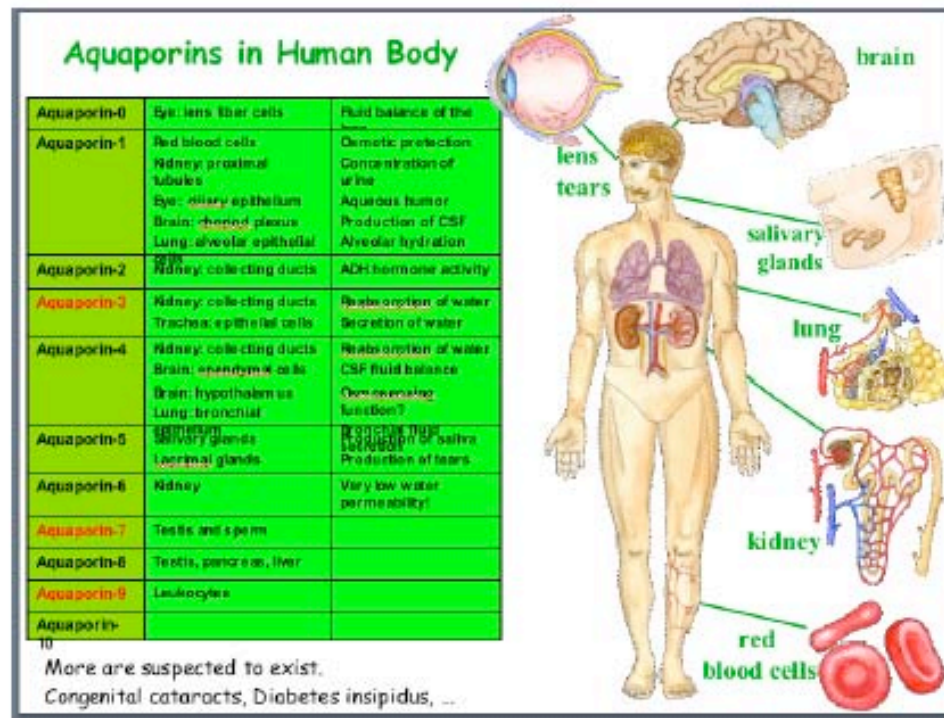


# Aquaporins



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## Physical Bioinformatics - A Case Study

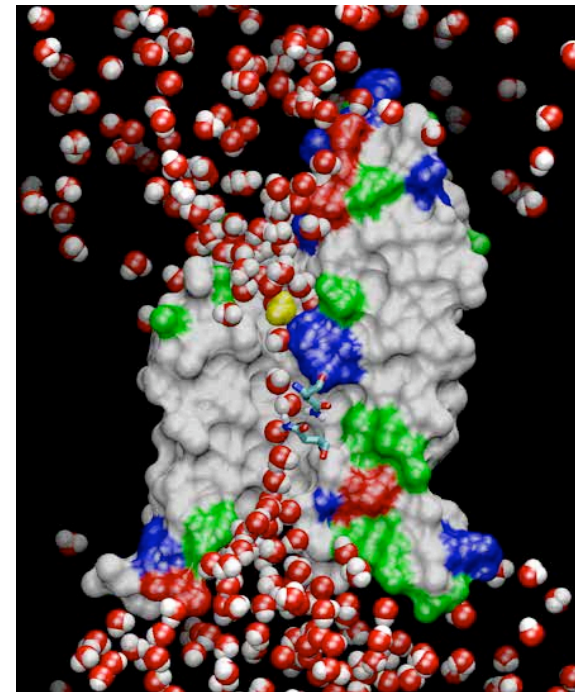
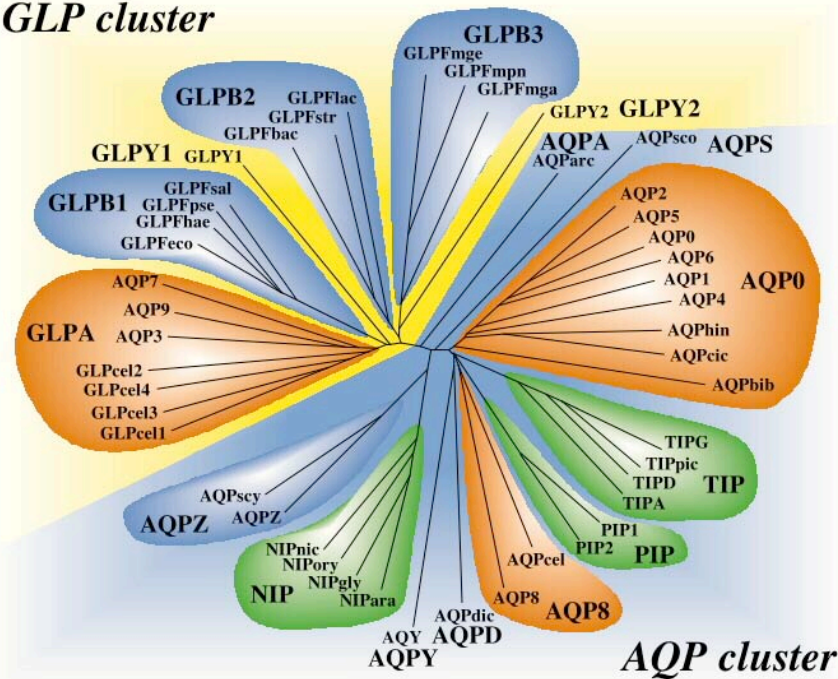
Sequence and structure information are the bedrock on which an understanding of cellular functions and the underlying physical mechanisms can be built. This lecture illustrates how the two sources of information are combined to investigate by means of the program VMD function and mechanism of the aquaporin 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 questions are addressed by means of molecular dynamics simulations using the program NAMD that reveal the physical principles behind water transport and highly selective solute co-transport in aquaporins. Sequence-structure information is viewed again to elucidate tetramer binding and pathologies connected with certain aquaporin mutants. The lecture introduces the concepts behind the programs employed and emphasizes those aspects of the case study that can be applied for investigations of other protein families.

# Physical Bioinformatics - A Case Study

## Aquaporin Family of Membrane Channels

Klaus Schulten, U. Illinois at Urbana-Champaign

*GLP cluster*

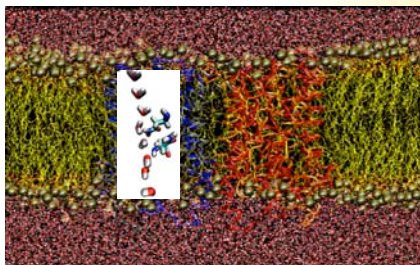
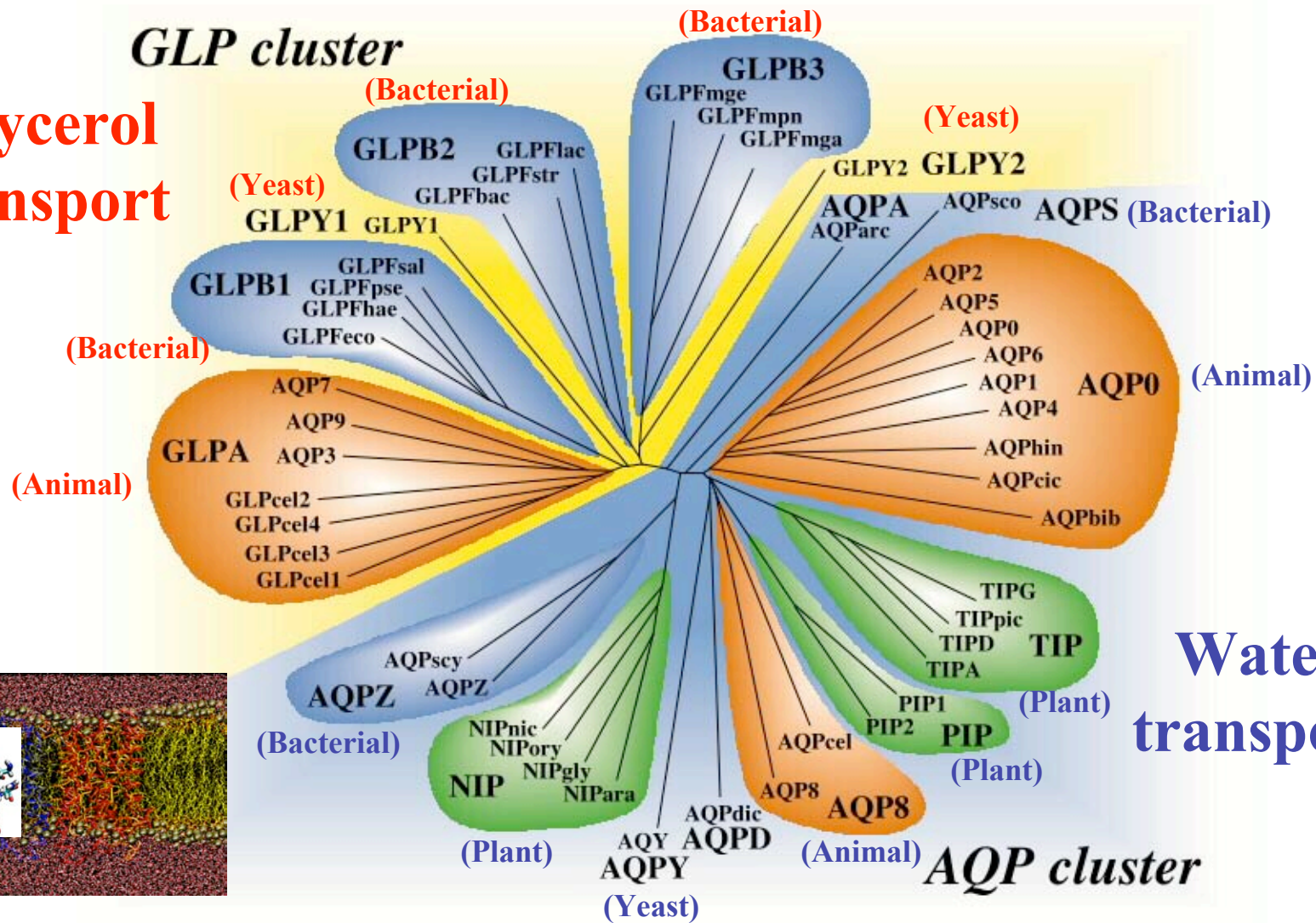


|            |     |                                     |                                   |                               |       |     |       |     |       |     |       |     |       |     |      |
|------------|-----|-------------------------------------|-----------------------------------|-------------------------------|-------|-----|-------|-----|-------|-----|-------|-----|-------|-----|------|
|            |     | .                                   | :                                 | *                             | :     | :   |       | .   | .*:   | :   | :     | .*  | :     |     |      |
| AQP0_HUMAN | --- | LNTLHPAVSVGQATTVEIFLTLQFVLCIFATYDE  | -                                 | RRNGQLGSVALAVGFSLALGHLFGMYT   | GAGM  |     |       |     |       |     |       |     | 183   |     |      |
| AQP1_HUMAN | --- | RNDLADGVNSGQGLGIEIIGTLQVLVLCVLATDR  | -                                 | RRRDLGGSAPLAIGLSVALGHLAIDYT   | GCGI  |     |       |     |       |     |       |     | 191   |     |      |
| AQP2_HUMAN | --- | VNALSNSTTAGQAVTVLFLTLQVLCIFASTDE    | -                                 | RRGENPGTPALSIGFSVALGHLGHIHYTG | CSM   |     |       |     |       |     |       |     | 183   |     |      |
| AQP3_HUMAN |     | GIFATYPSGHLDMINGFFDQFIGTASLIVCVLAI  | VDPYNNPVPRGLEAFTVGLVVLVIGTSMGFNS  | GYAV                          |       |     |       |     |       |     |       |     | 214   |     |      |
| AQP4_HUMAN | --- | VTMVHGNLTAGHLLVELIITFQLVFTIFASCDS   | -                                 | KRTDVTGSIALAIGFSAIGHLFAINYTG  | GASM  |     |       |     |       |     |       |     | 212   |     |      |
| AQP5_HUMAN | --- | VNALNNNTTQQAAMVVELILTFQALCIFASTDS   | -                                 | RRTSPVGSVALSIGLSVTLGHLVGIYFTG | CSM   |     |       |     |       |     |       |     | 184   |     |      |
| AQP6_HUMAN | --- | INVVRNSVSTGQAVAVELLTLQVLCVFASTDS    | -                                 | RQTS--GSPATMIGISWALGHLIGILFTG | CSM   |     |       |     |       |     |       |     | 195   |     |      |
| AQP7_HUMAN |     | GIFATYLPDHMTLWRGFLNEAWLTGMLQLCLFA   | ITDQENNPALPGTEALVIGILVVIIGVSLGMNT | GYAI                          |       |     |       |     |       |     |       |     | 225   |     |      |
| AQP8_HUMAN | -   | AAFVTVQEQGQVAGALVAEIIITLLALAVCMGAIN | -                                 | EKTKGPLAPFSIGFAVTVDILAGGPVSG  | GCM   |     |       |     |       |     |       |     | 209   |     |      |
| AQP9_HUMAN |     | HIFATYPAPYLSLANAFADQVATMILLIIVFAIF  | DSRNLGAPRGLEPIAIGLLIIVIASSLGLNSG  | CAM                           |       |     |       |     |       |     |       |     | 215   |     |      |
| GLPF_ECOLI |     | GTFSTYPNPHINFVQAFVEMVITAILMGLLILAL  | TDDGNGVPRGPLAPLLIGLLIAVIGASMGPLT  | GFAM                          |       |     |       |     |       |     |       |     | 202   |     |      |
| ruler      | ... | 180                                 | .....                             | 190                           | ..... | 200 | ..... | 210 | ..... | 220 | ..... | 230 | ..... | 240 | .... |



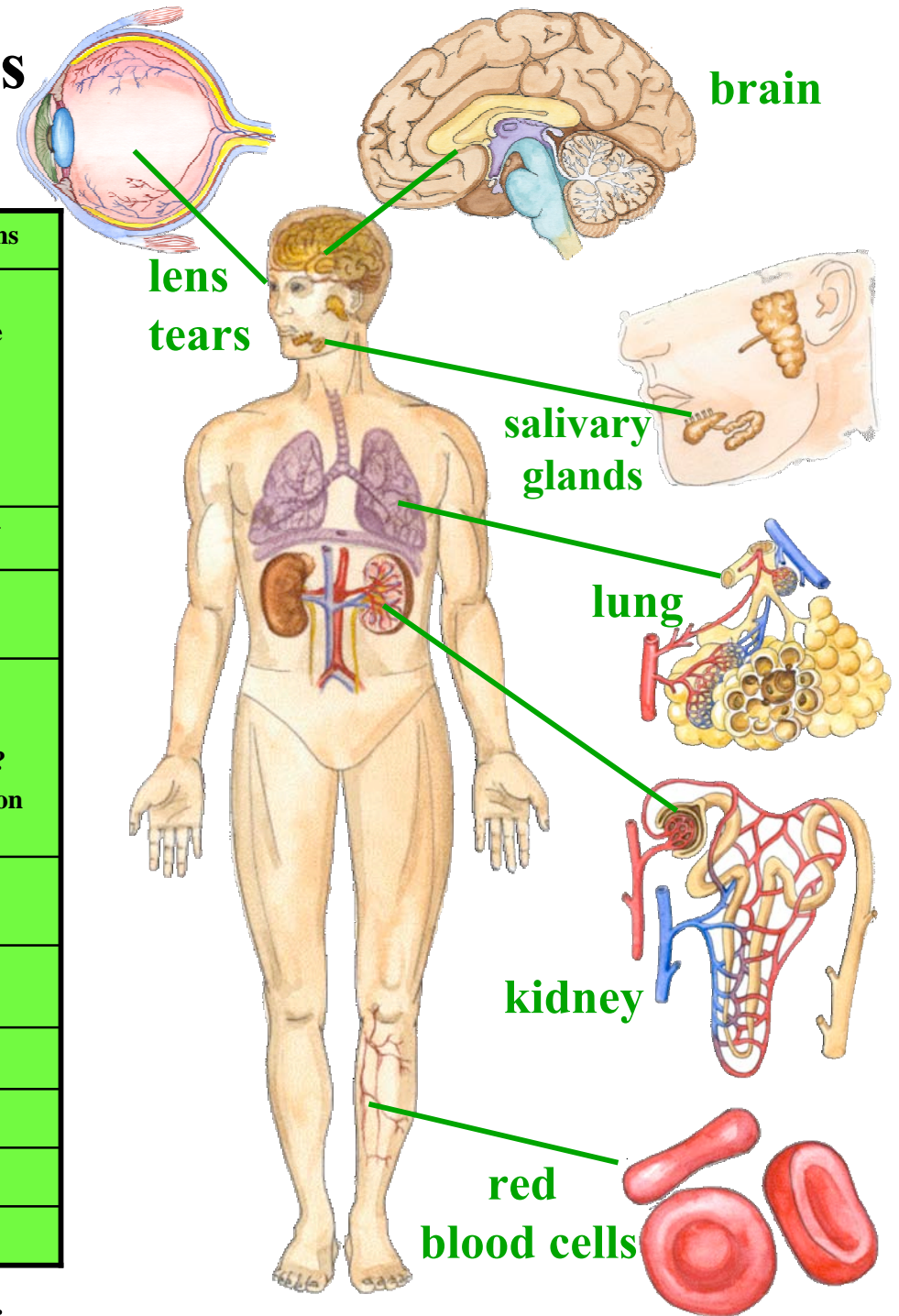
# The Aquaporin Superfamily

**Glycerol transport**



# Water and **Glycerol** Channels in the Human Body

|                     |  |  |
|---------------------|--|--|
| <b>Aquaporin-0</b>  | Eye: lens fiber cells  | Fluid balance of the lens  |
| <b>Aquaporin-1</b>  | Red blood cells<br>Kidney: proximal tubules<br>Eye: ciliary epithelium<br>Brain: choroid plexus<br>Lung: alveolar epithelial cells | Osmotic protection<br>Concentration of urine<br>Aqueous humor<br>Production of CSF<br>Alveolar hydration |
| <b>Aquaporin-2</b>  | Kidney: collecting ducts   | ADH hormone activity   |
| <b>Aquaporin-3</b>  | Kidney: collecting ducts<br>Trachea: epithelial cells  | Reabsorption of water<br>Secretion of water  |
| <b>Aquaporin-4</b>  | Kidney: collecting ducts<br>Brain: ependymal cells<br>Brain: hypothalamus<br>Lung: bronchial epithelium                            | Reabsorption of water<br>CSF fluid balance<br>Osmosensing function?<br>Bronchial fluid secretion         |
| <b>Aquaporin-5</b>  | Salivary glands<br>Lacrimal glands   | Production of saliva<br>Production of tears  |
| <b>Aquaporin-6</b>  | Kidney   | Very low water permeability!   |
| <b>Aquaporin-7</b>  | Testis and sperm   |  |
| <b>Aquaporin-8</b>  | Testis, pancreas, liver  |  |
| <b>Aquaporin-9</b>  | Leukocytes   |  |
| <b>Aquaporin-10</b> |  |  |



Additional members are suspected to exist.

# Functionally Important Features of Aquaporins

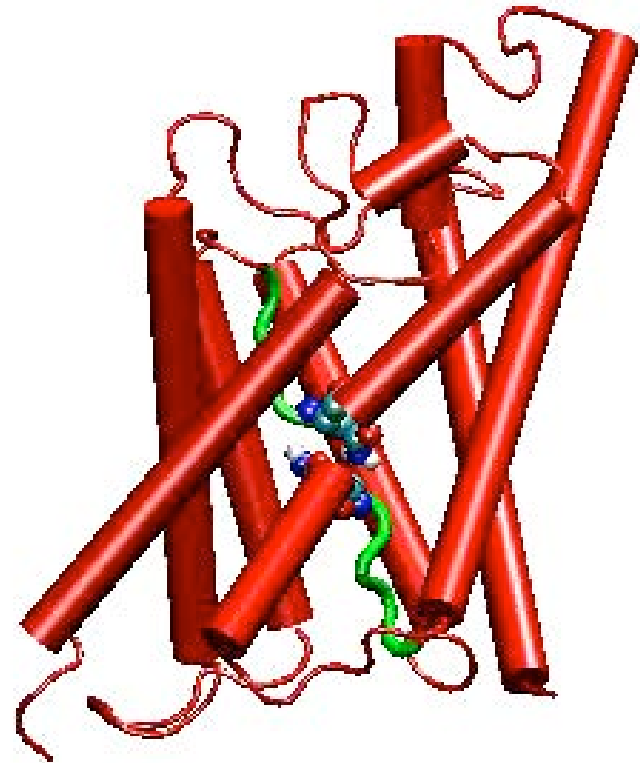
- Water and glycerol transport
- Exclusion of ions and protons
- Tetrameric arrangement in membrane

Aquaporins of known structure:

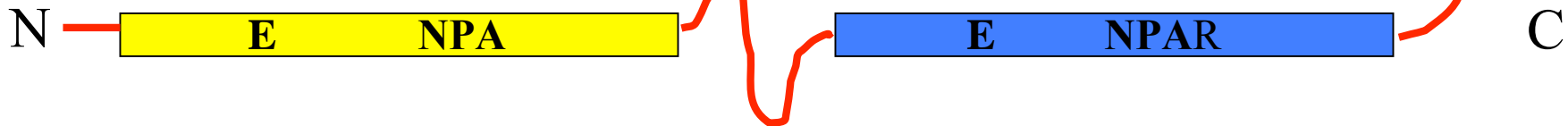
**GlpF** – E. coli glycerol channel (aquaglyceroporin)

– Fu, et al., Science (2000)

**AQP1** – Mammalian aquaporin-1 (pure water channel) -Sui et al, Nature (2001)



**~100% conserved -NPA- signature sequence**





# Load Aquaporin 1J4N into VMD

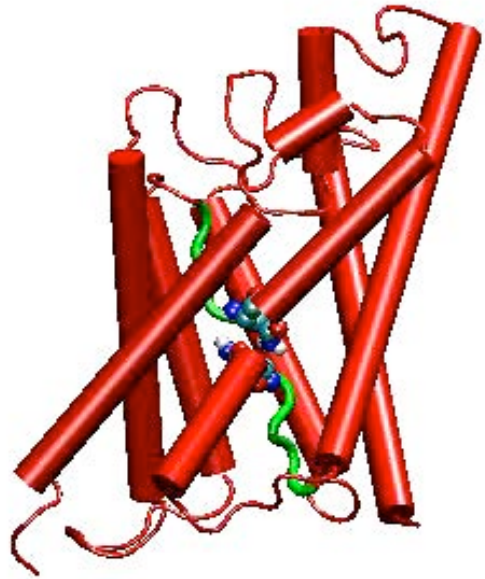
The image shows the VMD (Visual Molecular Dynamics) interface. The main window, titled "VMD Main", contains a menu bar (File, Molecule, Graphics, Display, Mouse, Extensions, Help) and a table of loaded molecules. The table has columns for ID, T, A, D, F, Molecule, Atoms, Frames, and Vol. The first row shows ID 1, T A D F, Molecule 1J4N, Atoms 2029, Frames 1, and Vol 0. Below the table are playback controls including a time slider at 0, zoom, Loop, step (set to 1), and speed controls.

The "Graphical Representations" window is open, showing the configuration for the selected molecule "1: 1J4N". It includes buttons for "Create Rep" and "Delete Rep", and a table with columns for Style, Color, and Selection. The first row is "Tube", "Name", and "all". Below this is a "Selected Atoms" field containing "all". The "Draw style" tab is active, showing "Coloring Method" set to "Name" and "Material" set to "Opaque". The "Drawing Method" is set to "Tube". At the bottom, there are sliders for "Radius" (set to 0.5) and "Resolution" (set to 11), and an "Apply Changes Automatically" checkbox with an "Apply" button.

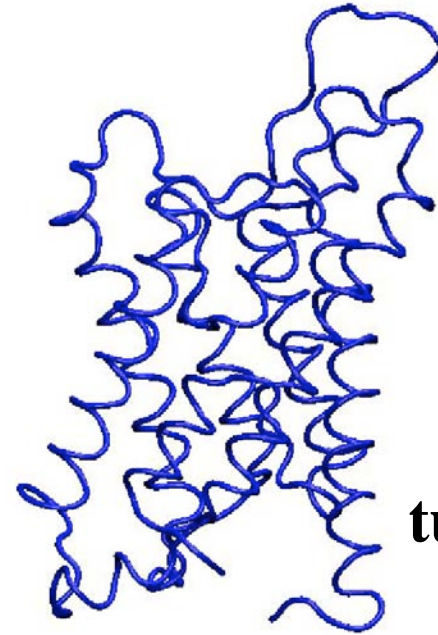
The "VMD 1.8.2b7 OpenGL Display" window shows a 3D rendering of the Aquaporin 1J4N protein structure as a cyan tube model. The structure is a complex, multi-domain protein with several alpha-helices and beta-strands. The system tray at the bottom right shows icons for VMD, a terminal, and a network connection.

# VMD Permits Different Rendering Styles

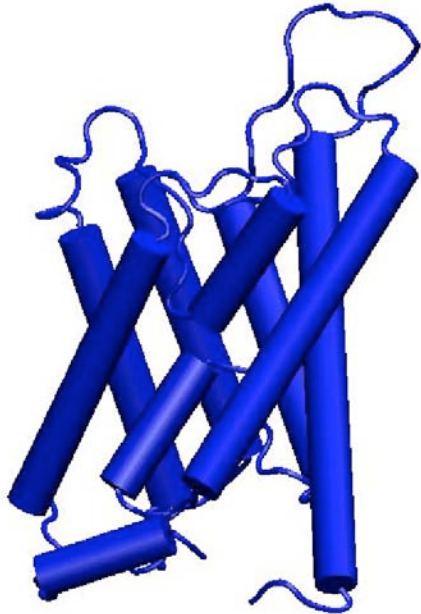
**movie**



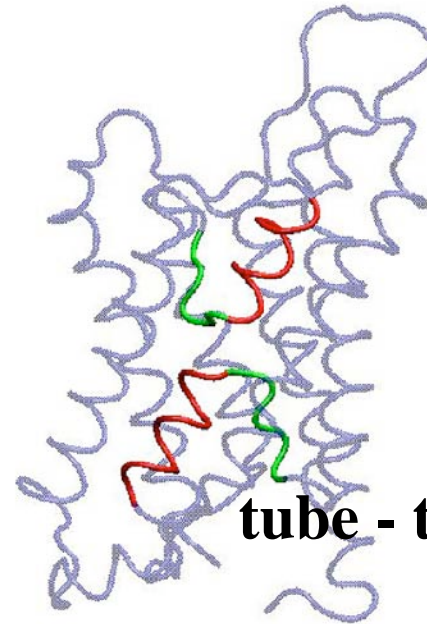
**tube**



**cartoon**



**tube - transparent**





# Comparing Sequences of Aquaporins

```

      :
      * : :
      : : : :
AQP0 HUMAN -----ASFWRRAIFAEFFA1LLFYVEFGLG2SLRWA-----PGPLHLVLCVAMAFGLALATLV3SVGHI 62
AQP1 HUMAN -----KKLFWRRAVVAEFLATLLFVFFSIGSALGFKY4PVGNNTAVQDNVQVSLAFGLSIATLAL5SVGHI 70
AQP2 HUMAN -----IAFSRAVFAEFLATLLFVFFGLGSALNWF-----QALPSVLGIAMAFGLIGITLV6QALGHI 62
AQP3 HUMAN -----IRYRLLRQALAECL7GLLILVMFCGCSVAQVV-----LSRGTGGFLTINLAFGFAVTL8GILIAQV 77
AQP4 HUMAN -----VWTQAFWKA9VLAFLAMLI10FVLLSLGSLINWG-----GTEKPLPVDMLISLCFGLSIATMV11QCFGHI 91
AQP5 HUMAN -----VAPLKAVFAEFLATLLFVFFGLGSALKWF-----SALPTILQIALAFGLAI12GLAALGPV 63
AQP6 HUMAN MLACRLWKATSRALFAEFLATGLYVFFGVG13SVMRWF-----TALPSVLQIAIT14FNLV15GLAMAV16QVTKW 76
AQP7 HUMAN KIQEILQRKMVREFLAEFMS17TYVMVFG18GLGSVAHMV-----LNK-KYGSVLGVNL19GF20FGVTMGVHVAGRI 88
AQP8 HUMAN RWRVSWYERFV21QCLVELLGSALFIFI22GCLSVIENG-----TDTGLLQ23PALAHGLALGLVIA24ILGNI 86
AQP9 HUMAN -----LKSSLAKETLSEFLGT25FILLIVLGC26CVAAQAI-----LSRGRFG27GVITIN28VGFSMAVAMAI29VAGGV 78
GLPF_ECOLI -----QTSTLKGQCI30AFLGTGLLIF31FGVGCVAALK-----VAGASFG-QWEISVIWGLGVAMAI32YL33AGV 62
ruler    ... 40.....50.....60.....70.....80.....90.....100....

```



```

      **.* *.* : :
      : : : :
AQP0 HUMAN SGAHVNP34AVTFAFLVGSQMSLLR35AFYMAAQLLGA36VAGA37AVLYSVTP-----PAVRCNLA----- 117
AQP1 HUMAN SGAHLNPAVTLGLLLSCQI38SIFRALMYIAACVGAIVATAILSGITS-----SLTGN39SLG----- 125
AQP2 HUMAN SGAHINPAVTVA40CLVGVCHVSVLRAAFYVAAQLLGA41VAGA42ALLHEITP-----ADIRGD43LA----- 117
AQP3 HUMAN SGAHLNPAVTIFAMCFLAREPWIK44LPIYTLAQLLGA45FLGAGIVFGLY46YDAIWHFADNQLFVSGP47NG-----TA 144
AQP4 HUMAN SGGHINPAVTIVAMVCTRKISIAK48SVPYIAAQLGAIIGAGILYLVTP-----PSVVG49GLG----- 146
AQP5 HUMAN SGGHINPAITLALLVGNQISLLR50APFYVAAQLVGA51IAAG52ILYGVAP-----LNARGNLA----- 118
AQP6 HUMAN SGAHANPAVTLAFLVGS53HISLPRAVAVAAQLVGA54TVGAALLYGVMP-----GDIRE55TLG----- 131
AQP7 HUMAN SGAHMNAAVTFANCALGRVPWRK56FPVYVLG57QFLGSFLAAAT58IYSLFY59TAILHFSGGQLM60VTGPVA-----TA 155
AQP8 HUMAN SGGHFNPAVSLAAMLI61GGLNLVMLLPYVWV62SOLLGGMLGAALAKVVS-----EERF63WNASC----- 142
AQP9 HUMAN SGGHINPAVSLAMCLFGRMKW64KLPPYVGAQFLGAFVGAALVFGIY65YDLMSFAGGKLLIVG66ENAT-----TA 145
GLPF_ECOLI SGAHLNPAVTIALLWLFAC67DKR68KVLPFIVS69QVAGAFCAALVYGLY70YNLFFDFEQTHIIVRGS71VEVDLA 132
ruler    ... 110.....120.....130.....140.....150.....160.....170....

```



```

      :
      * : :
      : : : :
AQP0 HUMAN ---LNTLHPAVSVGQAT72VEIFLTLQ73FLVLCIFATYDE-RRNGQLG74SVALAVG75PSLALGHLFGMYVTGAGM 183
AQP1 HUMAN ---RNDLADGVNSGGGLGIEII76GLQLVLCVLA77TDR-RRRDLGGSAPLAI78GLSVALGHLLAIDYTCGCI 191
AQP2 HUMAN ---VNALSNS79TAGQAVV80VELFLTLQ81LVLCIFASTDE-RRGENPGTPALSI82GF83SVALGHLLGIHYTGCSM 183
AQP3 HUMAN G84IFATY85PSGHLDMINGCFD86FIGTASLIVCVLA87IVDPYNNPVERGLEAF88VGLVVLVIG89TSMGFN90GGYAV 214
AQP4 HUMAN ---VTMVHG91NLTAGHGLLVELII92FLVFTIFAS93CDS-KRTDVTGSIALAI94GF95SVAIGHLFAINYTGASM 212
AQP5 HUMAN ---VNALNNT96TQGGAMVVELIL97FLQALCIFA98STDS-RRTSFVGS99PALSI100GLSVTLGHLVGIYFTGCSM 184
AQP6 HUMAN ---INVVRNSVSTGQAVAV101ELLTLQLVLCVFASTDS-RQTS-GSPA102MIGISWALGHLLIGILFTGCSM 195
AQP7 HUMAN G103IFATY104LPDHMLWRGFLNEAWL105GLMLQLCLFATLDQENN106PALPGTEALVIGILVVIIGVSLGMN107GYAI 225
AQP8 HUMAN -AAFVTVQEQGVAGALVAE108II109TL110LALAVCMGAIN--EKTGKPLA111PSI112GF113AV114VDILAGGPVSGGCM 209
AQP9 HUMAN HIFATY115PAPYLSLANAFAD116QVVA117TMILLIIVFAIFDSRNLGAP118RGLEPTAI119GLLIIVIAS120SLGLNSGCAM 215
GLPF_ECOLI GTFSTY121PNPHIN122FVQAF123AVEMVI124TAILMGLLILALDDGNGV125PRG126PLAPLLI127GLLIAVI128GASMG129PLTG130FAM 202
ruler    ... 180.....190.....200.....210.....220.....230.....240....

```



```

      **.* : :
      : : : :
AQP0 HUMAN NPARSFAPAIL131TGNFT-----NHWVYVWVGP132PIIGGGLGSLLYDFLL133FP----- 225
AQP1 HUMAN NPARSFSGSAVITHNFS-----NHWIFWVGP134PIIGALAVLIYDFIL135AP----- 233
AQP2 HUMAN NPARS136LAPAVVTGKFD-----DHWVFWVGP137PLVGAIGSLLYNVV138LP----- 225
AQP3 HUMAN NPARD139FGRPLFTALAGWGS140AVFTGCG--HWWWV141PVIVS142PLLGSIAGV143FVYQLMIG144C----- 267
AQP4 HUMAN NPARSFGPAVIMGNWE-----NHWIYVWVGP145PIIGAVLAGGLYEVV146FC147PD----- 255
AQP5 HUMAN NPARSFGPAVVMNRFSP-----AHWVFWVGP148PIVGA149VLAAILYV150YLL151FP----- 227
AQP6 HUMAN NPARSFGPAIIIGKFT-----VHWVFWVGP152PLMGALLASLI153NV154VL155FP----- 237
AQP7 HUMAN NPARDL156PRRIF157FIAGW158GKQVFSNGE--NWWWV159PVVAPLLGAYLGGI160INLV161FIGS----- 278
AQP8 HUMAN NPARAFGP162AVVANHNW-----FHWI163MWLG164PLLAGLLVGLL165IRCF166IGD----- 251
AQP9 HUMAN NPARDL167SPRLF168TALAGWCF169EVFRAGN--NFWWI170PVVG171PLVGA172VIGGLI173NV174VIEI----- 268
GLPF_ECOLI NPARD175FGRKVF176AWLAWGN177VAF178TGGRDIPY179FLVPLF180GP181IVGA182IVGAFAR183KLIGR----- 257
ruler    ... 250.....260.....270.....280.....290.....300....

```







# Load Aquaporins 1j4n, 1fqy, 1lda, 1rc2 into VMD

The image displays the VMD (Visual Molecular Dynamics) software interface. The main window, titled "VMD Main", shows a list of loaded molecules:

| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  |   | A | D | F | 1J4N     | 2029  | 1      | 0   |
| 2  |   | A | D | F | 1FQY     | 1661  | 1      | 0   |
| 3  |   | A | D | F | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

The "Graphical Representations" window shows the selected molecule "5: 1rc2" with the following settings:

- Style: Tube
- Color: ColorID 3
- Selection: chain A
- Coloring Method: ColorID
- Material: Opaque
- Drawing Method: Tube
- Radius: 0.5
- Resolution: 11

The "Multiple Sequence Alignment" window displays the following alignment:

| PDB code | Description                         |
|----------|-------------------------------------|
| 1j4n     | Bovine AQP1                         |
| 1fqy     | Human AQP1                          |
| 1lda     | E. coli Glycerol Facilitator (GlpF) |
| 1r2c     | E. coli AqpZ                        |

```
d1fqya_.ent KLFWRVAVAEFLATLTFVVISIGSALGFKYPVGNQTAVDNPKVSLAFGLSIATLA
d1j4na_.ent MASEFKKKLFWRAVVAEFLAHILFIFISIGSALGFHYPIKSNQTTGAVODNPKVSLA
d1lda_.ent TLFQGCIAEFLGTGLLFFGVGCVAAKLVAGASFGQWEISVINGLVAMATYLTAGV
d1rc2a_.ent MFRKLAESCFTFWLVPGGCSAVLAAGFPFELIGFAGVALAFGLTVLTHAFVAGHI
```



# Aligning Structures and Sequences

The image displays the VMD (Visual Molecular Dynamics) software interface, illustrating the process of aligning structures and sequences. The main window, titled "VMD 1.8.2b7 OpenGL Display", shows a 3D ribbon representation of a protein structure, colored by chain (blue, orange, red, yellow, green).

The "VMD Main" window shows a table of loaded molecules:

| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  | A | D | F |   | 1J4N     | 2029  | 1      | 0   |
| 2  | A | D | F |   | 1FQY     | 1661  | 1      | 0   |
| 3  | A | D | F |   | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

The "Graphical Representations" window shows the configuration for the selected molecule (5: 1rc2):

- Selected Molecule: 5: 1rc2
- Buttons: Create Rep, Delete Rep
- Table:

| Style | Color     | Selection |
|-------|-----------|-----------|
| Tube  | ColorID 3 | chain A   |
- Selected Atoms: chain A
- Draw style: Selections
- Coloring Method: ColorID 3, Material: Opaque
- Drawing Method: Tube, Default
- Radius: 0.5
- Resolution: 11
- Buttons: Apply Changes Automatically, Apply

The "Multiple Sequence Alignment" window shows a sequence alignment interface with buttons for "Align Molecules...", "FASTA", "Highlight PDB", "Pairwise RMSD", and "Sequence Display". The alignment display shows the following sequences:

```
1fgy -----KLFWRVVAEFLATTLFVFLSIGSAL-GF-KY---PVGNNQTAVDNPKVSLAPGLSIATLAQS-VGHISGAHLNPAVTLGILLSCQISIF-RAI
1j4n MASEFKKKLFWRAVVAEFLAMILFIFLISIGSAL-GF-HYPIKSNQT-TGAVQDNVKVSLAPGLSIATLAQSVGH-ISGAHLNPAVTLGILLSCQ-ISVLRAI
1lda -----TLNGQCIAEFLGTGLLIFFGVGCVVA-ALKVA-----G-A-SFGQWEISVINGLGVAMATYLTG-VVSGAHLNPAVTLALWLFQ-CFDKRRVI
1rc2 -----MFRKLAECFPTFWLVFGCCGSAVLA-AG-----FPE-LGIGFAGVALAPGLTVLTMFAVVG-HISGGHFNPAVTIGLWAGG-RFPAKEVV
```



# Comparing Structures by Similarity - Q Value

The image displays the VMD (Visual Molecular Dynamics) software interface, illustrating the process of comparing protein structures by similarity using the Q Value.

**VMD Main Window:** Shows a list of loaded molecules:

| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  | A | D | F |   | 1J4N     | 2029  | 1      | 0   |
| 2  | A | D | F |   | 1FQY     | 1661  | 1      | 0   |
| 3  | A | D | F |   | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

**Graphical Representations Window:** Shows the configuration for the selected molecule (5: 1rc2):

- Selected Molecule: 5: 1rc2
- Style: Tube
- Color: ColorID 3
- Selection: chain A
- Coloring Method: ColorID
- Material: Opaque
- Drawing Method: Tube
- Radius: 0.5
- Resolution: 11

**VMD 1.8.2b7 OpenGL Display Window:** Shows a 3D ribbon representation of the protein structure, colored by the Q Value (ranging from blue to red).

**Multiple Sequence Alignment Window:** Shows a sequence alignment of the four proteins (1f4y, 1j4n, 1lda, 1rc2). The alignment is displayed in a grid format, with the Q Value per residue highlighted in blue.

The alignment shows the following sequences:

```
1f4y -----KLFWAQVADFLATLLEVFSTIGSAL-QF-RY---PVDNRQTAVDQVWVSLAFGLS IATLAQS-VGHI SG AHLNFAVTLG LLLSCQISIF-RAI
1j4n MASEFKKLFWRVAVAEFLAMILFIFISIGSAL-GF-HYPIKSNQT-TGAVQDNVKS LAFGLS IATLAQSVGH-I SG AHLNFAVTLG LLLSCQ-I SVLRAI
1lda -----TLRGQCIAEPLGTGLLIFPGVGCVA-ALKVA-----G-A-SFGQWEISVIWGLGVAMA IYLT A-GVSG AHLNFAVTLALW LFA-CFDKRRV I
1rc2 -----MFRKLA AECPGTFWLVFGGCGSAVLA-AG-----FPE-LGIGFAGVALAPGLTVL TMAFAVG-HISGGHPNFAVTLGLWAGG-RFP AKEV I
```



# Comparing Structures by Similarity - Q Value

The image displays the VMD (Visual Molecular Dynamics) software interface, illustrating the process of comparing protein structures by similarity using the Q Value method.

**VMD Main Window:** Shows a table of loaded molecules and playback controls.

| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  | A | D | F |   | 1J4N     | 2029  | 1      | 0   |
| 2  | A | D | F |   | 1FQY     | 1661  | 1      | 0   |
| 3  | A | D | F |   | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

**Graphical Representations Window:** Shows the configuration for the selected molecule (5: 1rc2).

Selected Molecule: 5: 1rc2

Buttons: Create Rep, Delete Rep

| Style | Color     | Selection |
|-------|-----------|-----------|
| Tube  | ColorID 3 | chain A   |

Selected Atoms: chain A

Draw style: Selections | Trajectory | Periodic

Coloring Method: ColorID 3 | Material: Opaque

Drawing Method: Tube | Default

Radius: 0.5 | Resolution: 11

Apply Changes Automatically:  Apply

**VMD 1.8.2b7 OpenGL Display Window:** Shows a 3D ribbon representation of the protein structure, colored by Q value (ranging from blue to red).

**Multiple Sequence Alignment Window:** Shows a sequence alignment of four proteins (1f4y, 1j4n, 1lda, 1rc2) with a context menu open over the alignment.

Multiple Sequence Alignment

Context Menu:

- RMSD Per Residue
- Tree
- STAMP Parameters
- Bulk Residue Selection
- Molecule Coloring
  - Q per residue (checked)
  - Sequence Identity per residue
- Highlight Style

Buttons: Align Molecules..., FASTA, Highlight PDB, Distance, RMSD

Sequence Alignment:

```
1f4y -----KLFWAQVADFLATLLEVFSTIGSAL-QF-RY---PVRNQITAVQDQVQVSLAPGLSATLAQS-VGHIISGAHLNFAVTLGLLLSQGISIF-RAI
1j4n MASEFKKLFWRARVAEFLAMILFIFISIGSAL-GF-HYPIKSNQT-TGAVQDNVQVSLAPGLSIATLAQSVGH-IISGAHLNPAVTLGLLLSQGI-ISVLRAD
1lda -----TLRGQCIAEPLGTGLLIPFGVGCVA-ALKVA-----G-A-SFGQWEISVIWGLGVAMAIYLYTA-GVSGAHLNPAVTLALWLFA-CFDKRRVQ
1rc2 -----MFRKLAACECPGTFWLVFGGCGSAVLA-AG-----FPE-LGIGFAGVALAPGLTVLTMFAVVG-HISGGHPNPAVTLGLWAGG-RFPAKEVQ
```



# Exhibiting Sequence Identity - Side View

The image displays the VMD (Visual Molecular Dynamics) software interface. The main window, titled "VMD 1.8.2b7 OpenGL Display", shows a side view of a protein structure represented as a multi-colored ribbon. The structure is composed of several chains, with colors ranging from red to blue, indicating sequence identity. The ribbon is shown in a side view, highlighting the complex folding of the protein.

The "VMD Main" window in the top left corner contains a table with the following data:

| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  | A | D | F |   | 1J4N     | 2029  | 1      | 0   |
| 2  | A | D | F |   | 1FQY     | 1661  | 1      | 0   |
| 3  | A | D | F |   | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

The "Graphical Representations" window in the middle left shows the configuration for the selected molecule "5: 1rc2". The "Style" is set to "Tube", the "Color" is "ColorID 3", and the "Selection" is "chain A". The "Drawing Method" is also set to "Tube". The "Radius" is 0.5 and the "Resolution" is 11. The "Apply Changes Automatically" checkbox is checked.

The "Multiple Sequence Alignment" window in the bottom right shows a sequence alignment of four proteins: 1fqy, 1j4n, 1lda, and 1rc2. The alignment is displayed as follows:

```

1fqy  -----KLFWRVVAEFLATTLFVFISISGAL-GF-KY---PVGNQTAVDNRVKVSLAFGLSIATLAQS-VGHSI SGAEINPAVTLG LLLSCOISIF-RV
1j4n  MASEFKKLLFWRVVAEFLAMILFIFISISGAL-GF-HYPIKSNQ-TGAVQDNVKVSLAFGLSIATLAQSVGH-I SGAEINPAVTLG LLLSCO-ISVLRV
1lda  -----TLRGQCIAEPLDGLLIFFGVGVVA-ALKVA-----G-A-SFGQWEISVINGLVMAIYLTA-GVSGAEINPAVTIALWLFV-CFDKRRV
1rc2  -----MFRKLAECFGTFWLVFGCCSAVLA-AG-----FPE-LGIGPAGVALAFGLTVLTMFAVVG-HISGGHFNPAVTIGLWAGG-RFPAREV
  
```

The alignment shows high sequence identity between the proteins, with several conserved residues highlighted in yellow. The "Sequence Display" window is currently set to "FASTA" format.



# Exhibiting Sequence Identity - Top View

The image displays the VMD (Visual Molecular Dynamics) software interface. The main window, titled "VMD Main", shows a table of loaded molecules:

| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  | A | D | F |   | 1J4N     | 2029  | 1      | 0   |
| 2  | A | D | F |   | 1FQY     | 1661  | 1      | 0   |
| 3  | A | D | F |   | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

The "Graphical Representations" window shows the selected molecule "5: 1rc2" with a "Tube" style and "ColorID 3" color. The "Multiple Sequence Alignment" window displays the following sequence alignment:

```
1fqy  -----KLFWRVVAEFLATTLFVETISIGSAL-GF-KY---PVGNQTAVDNRVKVSLAFGLSIATLAQS-VGHSAGELNPAVTLGLLSCOISIF-RV
1j4n  MASEFKKLFWRVVAEFLAMILFVETISIGSAL-GF-HYPIKSNQ-TGAVQDNVKVSLAFGLSIATLAQSVGH-I SAGELNPAVTLGLLSCO-ISVLRV
1lda  -----TLRGQCIAEPLDGLLFTGVGVA-ALKVA-----G-A-SFGWEISVINGLVMAIYLTA-GVSGAELNPAVTIALWLFV-CFDKRV
1rc2  -----MFRKLAECFGTFWLVFGCCSAVLA-AG-----FPE-LGIGPAGVALAFGLTVLTMFAVVG-HISGGHFNPAVTIGLWAGG-RFPAREV
```



# Showing Conserved Residues - Monomer

The screenshot displays the VMD (Visual Molecular Dynamics) software interface. The main window, titled 'VMD 1.8.2b7 OpenGL Display', shows a 3D ribbon representation of a protein monomer. The protein is colored by residue type: red for alpha-helices, green for beta-strands, and yellow for loops. The 'VMD Main' window shows a table of loaded molecules:

| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  | A | D | F |   | 1J4N     | 2029  | 1      | 0   |
| 2  | A | D | F |   | 1FQY     | 1661  | 1      | 0   |
| 3  | A | D | F |   | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

The 'Graphical Representations' window is configured for molecule '5: 1rc2'. The 'Selected Molecule' is '5: 1rc2'. The 'Style' is 'Tube', 'Color' is 'ColorID 3', and 'Selection' is 'chain A'. The 'Selected Atoms' field contains 'chain A'. The 'Drawing Method' is 'Tube'. The 'Radius' is set to 0.5 and 'Resolution' is 11. The 'Multiple Sequence Alignment' window shows the following alignment:

```

1fqy  -----KLFWRVVAEFLATTLFVFIISIGSAL-GF-KY---PVGNQTAVDNRKVSIAFGLSIATLAQS-VGHSIIGAELNPAVTLGILLSCOISIF-RV
1j4n  MASEFKKLFWRVVAEFLAMILFIFISIGSAL-GF-HYPIKSNQ-TGAVQDNKVSIAFGLSIATLAQSVGH-IIGAELNPAVTLGILLSCO-IVLVRV
1lda  -----TLKGQCIAEPLDGLLIFFGVGVVA-ALKVA-----G-A-SFGQWEISVINGLVMAIYLTA-GVSGAELNPAVTIALWLFV-CFDKRRV
1rc2  -----MFRKLAECFPTFLVIFGCGSAVLA-AG-----FPE-LGIGPAGVALAFGLTVLTMFAVVG-HISGGHFNPAVTIGLWAGG-RFPAREV
  
```



# Showing Conserved Residues - Tetramer

The image displays the VMD (Visual Molecular Dynamics) interface. The main window, titled "VMD Main", shows a table of loaded molecules:

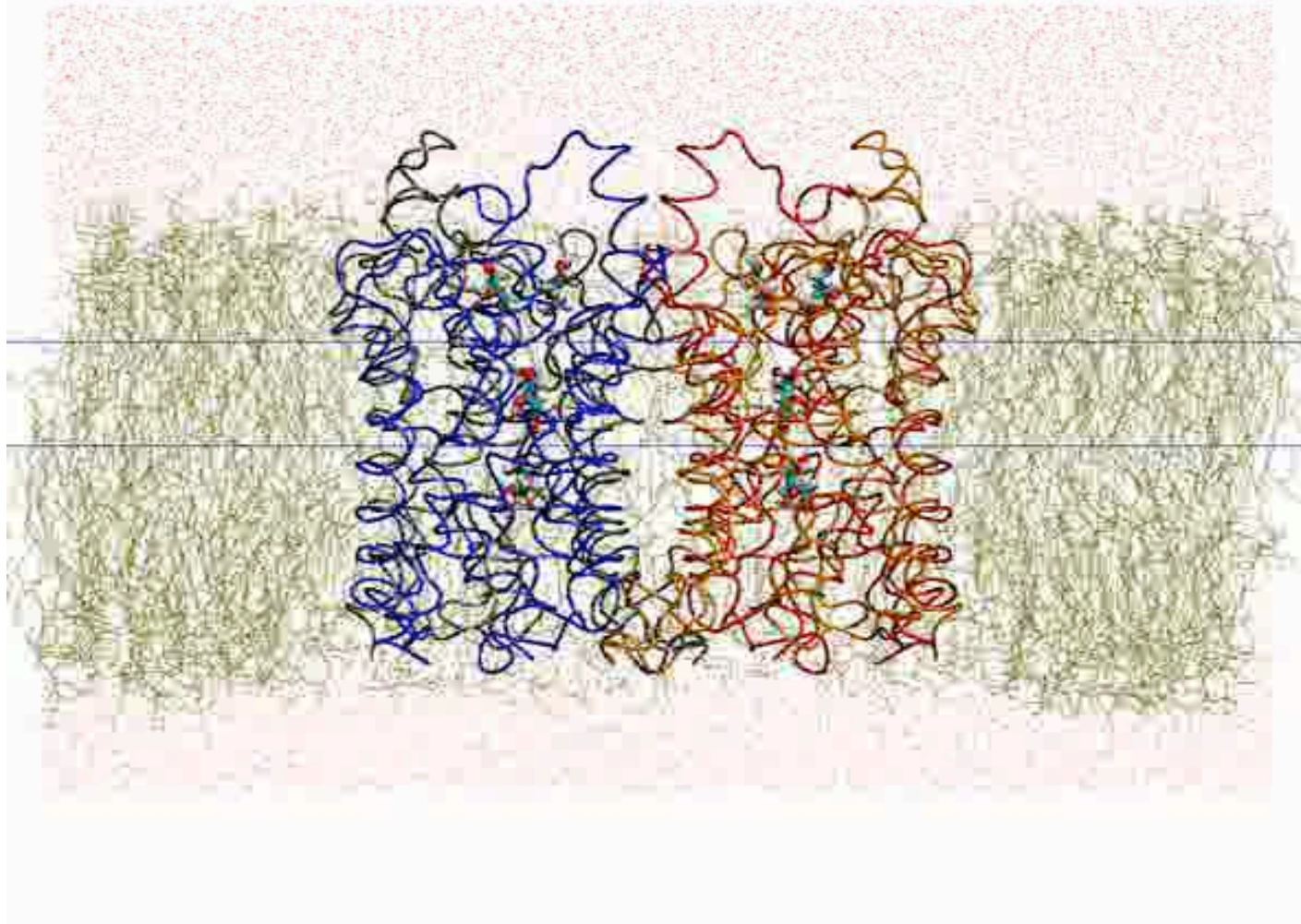
| ID | T | A | D | F | Molecule | Atoms | Frames | Vol |
|----|---|---|---|---|----------|-------|--------|-----|
| 1  | A | D | F |   | 1J4N     | 2029  | 1      | 0   |
| 2  | A | D | F |   | 1FQY     | 1661  | 1      | 0   |
| 3  | A | D | F |   | 1lda     | 1997  | 1      | 0   |
| 5  | T | A | D | F | 1rc2     | 3530  | 1      | 0   |

The "Graphical Representations" window shows the configuration for the selected molecule "5: 1rc2". The representation is set to "Tube" with "ColorID 3" and "chain A" selected. The drawing method is also set to "Tube". The radius is 0.5 and the resolution is 11. The conserved residues are highlighted in yellow in the protein structure.

The "VMD 1.8.2b7 OpenGL Display" window shows a 3D rendering of the tetramer protein structure. The structure is composed of four subunits, each represented by a different color: red, blue, orange, and grey. The conserved residues are highlighted in yellow. The structure is shown in a ribbon representation, with the conserved residues highlighted in yellow.



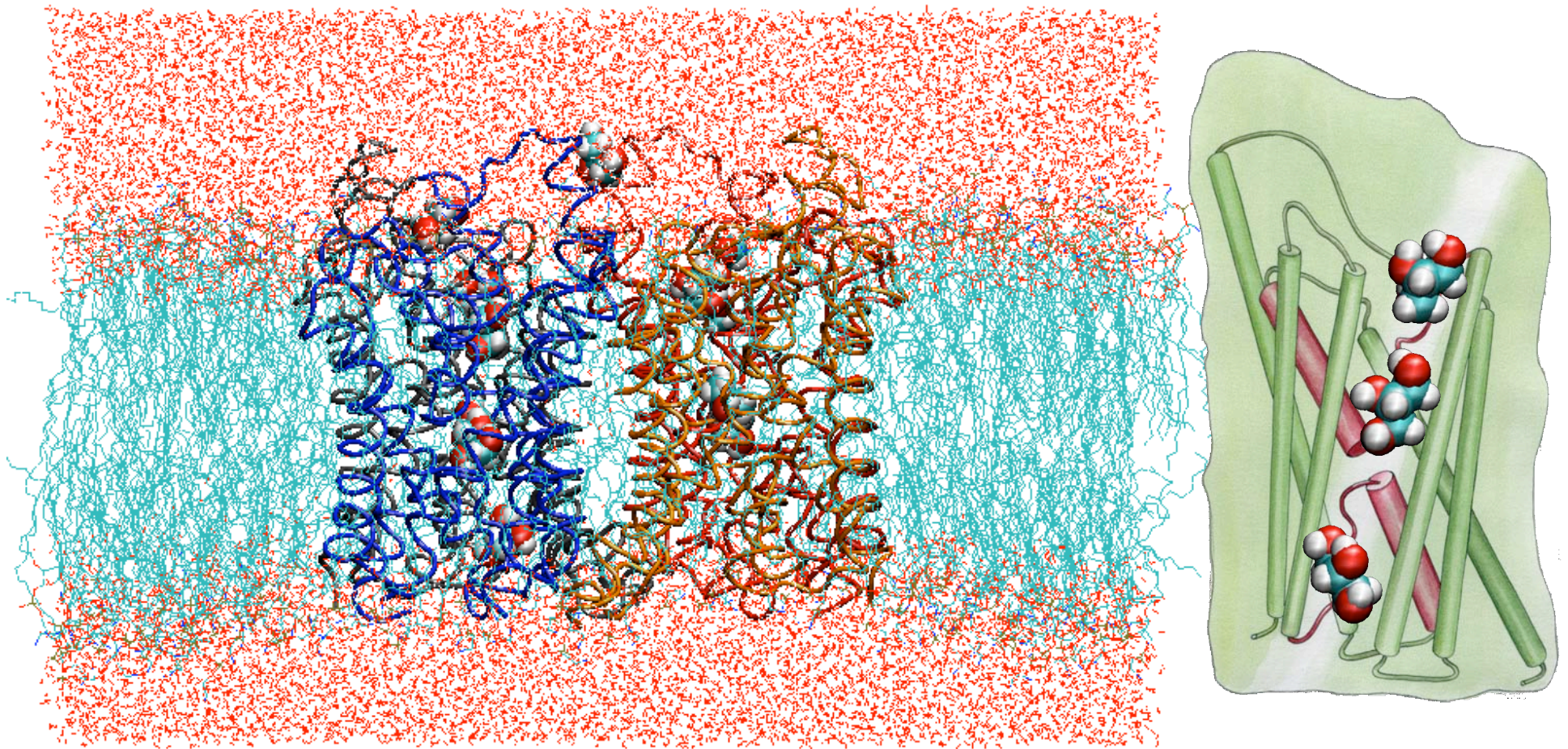
# Dynamics of Protein, Lipid, Water System



M. Jensen, E. Tajkhorshid, K. Schulten, *Structure* 9, 1083 (2001)



# Equilibrated Structure after 1 ns



*note the curved adjustment between lipids-protein*

**Morten Jensen, Emad Tajkhorshid**



# Glycerol Conduction



- Spontaneous glycerol conduction on ns time scale;
- **Conduction occurs independently in each monomer;**
- Exposed backbone carbonyl oxygen atoms dictates glycerol and water pathway; this explains the non-helical secondary structure in the aquaporin family;
- Glycerol resides at the positions of conserved motif for the longest time during simulation = minimum energy sites;
- **Water molecules are essential for the glycerol transport.**

