

Exploring Aquaporin

with the Protein Exploratorium

***"Well, all life forms are
dependent upon water."***

Peter Agre, American physician, Nobel Laureate, and molecular biologist



Kit name here



Molecular Story

A young mother of two small children visits her doctor with complaints of:

- trouble sleeping (insomnia)
- leg pain
- muscle weakness (paresis)
- tingling and numbness in her hands and feet (paresthesia and neuropathy)

Since this was not her first visit associated with these symptoms, the doctor ordered a urine and blood test.



***What conditions might cause the symptoms she was experiencing?
What additional information do you need?***

The Results For The Urine Test Come Back Quickly



(Chaurasiya, Urine sample for Culture and Sensitivity 2021)

Urine Test Sample	
Appearance	Yellow
pH	6.9
Specific Gravity	1.010
Protein	100 mg/deciliter
Glucose	105 mg/deciliter
RBCs	3
WBCs	3
Mercury	23 mcg/L



Are the results within an acceptable range?

At first glance, does anything seem out of the ordinary?

Urine Test Results

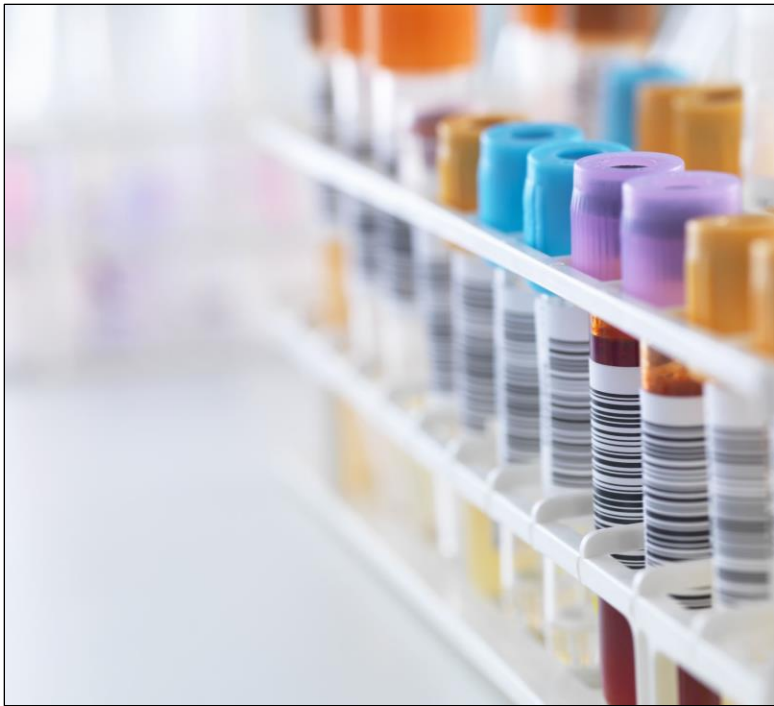
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Urine Base Sample	
Appearance	Clear to Light Yellow
pH	4.5-7.2
Specific Gravity	1.005-1.025
Protein	<150 mg/deciliter
Glucose	130 mg/deciliter
RBCs	0 to 3 RBCs
WBCs	<2-5 WBCs/hpf
Mercury	5 mcg/L



Are the results within an acceptable range?
At first glance, does anything seem out of the ordinary?

Over the next year the woman continued to experience the same worsening symptoms. She was also losing her eyesight. A new urine test was ordered.



Urine Test Sample	
Appearance	Dark Yellow
pH	6.7
Specific Gravity	1.050
Protein	101 mg/deciliter
Glucose	105 mg/deciliter
RBCs	2
WBCs	5
Mercury	46.6 mcg/L



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Second Home Visit To Look For Sources Of Mercury

The State Pollution Control Agency visited the home a year later and found the levels of mercury in the home to have risen significantly.

Normal background mercury level= 200 ng/m^3



House Search Results



Location	Level	How much higher?
Children's Bedroom	400 ng/m ³	
Towels	600 ng/m ³	
Washing Machine	300 ng/m ³	



What might be causing the elevated values?

Skin-whitening Creams

FDA acceptable allowance for Hg: 1 ppm

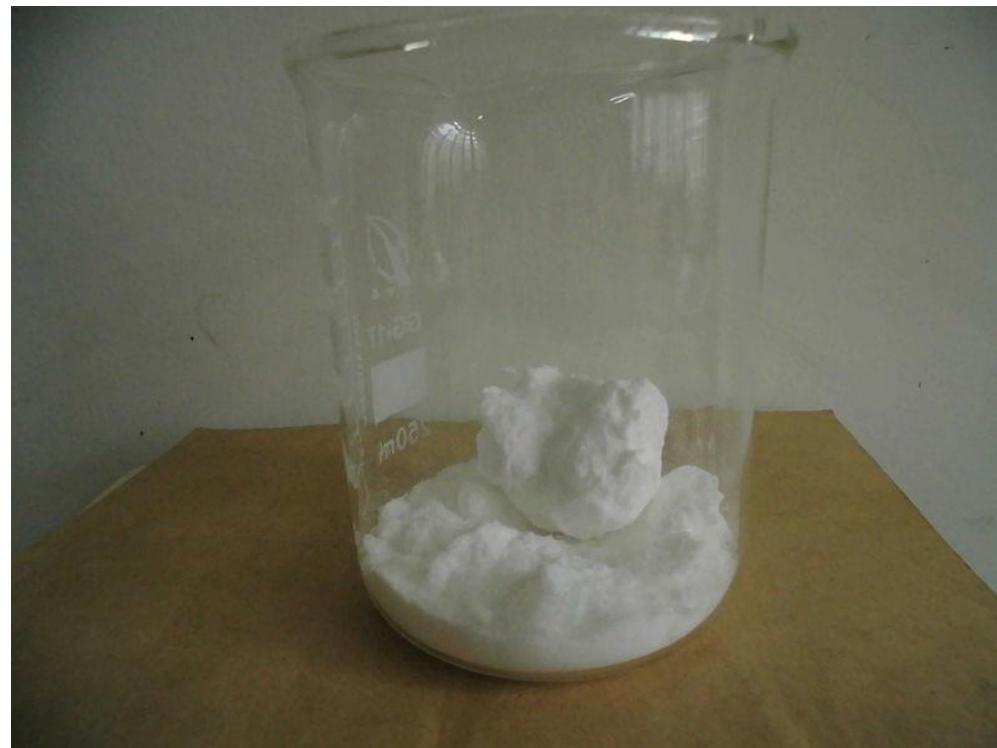


Whitening Cream	Amount of Mercury
Product 1	4,590 ppm (Opened, partially used bottle)
Product 2	7,440 ppm (Opened, partially used bottle)
Product 3	11,000 ppm (New, unopened bottle; same as product one)
Product 4	18,000 ppm (New, unopened bottle; same as product one)



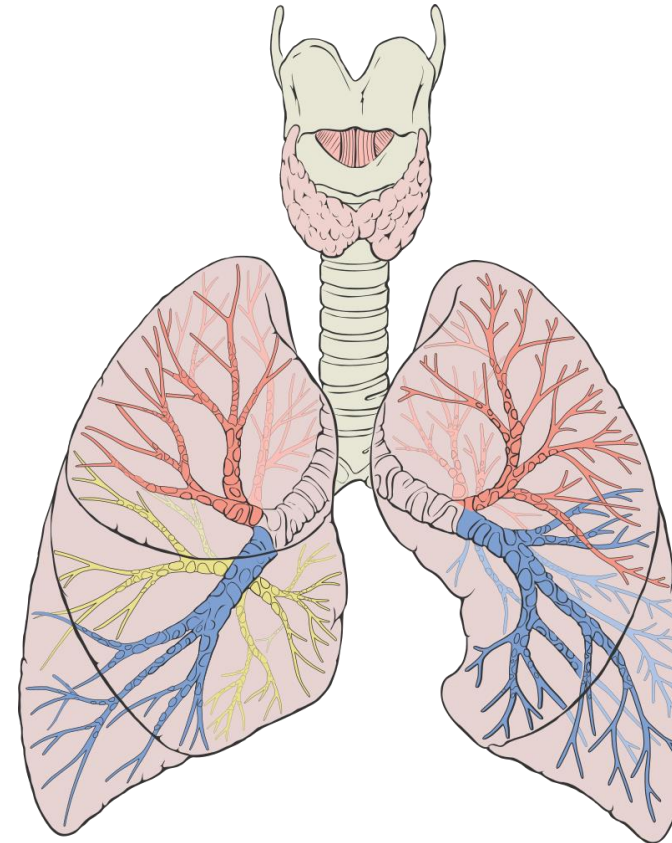
Where is the mercury going?

Inorganic mercury in the cream is absorbed by the skin

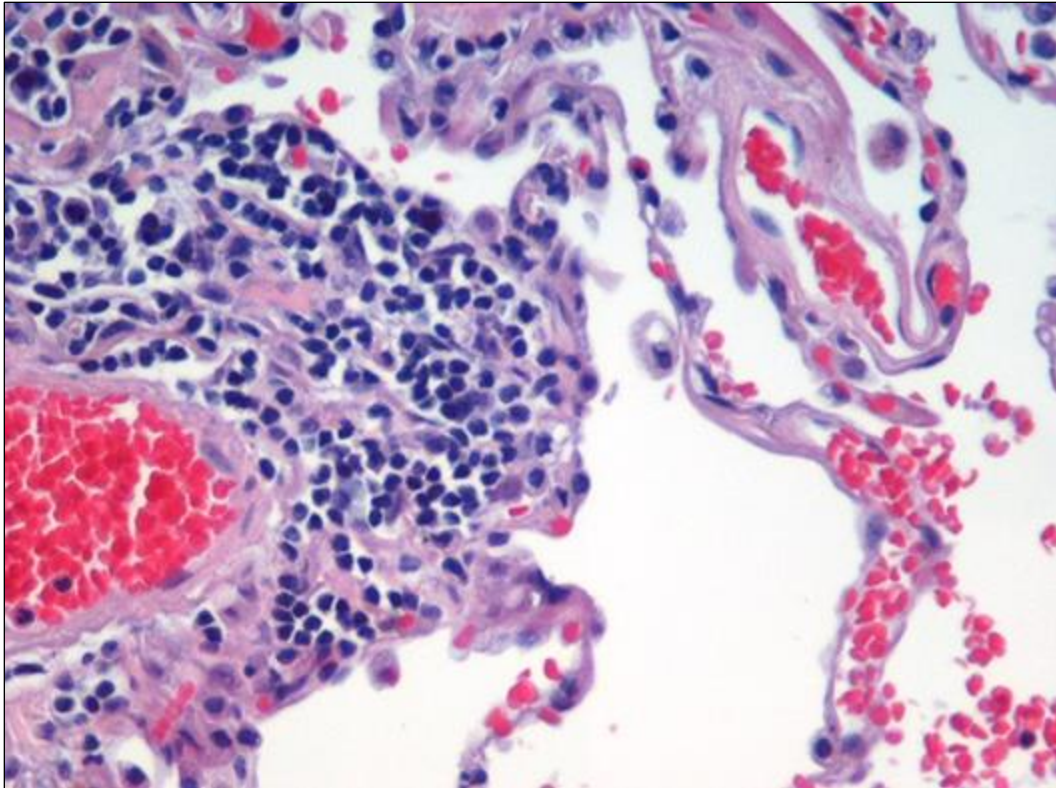


(Lühuagong(II) 2014)

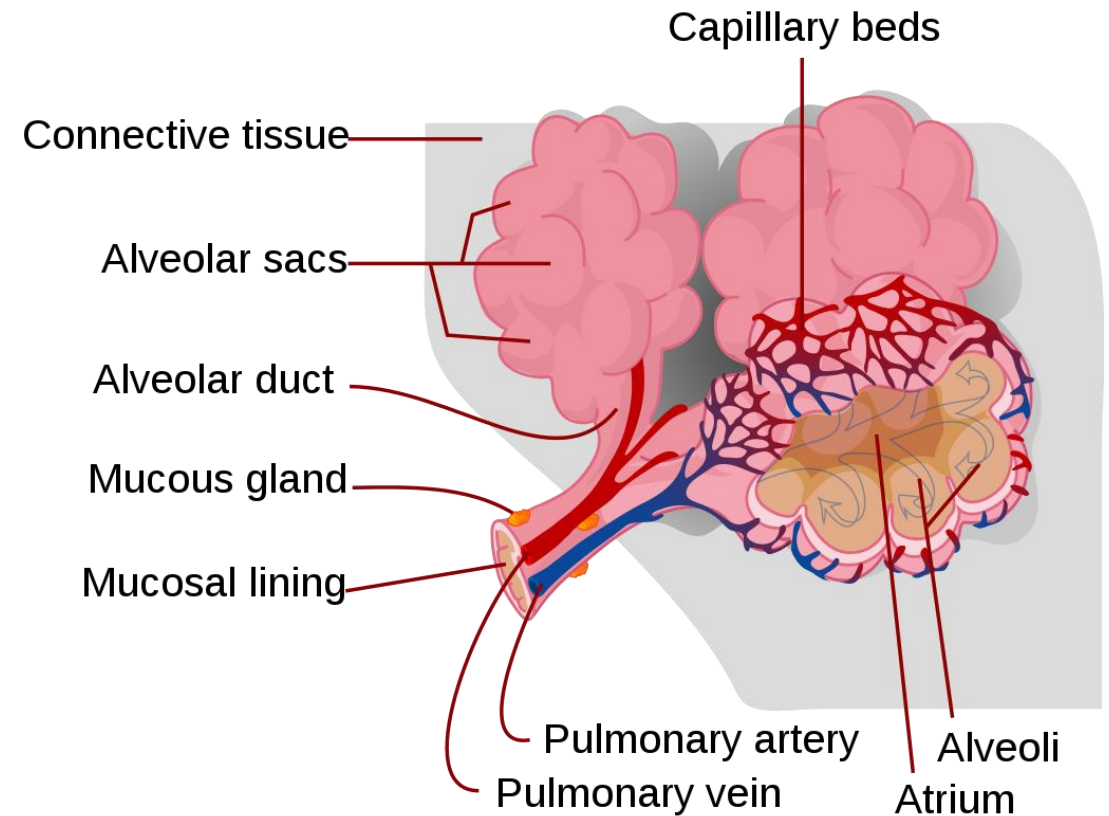
Mercury in the cream can also become vapor and is inhaled.



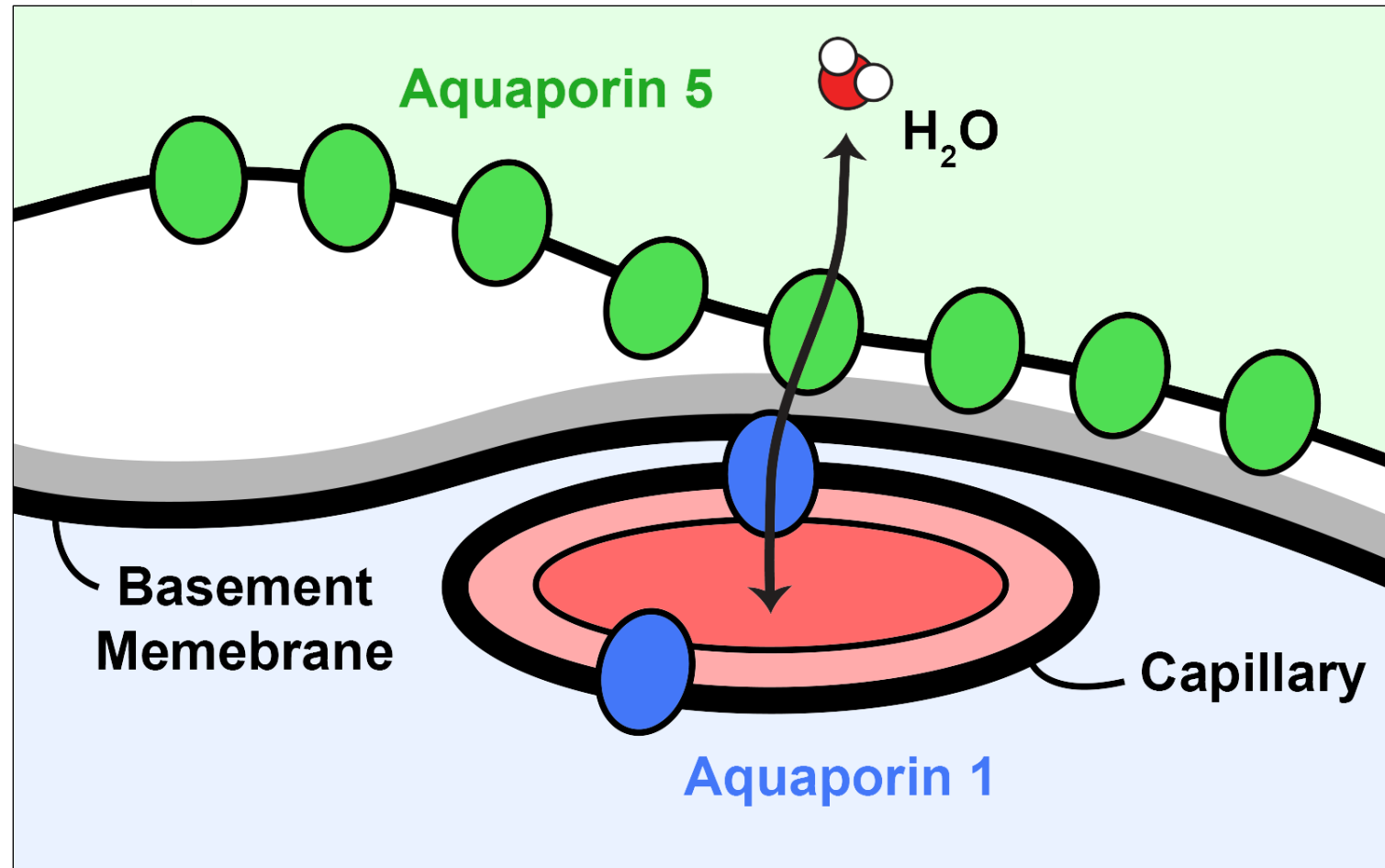
After It Is Inhaled, Where Does It Go?



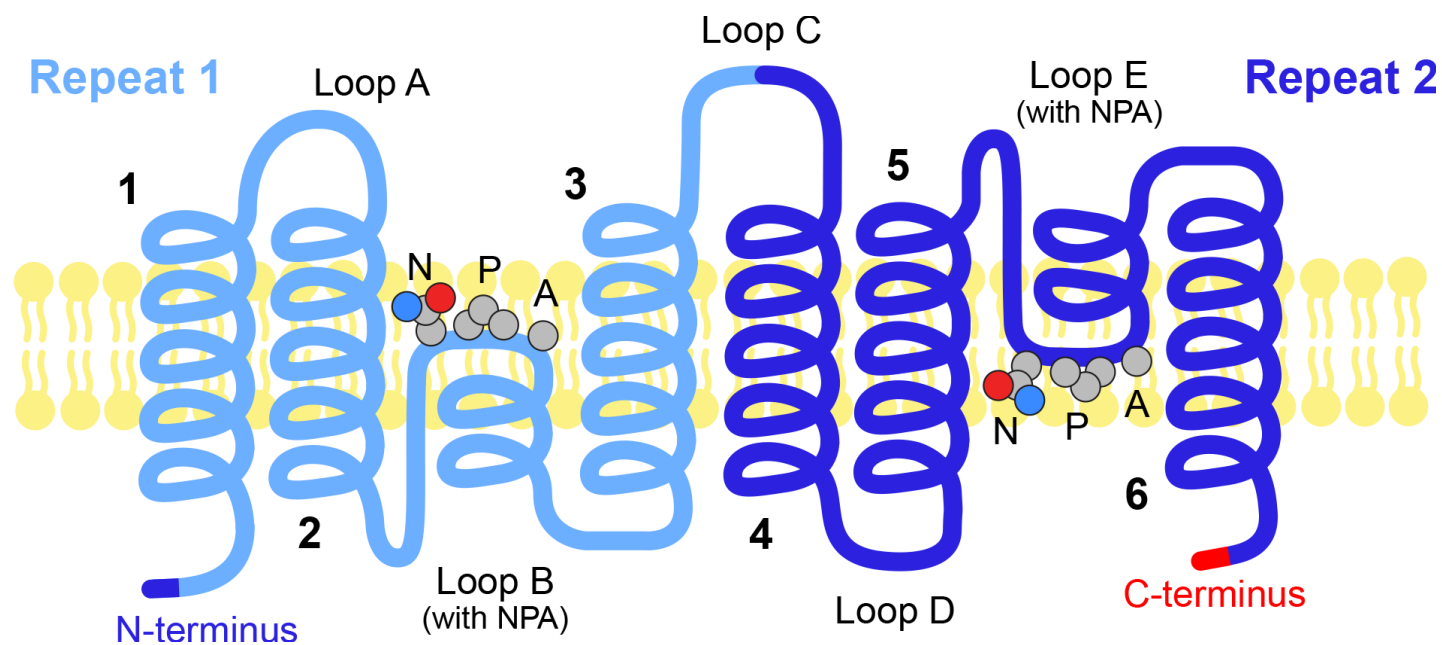
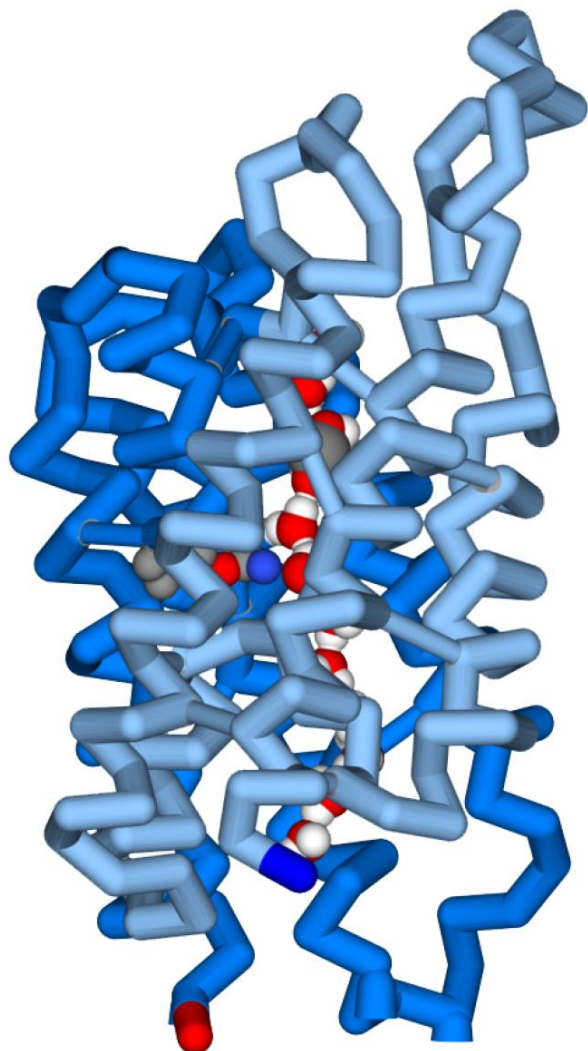
(Public Library of Science, Emphysema H and E 2004)



(Villarreal, Alveolus diagram 2007)

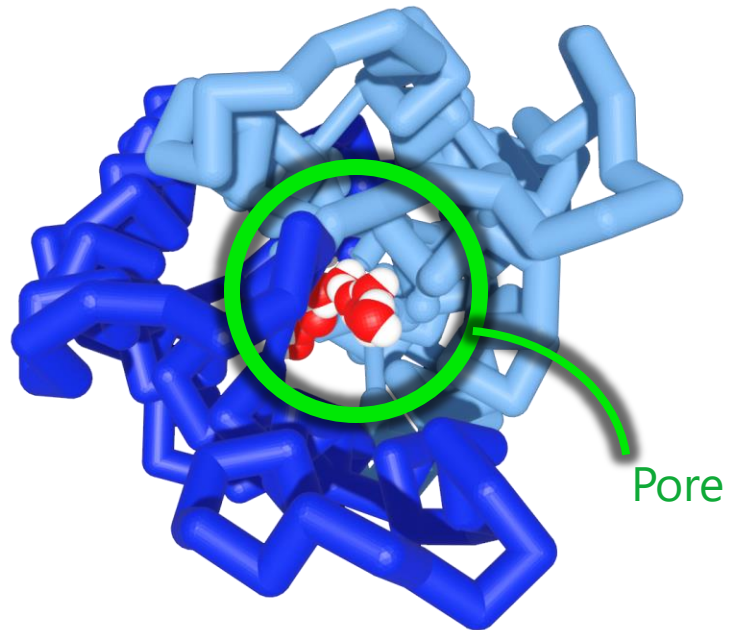


What is Aquaporin?

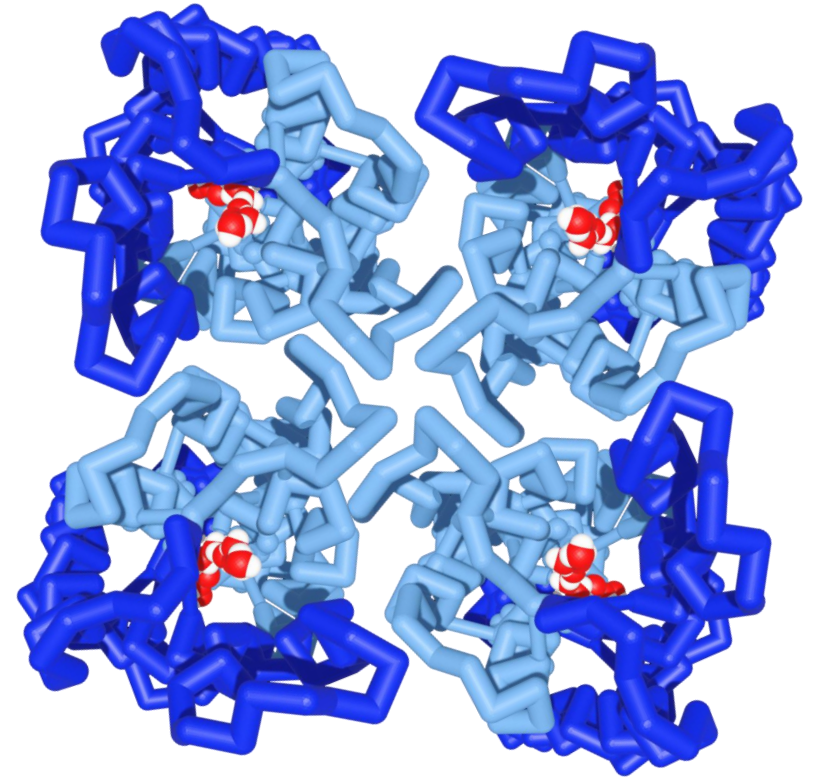


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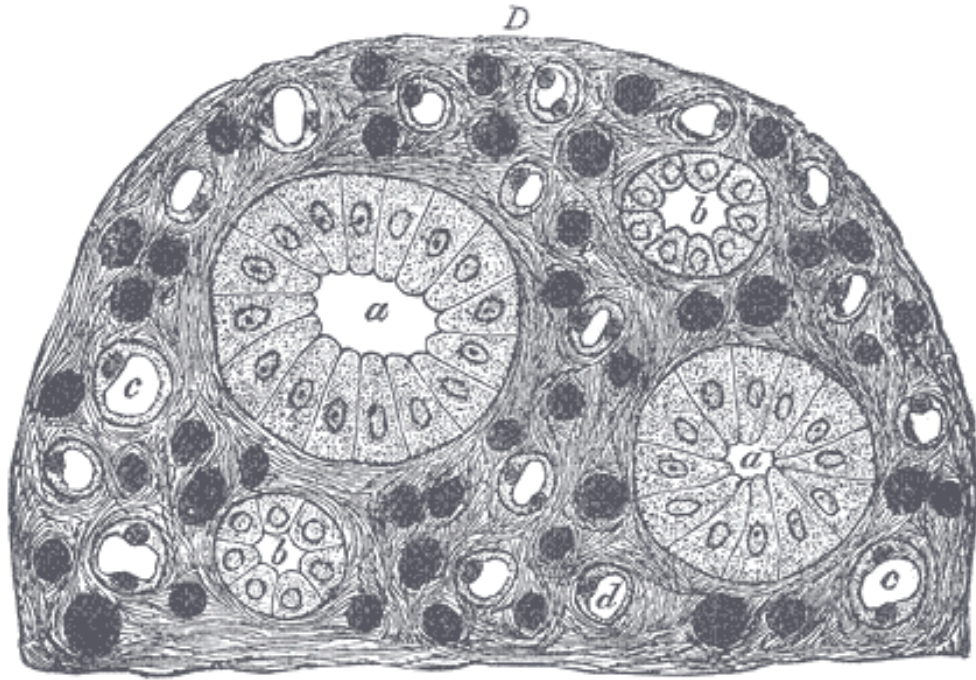
Monomer



Tetramer
(Quaternary structure)

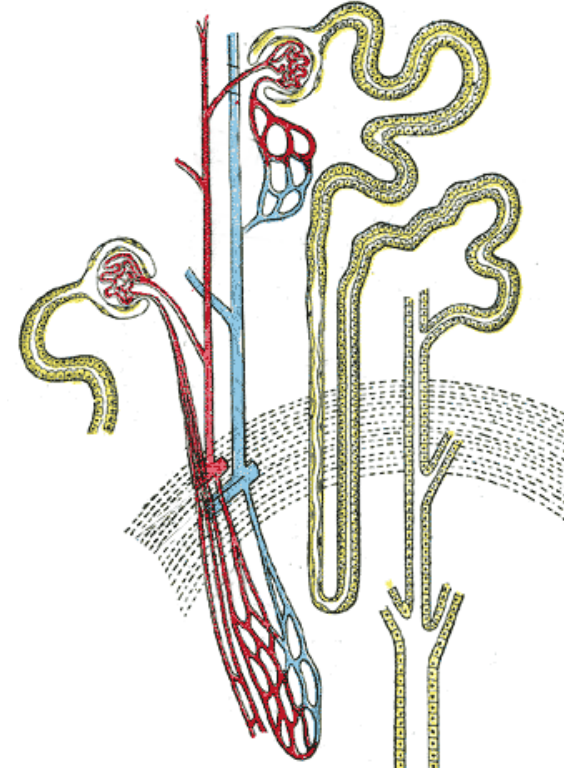


Where Else Is Aquaporin-1 Found?



(Gray, Gray1133)

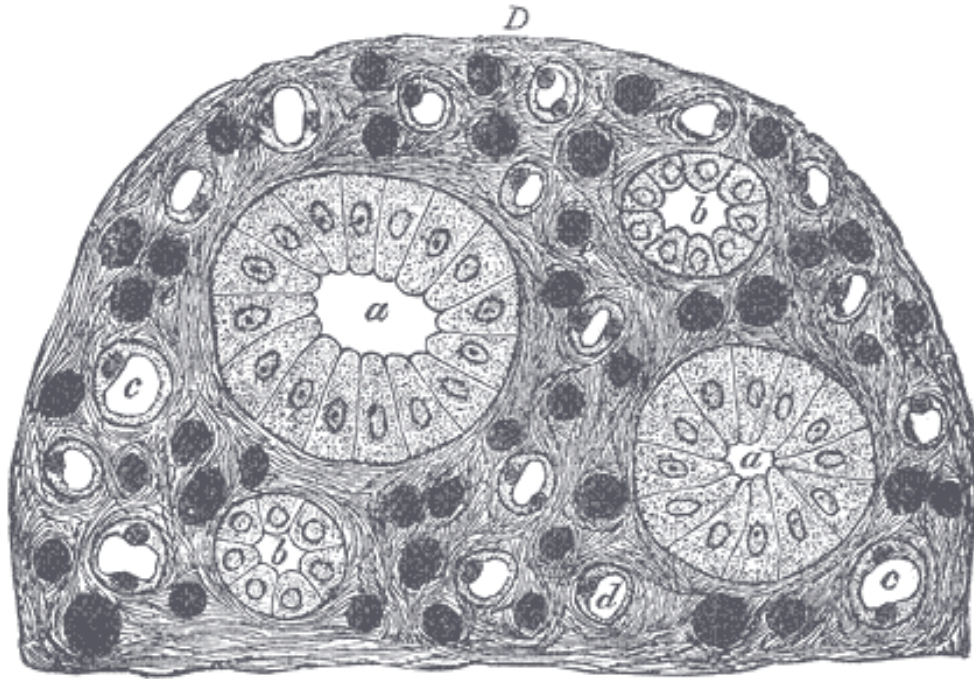
Cuboidal epithelium in the collecting ducts of the kidney



(Gray, Gray1128)

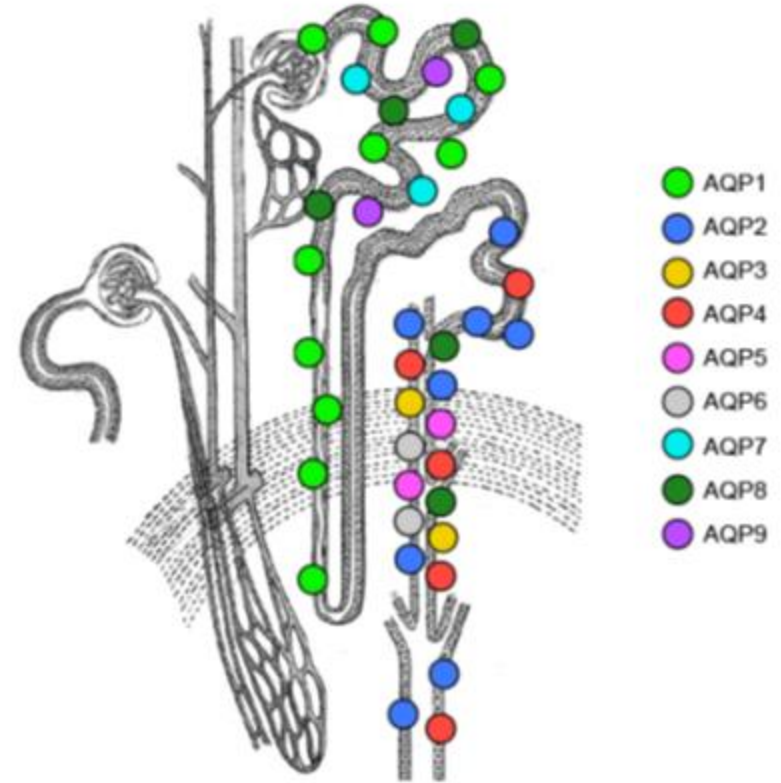
Nephron of the kidney

Where Else Is Aquaporin-1 Found?



(Gray, Gray1133)

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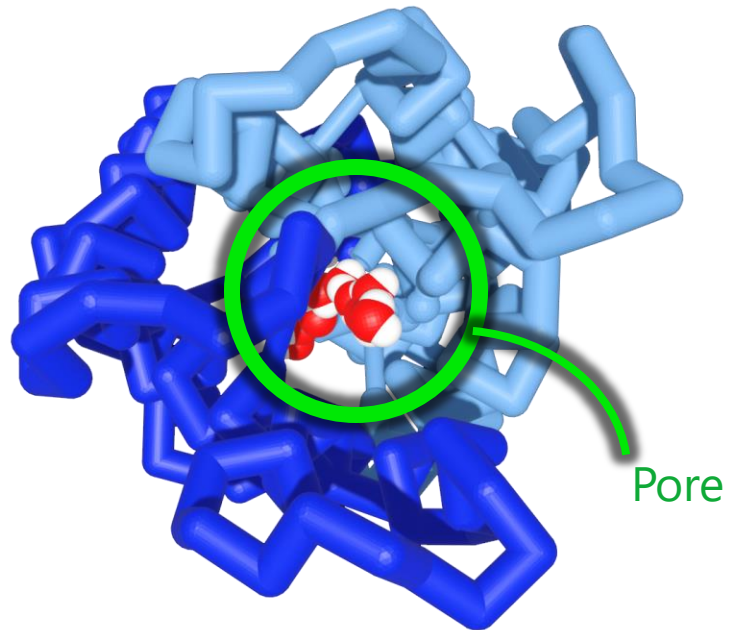


(Gray, Gray1128)

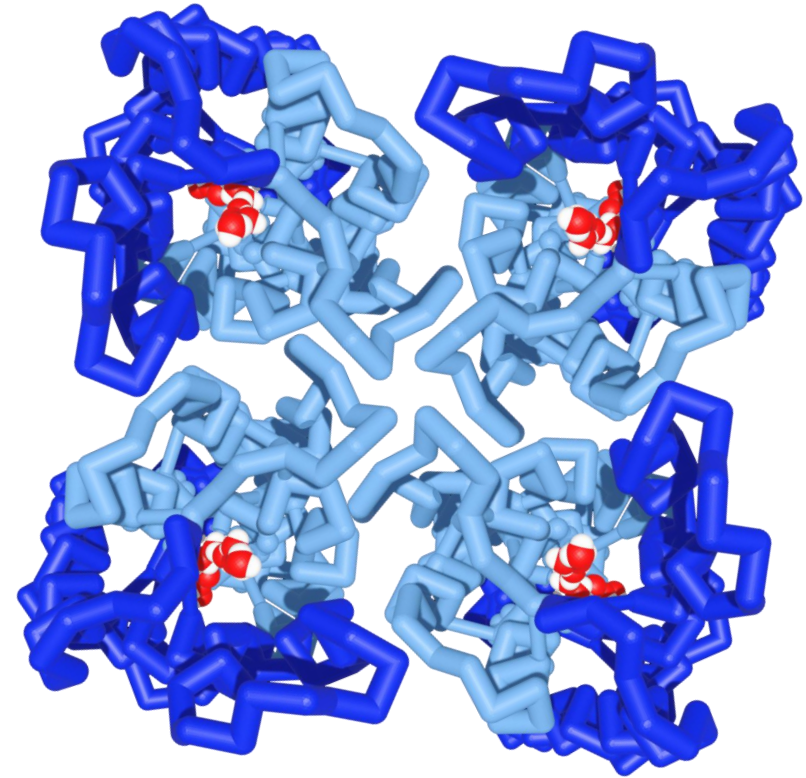
Nephron of the kidney

Homotetrameric structure

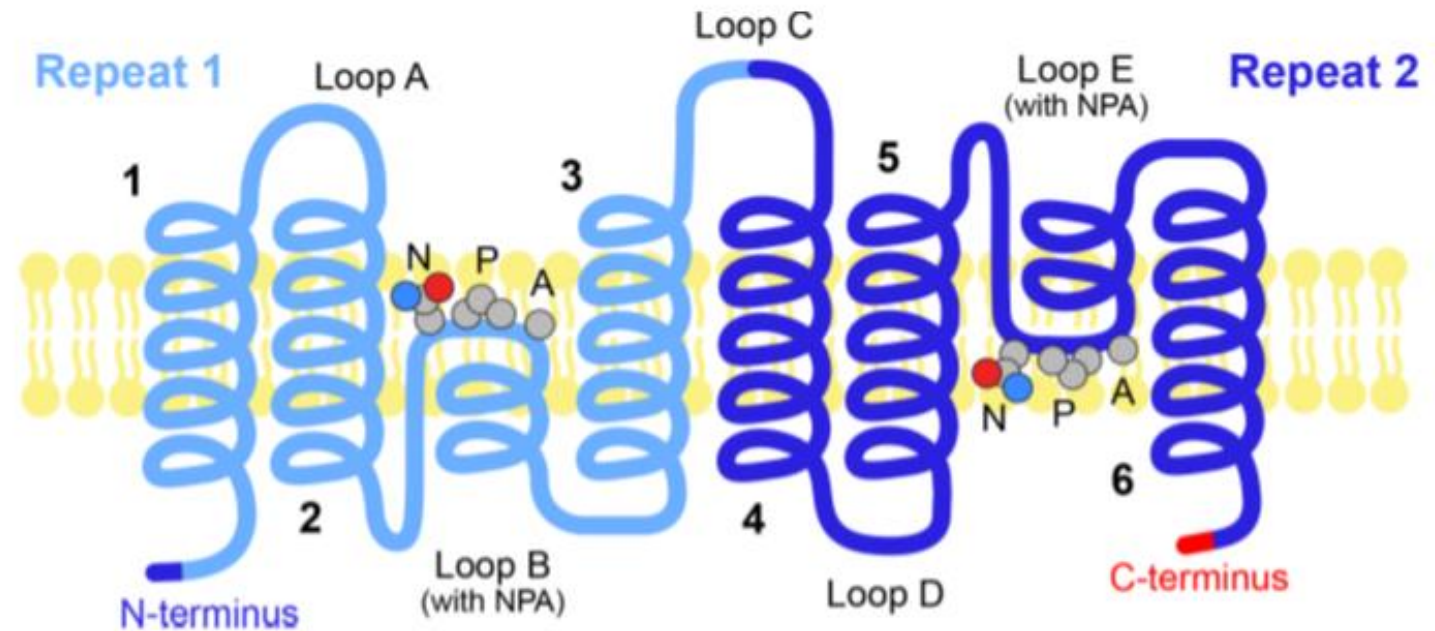
Monomer



Tetramer
(Quaternary structure)



What is Aquaporin?



Monomeric Repeats



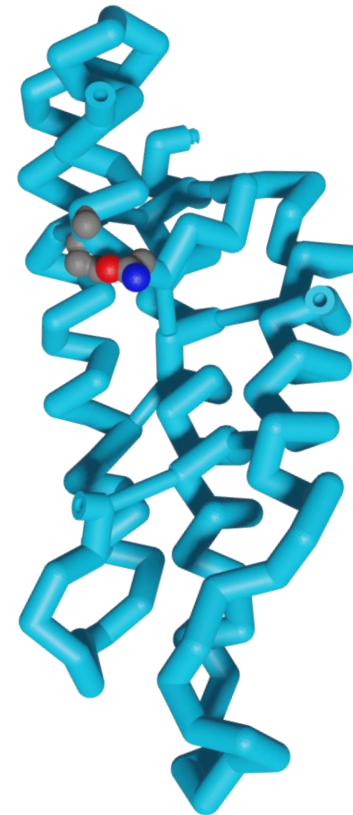
- Open the model so the **amino acid** side chains are facing you.
- Rotate one of the sections 180 degrees.

Explain where the sections are similar.

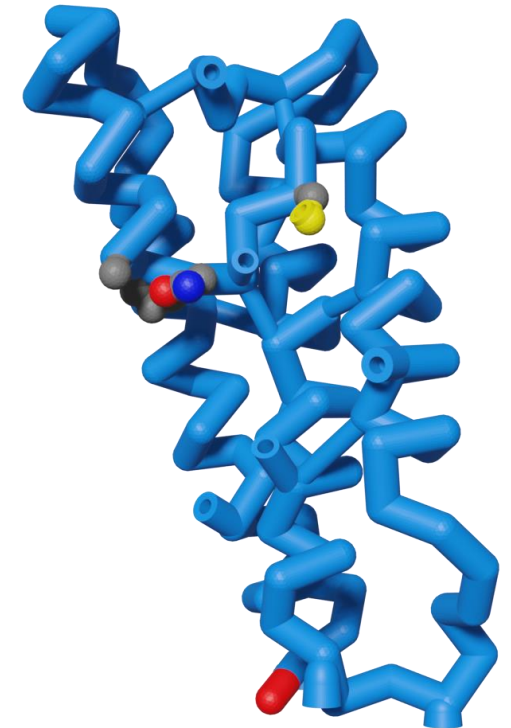
- Turn both section over so you can see the exterior of the monomer.

*What do you notice about the helices on both sections?
What might have caused this to occur in the protein?*

Monomer Repeats

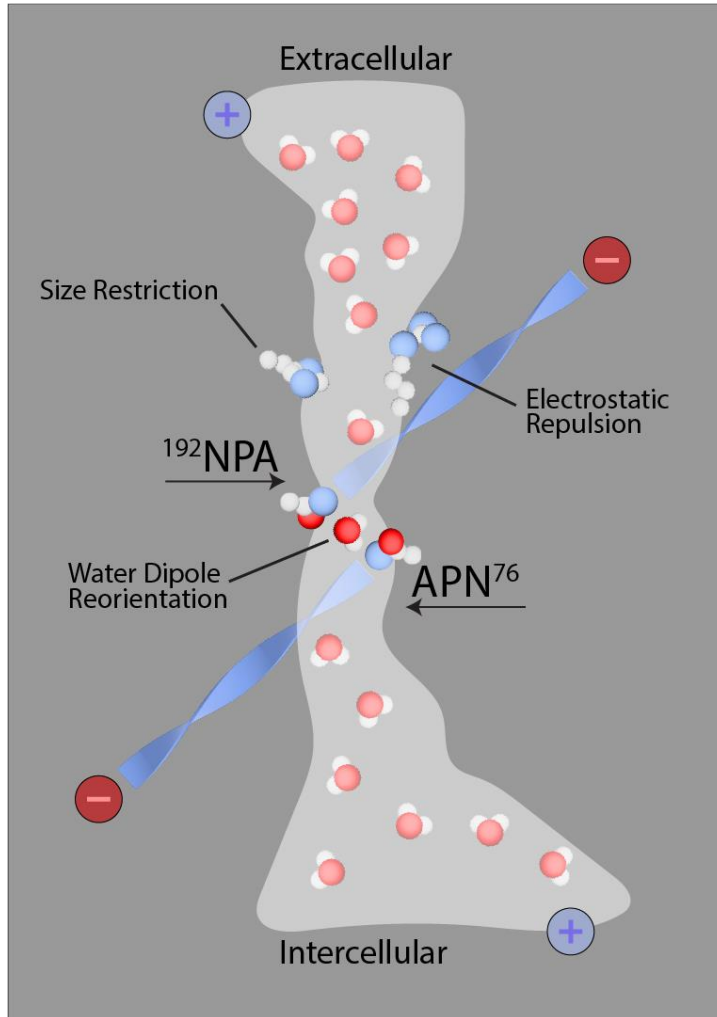


Repeat 1



Repeat 1

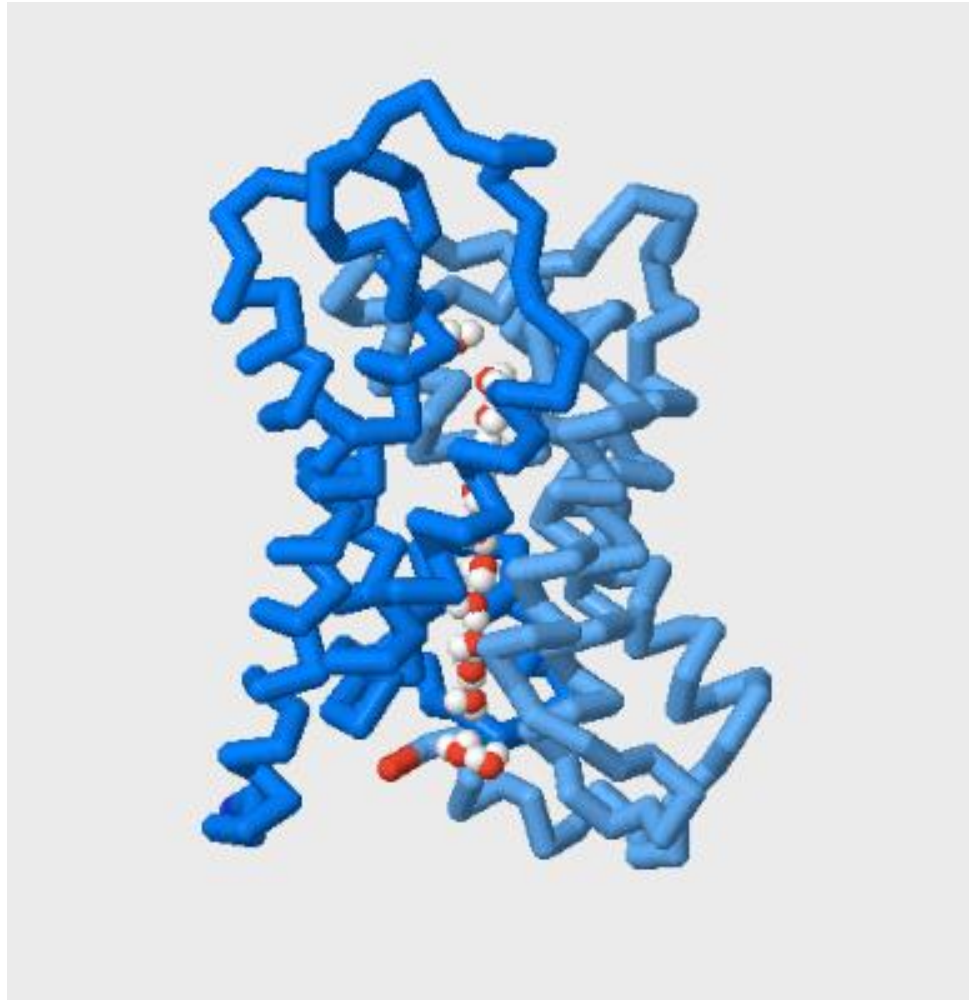
A closer look at NPA



- Two **asparagine** side chains (N78 and N194) are important because they **hydrogen bond** with the water
- Water is in bulk in the inner and outer vestibule
- Water moves in single file through the channel with **oxygen atom** facing down
- When a water molecule encounters arg195 side chain, the **dipole** is reoriented.
- Water turns and ends up with the hydrogen atoms facing down toward the interior of the cell.

How could you model this?

Exploring the Protein Exploratorium

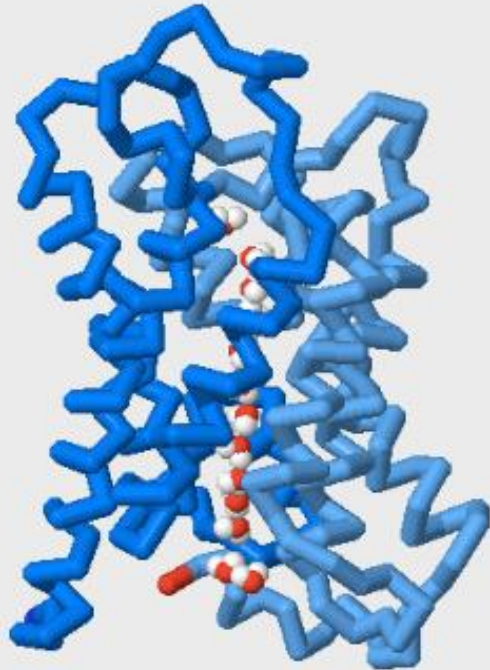


- Familiarize yourself with the tools available on the screen.
- Look the Display Format Box
- Backbone is the default
- Select Spacefill

How does the image on the screen change?

What is the difference between backbone and spacefill?

How Does Aquaporin-1 Help Maintain Water Homeostasis?

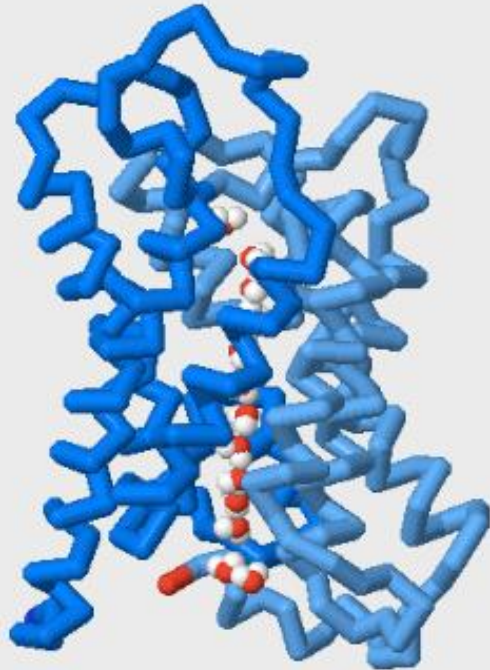


- Scroll through the primary sequence at the bottom of the screen.
- When you find the NPA sequence, click on the blue amino acid box to show the side chains.



Where does it appear in the Exploratorium?

How Does Aquaporin-1 Help Maintain Water Homeostasis?



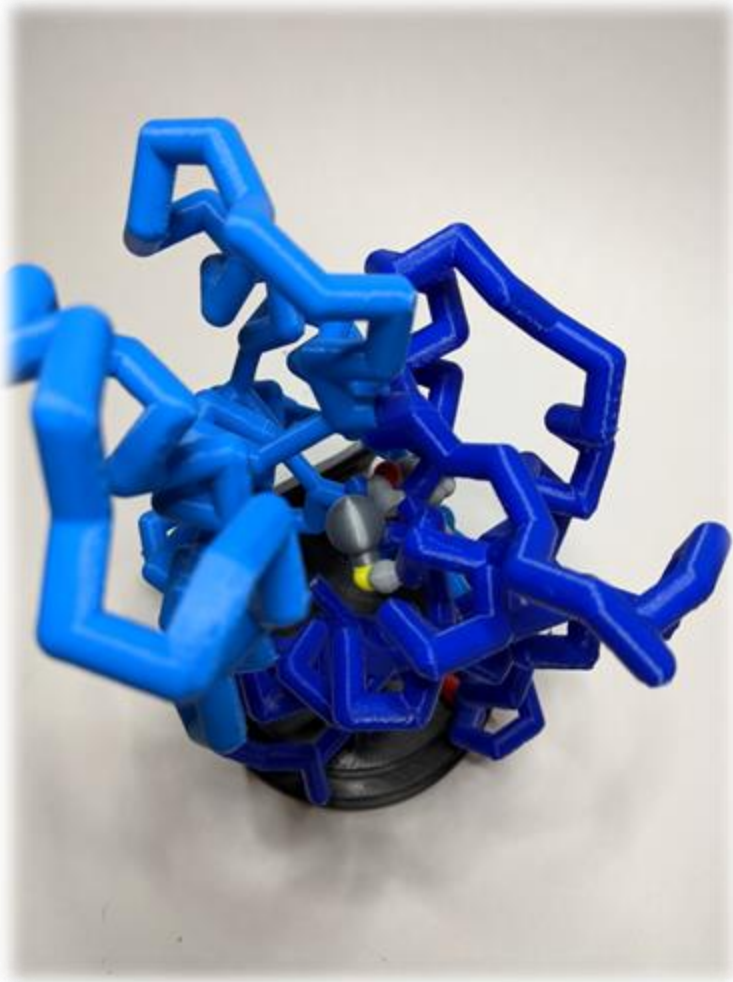
- Let's continue scrolling through the primary sequence at the bottom of the screen
- When you find additional NPA sequences, click on the blue amino acid box to show the side chains.



***Where do they appear
in the Exploratorium?***

***How might this help water
move through the pore?***

A Search For Cysteines



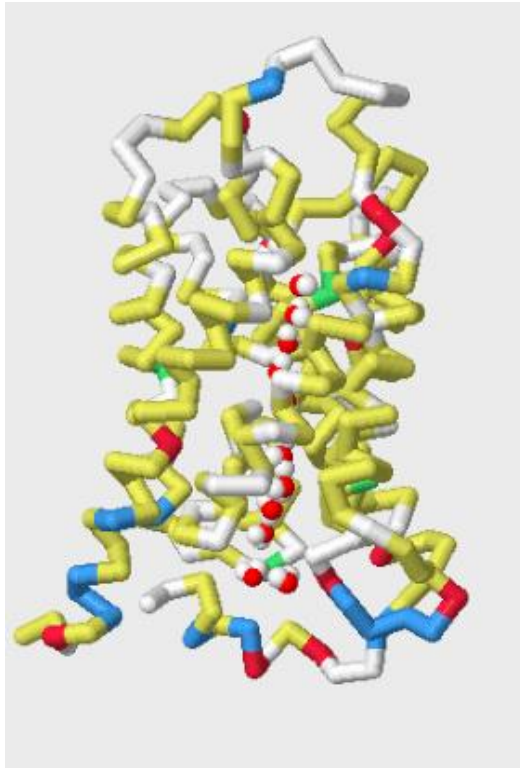
- Scan through the amino acid sequence.
- Enable all the cysteines [C] that you find.
- Notice where they are located on the protein backbone.



How many cysteines are in this sequence?

Which cysteine would most affect water movement into and out of the cell?

What is Aquaporin-1?



Display Format:

- ☒ Backbone
- ☐ Spacefill

Color Scheme:

- ☐ by Chain
- ☒ By Secondary Structure
- ☐ by Sidechain Property
- ☐ by Gradient

Printable Sequence (PDF)

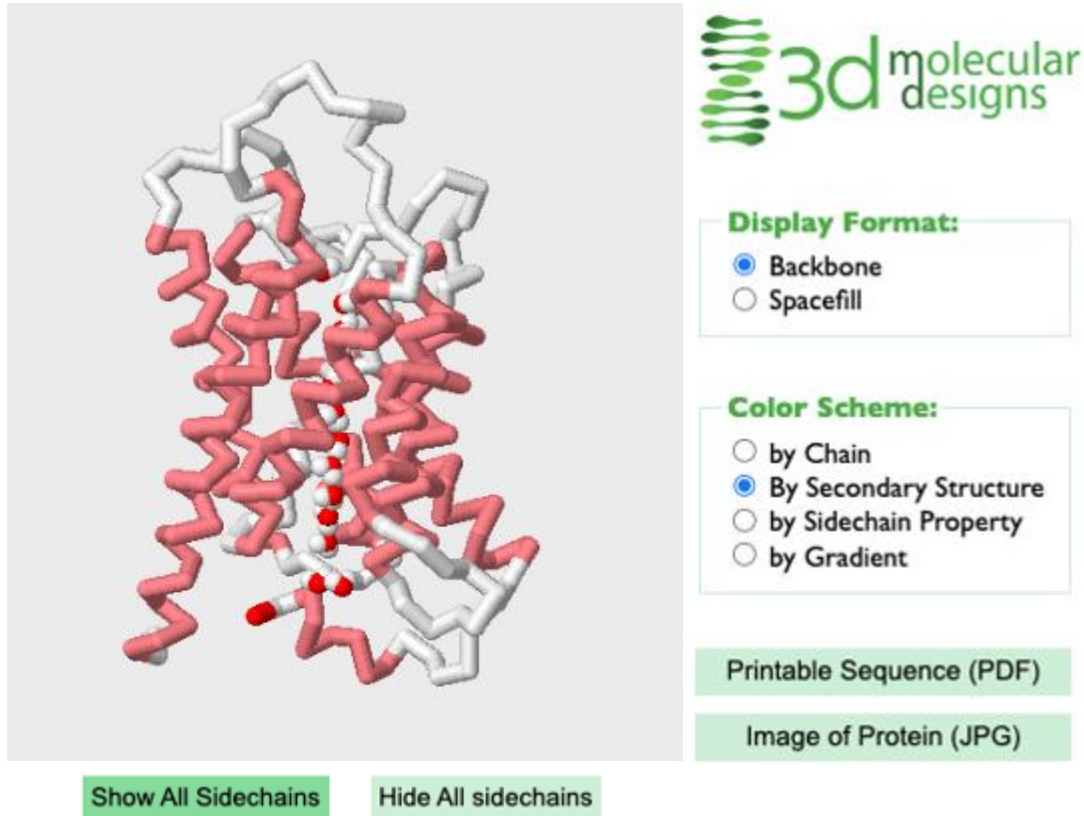
Image of Protein (JPG)

- Open the protein sequence viewer
- Select backbone in the display format.
- Select by side chain property in color scheme
- Scroll through the primary sequence of the polypeptide and notice the colors of the helices and loops.



What do the color indicate in terms of side chain property?

Exploring Secondary Structure



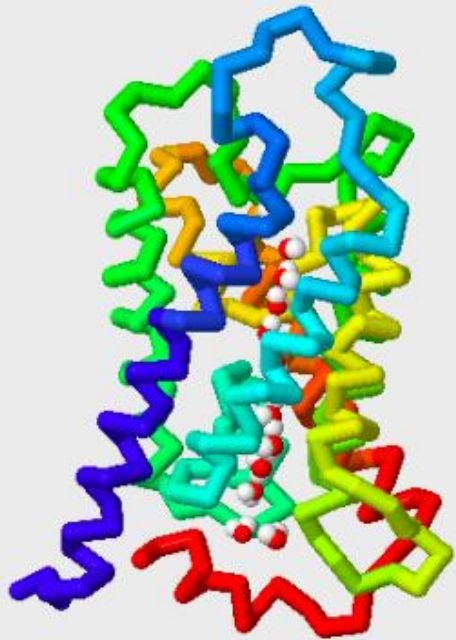
- Select Backbone under Display Format
- Select to display by Secondary Structure under Color Scheme



What types of secondary structures do you notice?

How many helices? How many sheets? Is there anything else that you notice?

Exploring Gradient



Show All Sidechains

Hide All sidechains



Display Format:

- ☒ Backbone
- ☐ Spacefill

Color Scheme:

- ☐ by Chain
- ☐ By Secondary Structure
- ☐ by Sidechain Property
- ☒ by Gradient

Printable Sequence (PDF)

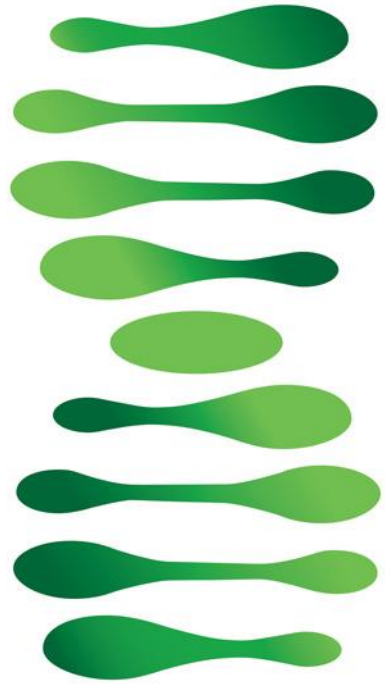
Image of Protein (JPG)

- Select Backbone under Display Format
- Select to display by Gradient under Color Scheme



What can gradient tell you about aquaporin's structure?

Why would scientists want to use such a tool?



Transforming Science Learning

