Sequence and Structure Alignment
- Illustrated for the Water Channel Aquaporin
Sequence and structure information are the bedrock on which an understanding of cellular functions and the underlying physical mechanisms can be built. This lecture illustrates how the two sources of information are combined to investigate by means of the program VMD function and mechanism of the aquaporin family of membrane channels that transport water and certain small solutes across cell walls. Introducing first the key architectural features of a single aquaporin, structures and sequences of four aquaporins are aligned and common features recognized. The shared and distinct features are examined closely and used as guideposts leading quickly to key questions regarding the mechanism underlying aquaporin's efficient conduction and selection.
The Aquaporin Superfamily

Aquaporins are also functioning as gas conductors

Aquaporin Function and Human Aquaporins

AQP cluster

GLP cluster
## Water and Glycerol Channels in the Human Body

<table>
<thead>
<tr>
<th>Aquaporin</th>
<th>Location</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aquaporin-0</td>
<td>Eye: lens fiber cells</td>
<td>Fluid balance of the lens</td>
</tr>
<tr>
<td>Aquaporin-1</td>
<td>Kidney: proximal tubules, Eye: ciliary epithelium, Brain: choroid plexus, Lung: alveolar epithelial cells</td>
<td>Osmotic protection, Concentration of urine, Aqueous humor, Production of CSF, Alveolar hydration</td>
</tr>
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<td>Aquaporin-2</td>
<td>Kidney: collecting ducts</td>
<td>ADH hormone activity</td>
</tr>
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<td>Aquaporin-3</td>
<td>Kidney: collecting ducts, Trachea: epithelial cells</td>
<td>Reabsorption of water, Secretion of water</td>
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<tr>
<td>Aquaporin-5</td>
<td>Salivary glands, Lacrimal glands</td>
<td>Production of saliva, Production of tears</td>
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<td>Aquaporin-6</td>
<td>Kidney</td>
<td>Very low water permeability!</td>
</tr>
<tr>
<td>Aquaporin-7</td>
<td>Testis and sperm</td>
<td></td>
</tr>
<tr>
<td>Aquaporin-8</td>
<td>Testis, pancreas, liver</td>
<td></td>
</tr>
<tr>
<td>Aquaporin-9</td>
<td>Leukocytes</td>
<td></td>
</tr>
<tr>
<td>Aquaporin-10</td>
<td>Intestines</td>
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Additional members are suspected to exist.
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<td>Brain: hypothalamus</td>
<td>Osmosensing function?</td>
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Functionally Important Features of Aquaporins

- Water, gas, and glycerol transport
- Exclusion of ions and protons
- Tetrameric arrangement in membrane

Aquaporins of known structure:
- AQP1 – Mammalian aquaporin-1 (pure water channel) -Sui et al, Nature (2001)

~100% conserved -NPA- signature sequence
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Load Aquaporin 1J4N into VMD
Load Aquaporins 1j4n, 1fqy, 1lda, 1rc2 into VMD
Aligning Structures and Sequences
Comparing Structures by Similarity - Q Value
Comparing Structures by Similarity - Q Value
Exhibiting Sequence Identity - Side View
Exhibiting Sequence Identity - Top View
Showing Conserved Residues - Monomer
Showing Conserved Residues - Tetramer
Water Transport in Aquaporins

Simulation:
Apply constant force on bulk water molecules

100,000 atoms
Osmotic permeability of water channels

\[ p_f: 7.0 \pm 0.9 \times 10^{-14} \text{ cm}^3/\text{s} \]

Exp: \[ 5.4 - 11.7 \times 10^{-14} \text{ cm}^3/\text{s} \]

Aquaporin-1

Dynamics of Protein, Lipid, Water System

Glycerol Conduction

Inverted helices guide glycerol

Aquaporins

Case study, see at http://www.ks.uiuc.edu/Training/CaseStudies/

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Brijeeet Dhalwal
Zan Luthey-Schulten