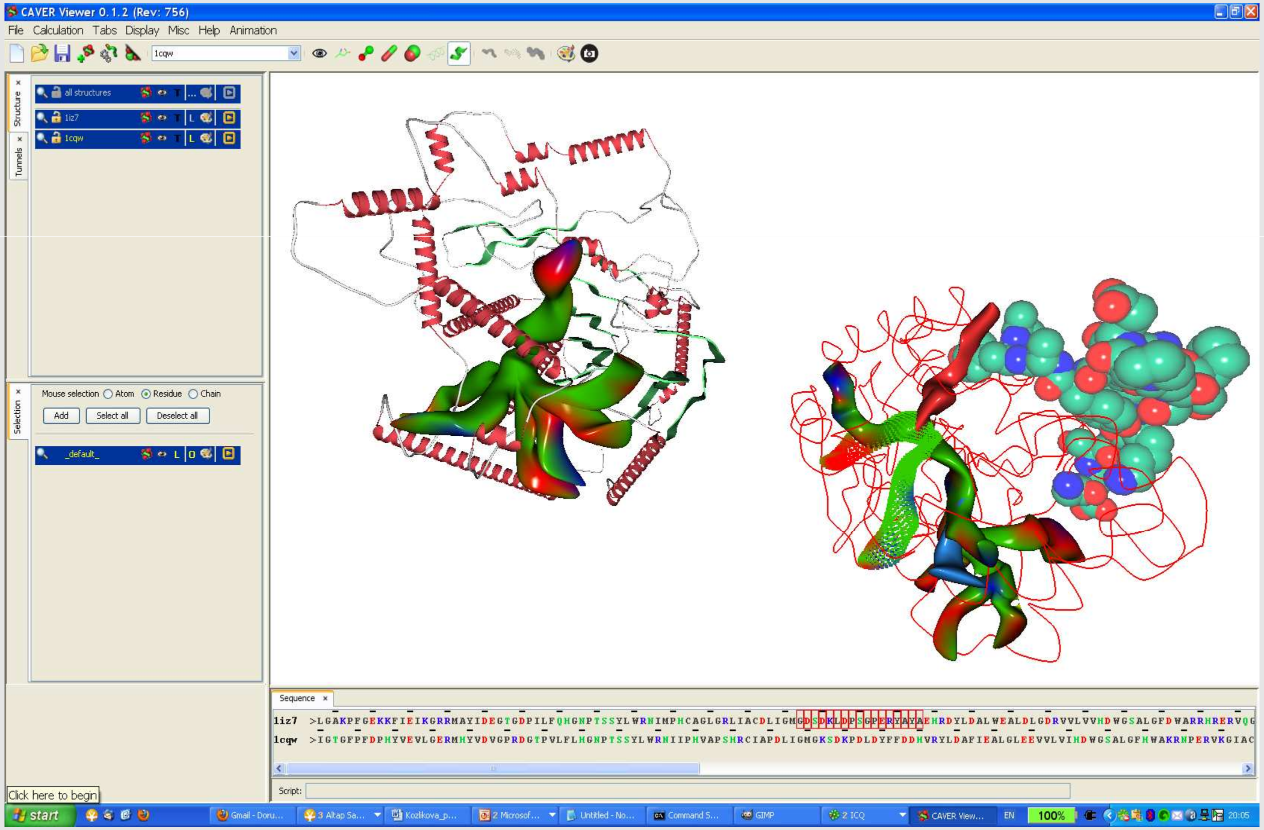


FUTURE WORK

- Analysis and visualisation of large proteins and other biochemical strucures (e.g. Ribosoms (~ 100 000 atoms)
- Visualisation of large dynamic molecular trajectories (~ 100 000 snapshots)
- 100 000 atoms in 100 000 frames means ~ 120 GB of data (3 floating point coordinates for each atom and frame)
- Design and implementation of extremly effective data structures for such bulky structures enabling real-time visualisation of dynamics
- Development of new visualisation techniques

CONCLUSION

- Thank you!
- Questions?



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1cqw  >IGTGFPFDPHYVEVLGERMHYVDVGPRDGTPVLFLHGNPTSSYLWRNIIPHVAPSHRCIAPDLIGMGKSDKPDLDYFFDDHVRYLDAFIEALGLEEVVLVIHDWGSALGFHWAKRNPERVKGIAC
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XYZ

- abc
- def