# Geometric and topological methods for visualizing channel and cavity structures in biomolecules

## Primary Goals
- We aim to devise novel geometric and topological techniques to understand the structure of biomolecules.
- In particular, we focus on the study of cavities and channels in proteins.
- We also aim to design interactive visualization tools which enable biologists to conduct detailed visual analysis of biomolecules.

## Motivation
- Biomolecules (e.g., proteins) are the basic building blocks of living systems.
- It has been observed that structure of biomolecule plays an important role in defining its function.
- Analysis of structural features is very important for understanding of structure-function relationships, engineering new proteins with required functional properties, or designing inhibitors for existing proteins.

## Challenges
- Size: Biomolecules consist of thousands of atoms. Identifying interesting features and ranking them based on their significance is non-trivial.
- Dynamic nature: In biomolecules move over time resulting in dynamic structural features.
- Uncertain data: Protein structures are obtained experimentally and thus have uncertainty associated with atomic positions and radii.

## Alpha Complex based framework
- Molecules can be represented using union of balls model.
- Each atom is represented as a sphere whose radius is von der Waals radius.
- Weighted Voronoi diagram partitions the space based on proximity to these atoms.
- The dual is called weighted Delaunay triangulation.
- Alpha complex is a filtration of Delaunay complex.
- Alpha complex at α = 0 partitions the molecular space into Occupied and Empty regions (O'R and E'R).
- Cavities are maximally connected regions in E'R.
- Channels are pathways in E'R.

## Channel Extraction and Visualization
- Contributions:
  - Using alpha complex based framework, we design a method to capture all geometrically feasible channels in a concise representation called channel network which supports querying for specific channels. The extracted channels are represented as set of connected tetrahedra.
  - We developed novel methods to automatically identify important channels within the network and rank them based on their significance.
  - We also proposed novel visualization methods to facilitate detailed study of the extracted channels.
- Evaluation:
  - The integrated channel extraction and visualization framework was successfully used to study multiple transmembrane pores and channels leading to active site.
  - The channel extraction method was compared with four existing software tools.
- Web-server: [http://vgl.csa.iisc.ac.in/chexvis/](http://vgl.csa.iisc.ac.in/chexvis/)

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**Connecting cavities**

## Method
- **Input**: PDB structure
- **Output**: Simplified network, Identified set of pores, The top TM pore

## Results
- The permanent liganded ion channels
- The comparison of KcsA potassium channels

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**Contributions**
- We propose a simple and flexible method for extracting cavities in biomolecules from uncertain data with guaranteed bounds on the perturbation required.
- We also propose efficient algorithms to compute a conduit between user selected cavities that satisfies well defined optimality criteria.
- We develop an interactive visualization of cavities in a molecule with multiple linked views that facilitates identification of disconnected cavities.

## Evaluation
- Case studies that demonstrate the benefits of the cavity connection based method.
- Web-server: [http://vgl.csa.iisc.ac.in/robustCavities/](http://vgl.csa.iisc.ac.in/robustCavities/)

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