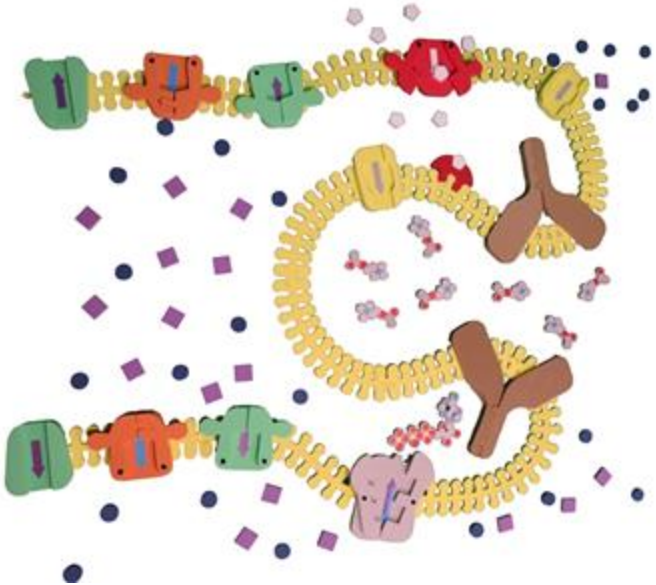
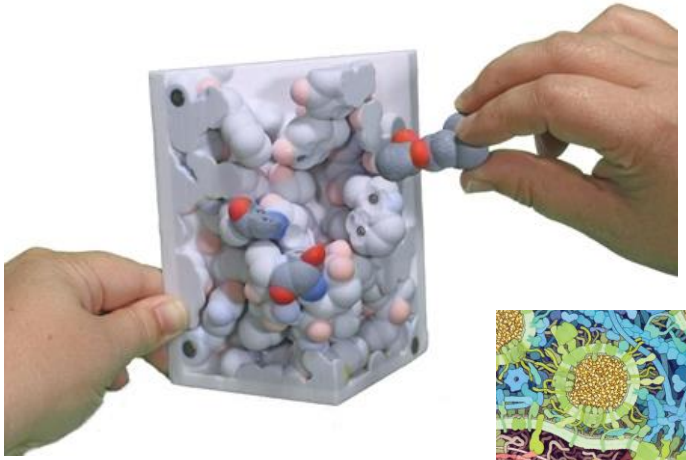
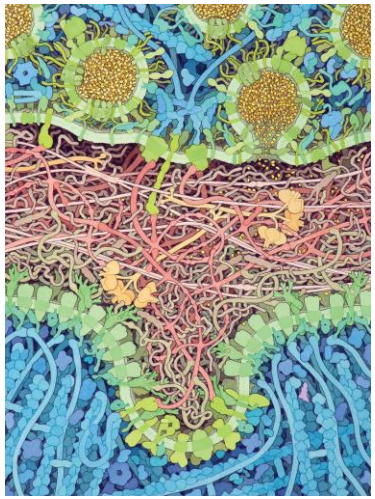
Neurotransmitters, Synapses & Acetylcholinesterase





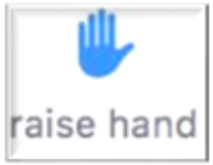


Digital Resources

Webinar norms

Comments and Questions for 3D Molecular Designs Staff should be entered into the Chat box.

Questions for the Speaker should be entered into the Q&A box.



Use the Raise Hand button to participate in discussion when applicable.

Dan Williams

BS, MA Biology

High School Teacher

NYS Master Teacher, SAR Biology STANYS

Shelter Island High School

Shelter Island, New York

Karen Avery

BA, MS Biology,

EdD Student, STEM Education

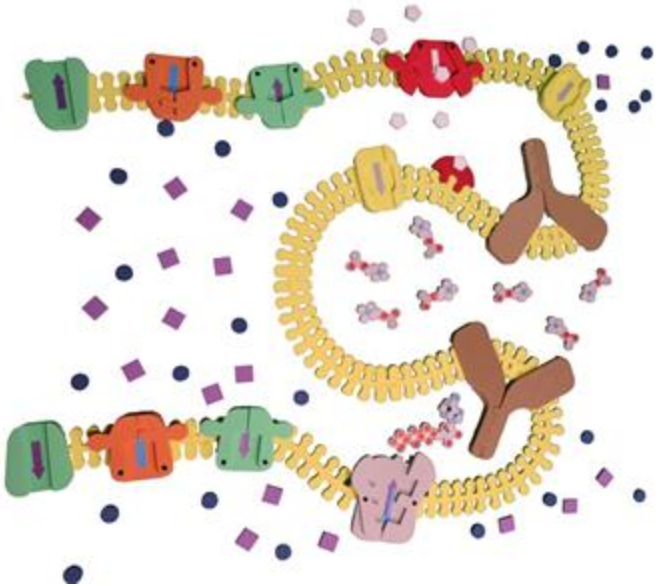
The Pennsylvania College of Technology

Williamsport, Pennsylvania

Instructor: Biology, Microbiology

High School Biology

How Cells Talk



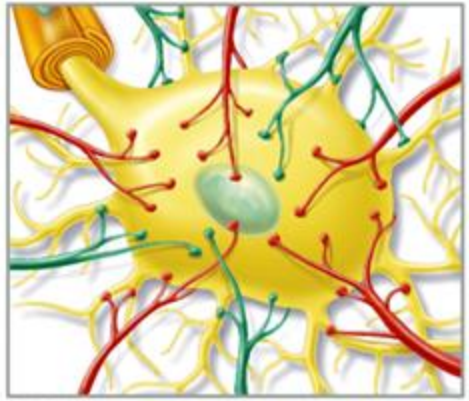
Modeling how cells talk: making sense of synapses and signals

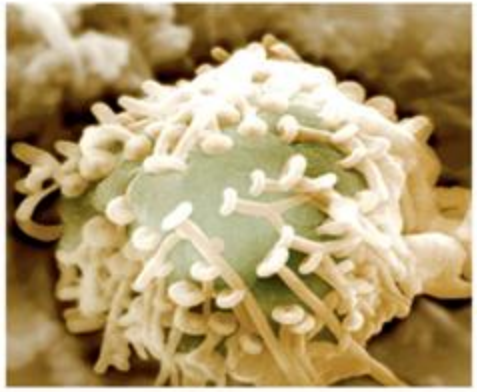
What questions will we answer today? (workshop goals)

- What makes a good model?
- What can we learn from the synapse model?
- What do you find difficult when you are teaching about cell interactions?
- Where do multidimensional models help with this topic?
- How can you show cell communication, synapses, disruptions of communication between cells and signal transduction using this model?


20 Years
3-D Molecular Designs
MSOE
Center for BioMolecular Modeling


A B C D E F
G H I J K
L M N O P
Q R S T U
V W X Y Z

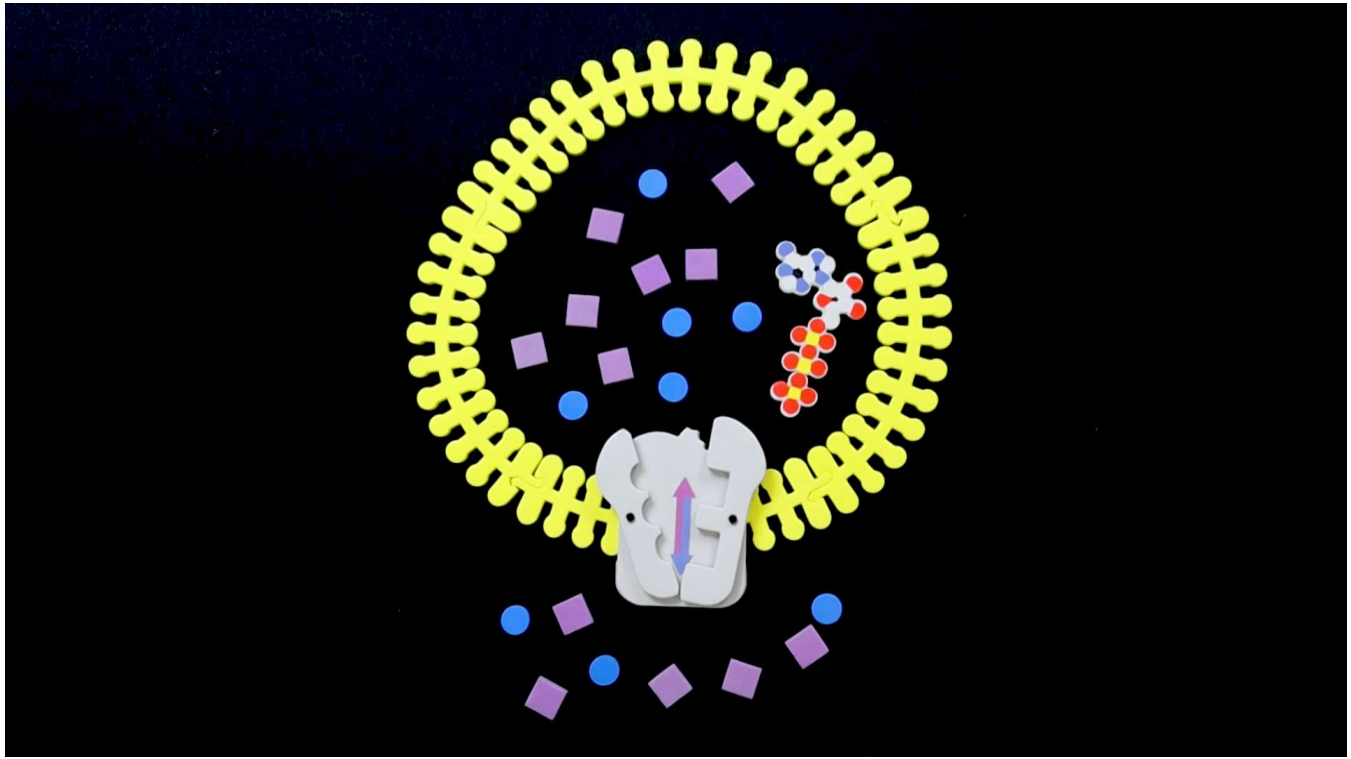





twitter
in
You Tube
digg
Q

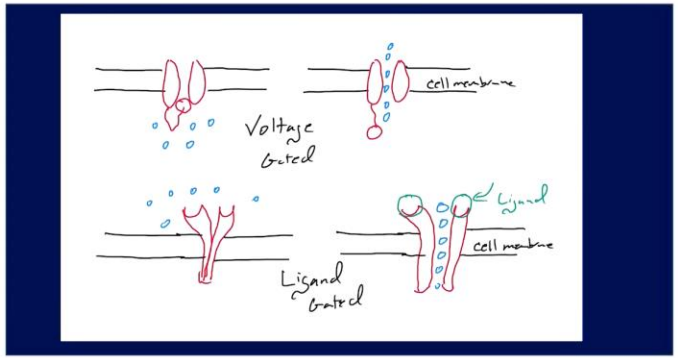
Synapse Construction Kit Walkthrough

Laying the Foundation: The Sodium Potassium Pump

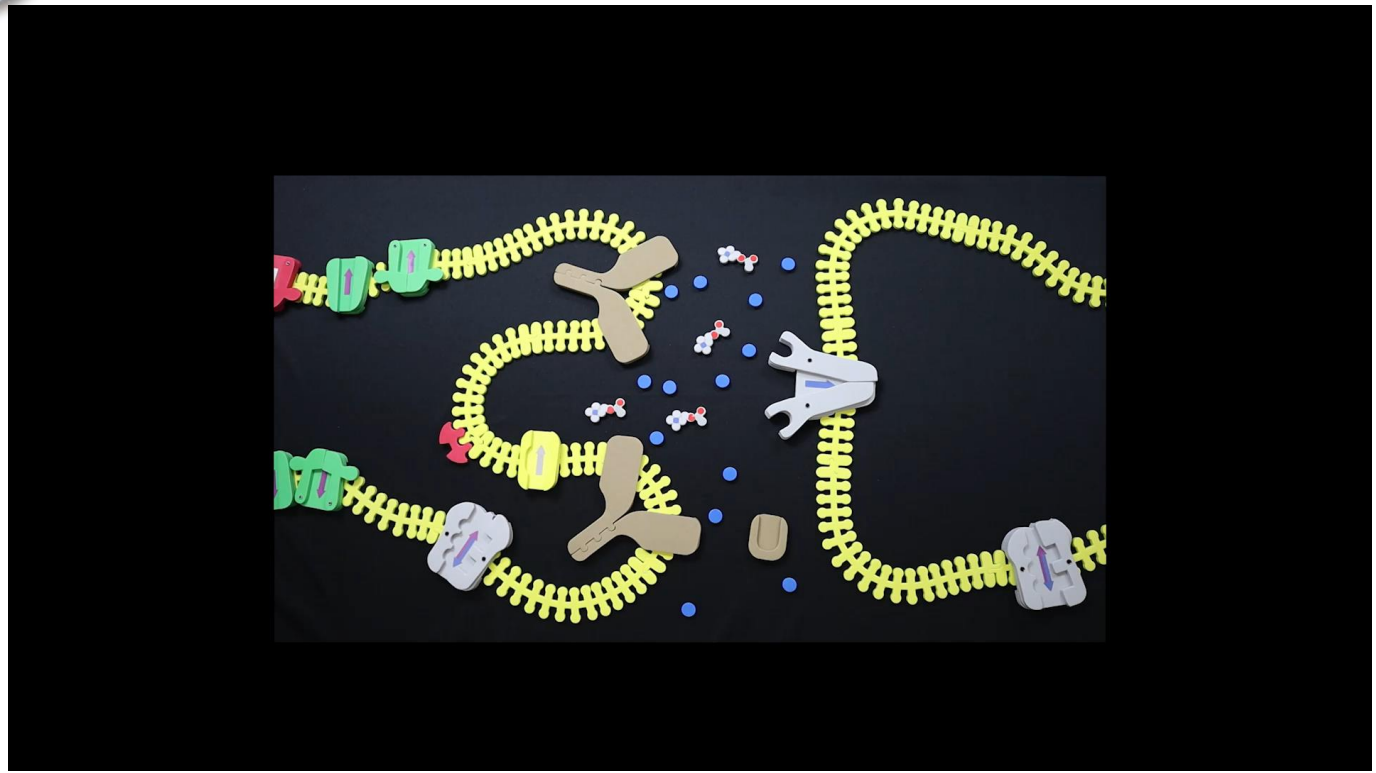


Cell Communications Basics

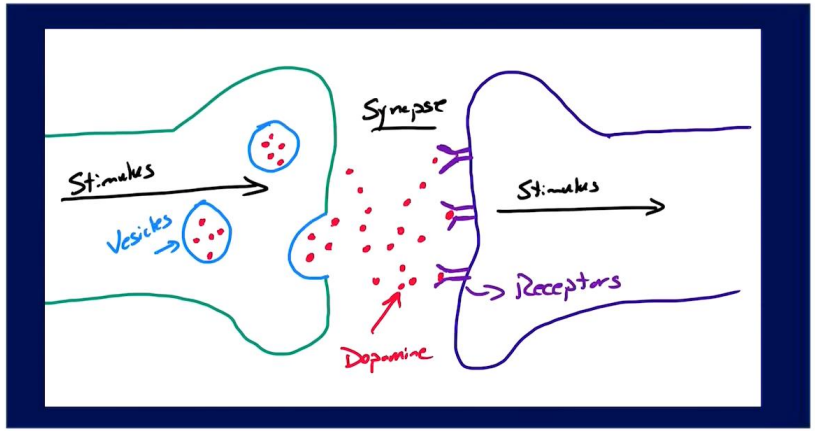
Voltage gated vs. Ligand gated



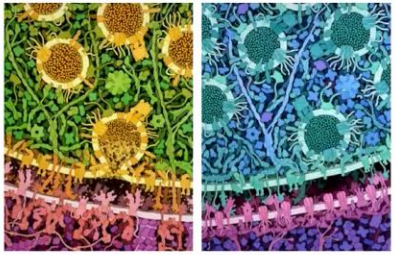
Allosteric and Competitive interactions



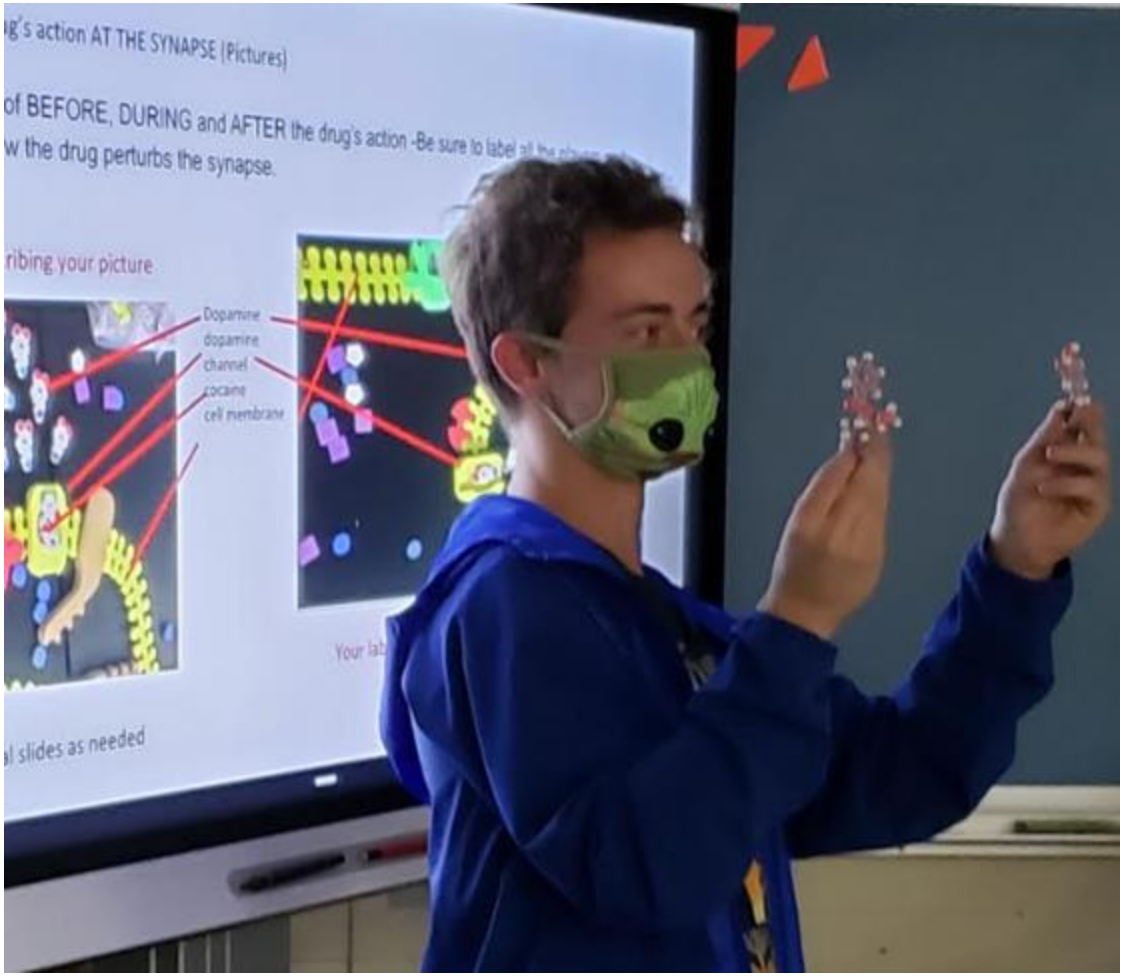
Signal Transduction and Applications to other systems



Inspires questioning

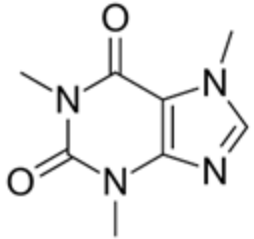


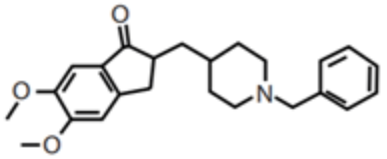
Making claims



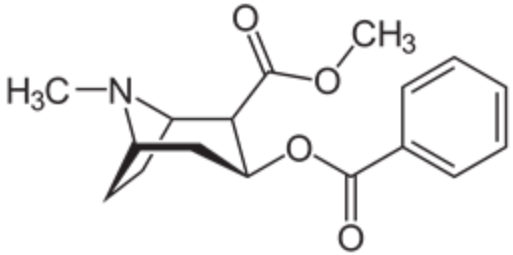
Rich Story Lines

Discuss membrane kit adaptation to model disruptions

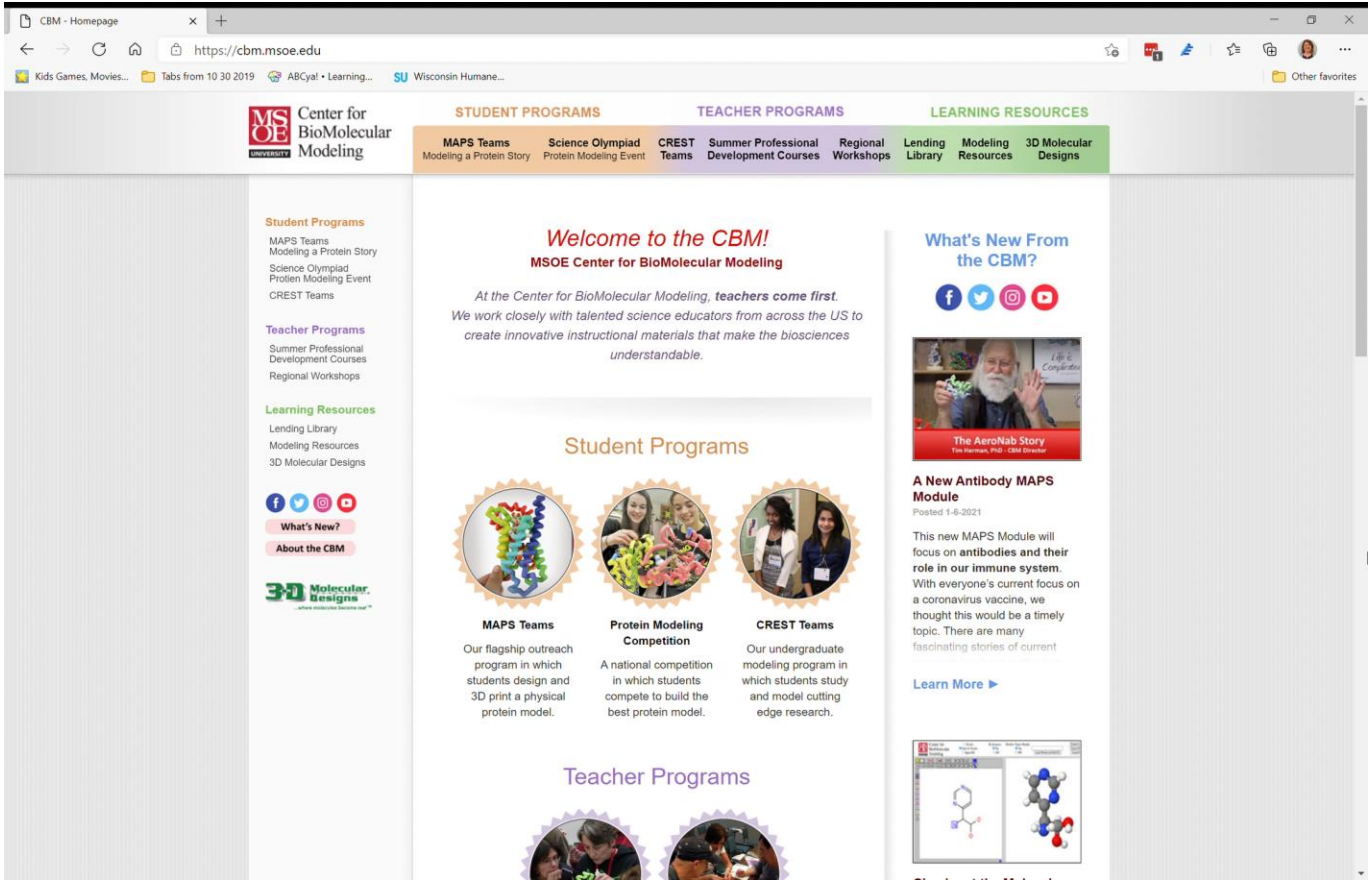


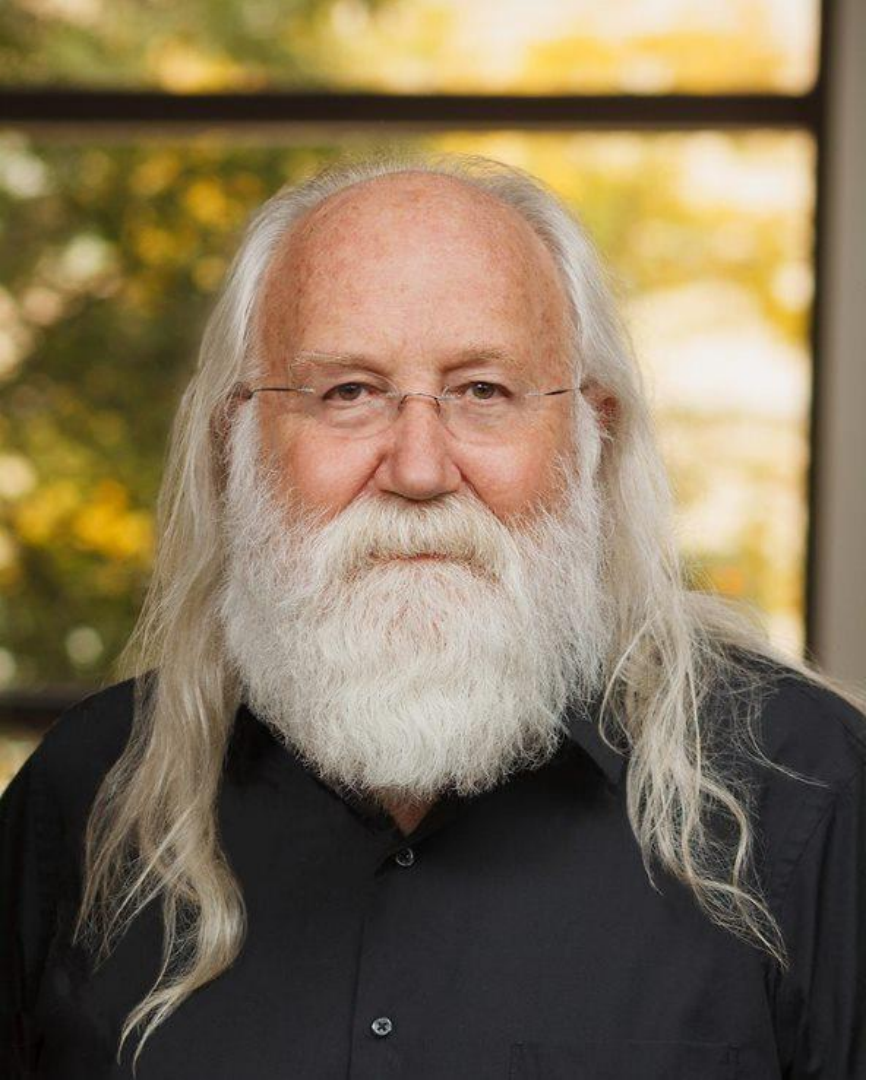


Aricept



Check out the CBM's Model Lending Library





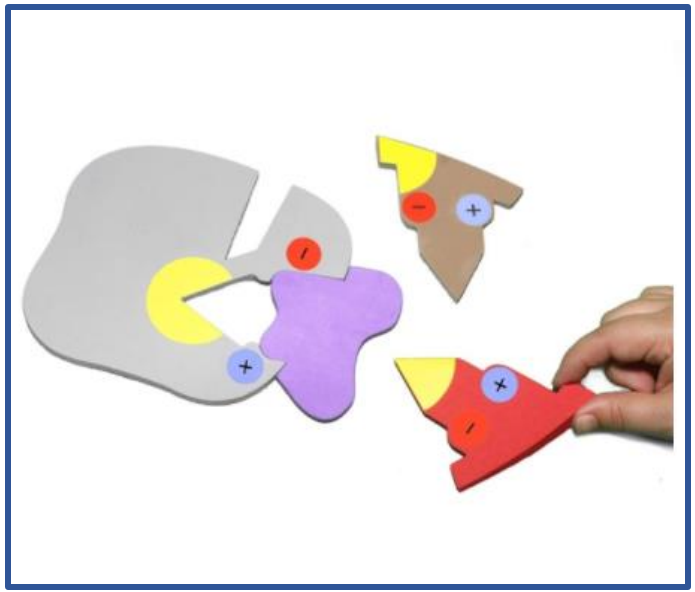
Timothy Herman, PhD

- Director of the Center for BioMolecular Modeling at MSOE
- Founding Partner of 3D Molecular Designs
- B.S. in Chemistry from the University of Nebraska
- Ph.D. in Biochemistry from Oregon State University.
- Post-doctoral studies in Molecular Biology at Harvard Medical School.

Acetylcholinesterase (ACHE)

an enzyme active site

From the Simple >>>>>>>>>>>>>>>>>>> to the Sublime



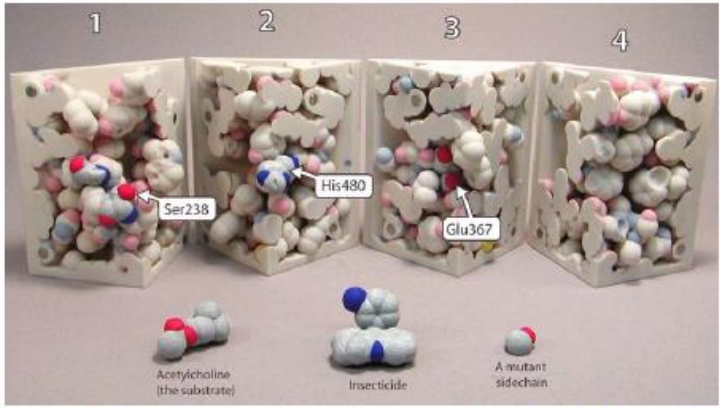
Evolution In Action

Emerging Insecticide Resistance in Mosquitoes

A three-dimensional molecular story about the acetylcholinesterase active site

Organophosphate insecticides are routinely used to control mosquito populations in areas where malaria is endemic. Many of these insecticides target the enzyme acetylcholinesterase --- which normally cleaves the acetylcholine neurotransmitter, and terminates synaptic transmission. A recent report by Weil et. al. (Nature, 423, pp136-137, 2003) described the molecular basis for this insecticide resistance --- a Gly119Ser mutation. Because it is difficult to communicate the close-packed nature of an enzyme active site, and the specific interactions between active site residues and the substrate/inhibitor with 2D illustrations and computer graphics, we have constructed a physical model of this enzyme active site.

This space-filled model of the active site "unfolds" to reveal the catalytic triad of active site residues Ser238, His480 and Glu367. The substrate and inhibitor can be alternatively docked into the active site. Replacement of the normal Gly119 sidechain with a serine sidechain blocks the binding of the insecticide, without interfering with substrate binding. This physical model is based on coordinates from 1qon.pdb.



This model can be borrowed from the MSOE Model Lending Library.

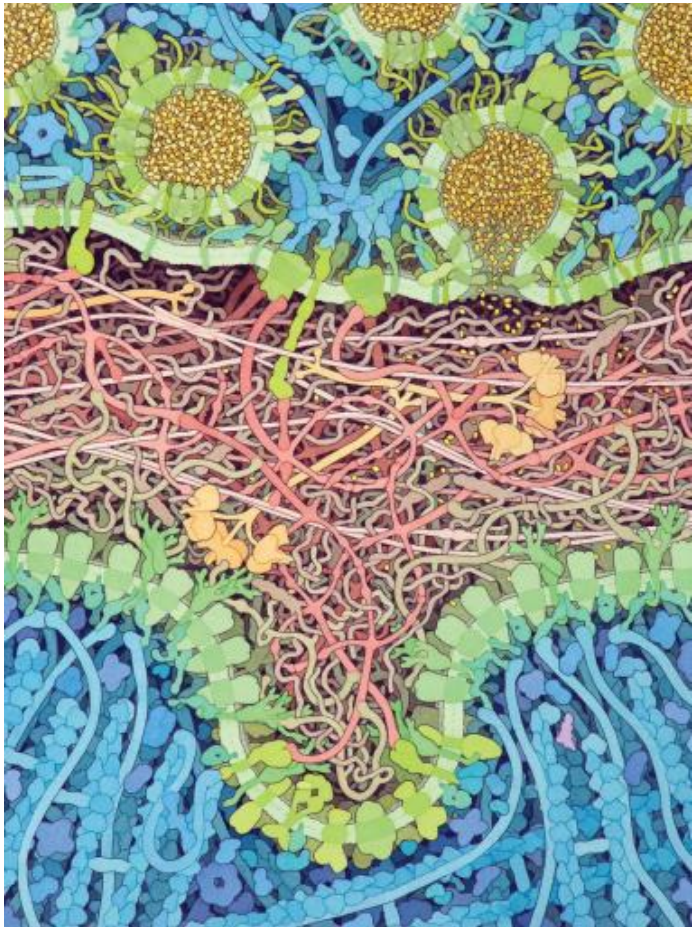
MSOE Center for BioMolecular Modeling
...where teachers come first

www.msoe.edu/cbm

An NIH NCRR SEPA Project

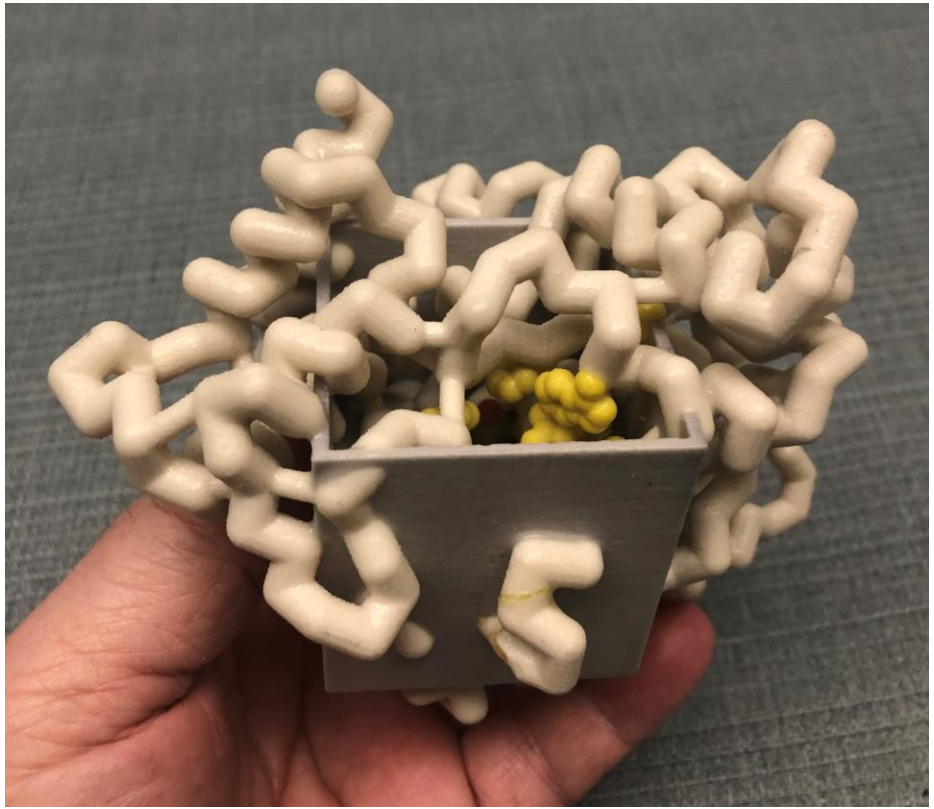
Neuromuscular Synapse Poster

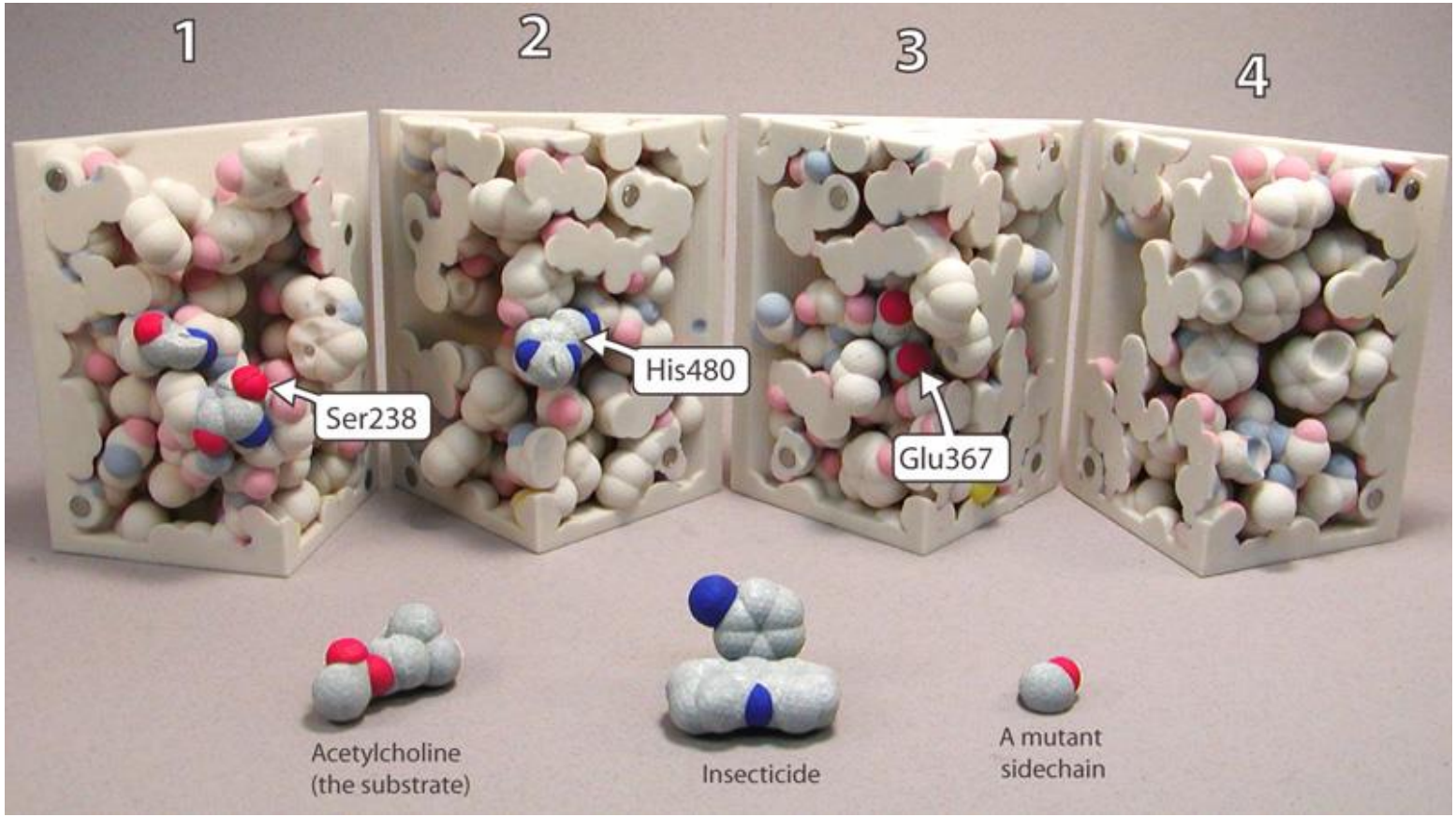
David Goodsell Cellular Landscapes



Acetylcholinesterase

- globular structure
- deeply buried active site




1
2
3
4
Ser238
His480
Glu367
Acetylcholine
(the substrate)
Insecticide
A mutant
sidechain

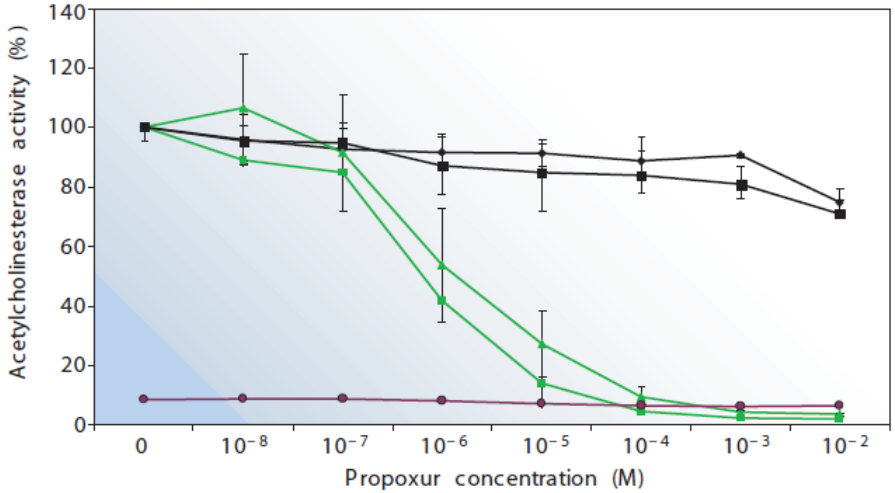


Figure 1 Residual acetylcholinesterase activity of susceptible (green squares) and resistant (black diamonds) mosquitoes assayed in homogenates and lysates from transfected S2 cells in the presence of increasing concentrations of the carbamate insecticide propoxur. S2 cells were transfected with the recombinant pAc5.1/V5-His vector (Invitrogen) either alone (purple circles) or with expression of either sensitive acetylcholinesterase-1 (green triangles) or insensitive G119S-mutant enzyme (black squares). Residual enzyme activity was assayed after incubation with Propoxur for 15 min (ref. 5). Three independent experiments were carried out using different volumes of lysate.

Comparative genomics

Insecticide resistance in mosquito vectors

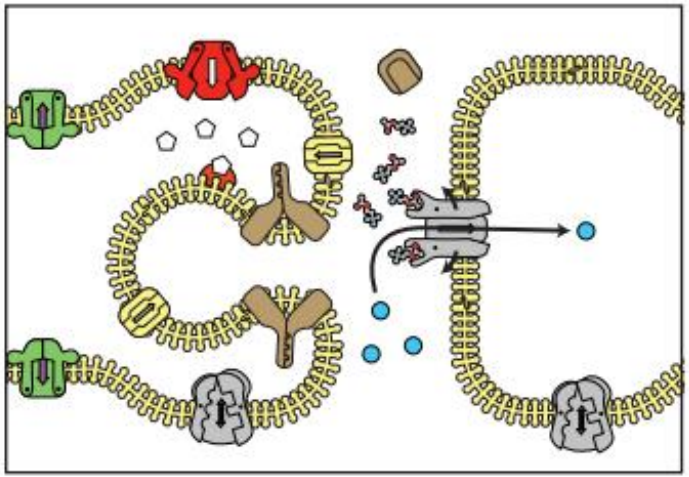
Resistance to insecticides among mosquitoes that act as vectors for malaria (*Anopheles gambiae*) and West Nile virus (*Culex pipiens*) emerged more than 25

which generates an amino-acid substitution: the GGC (glycine) codon at position 119, according to the nomenclature for *Torpedo* acetylcholinesterase[1], is replaced by an

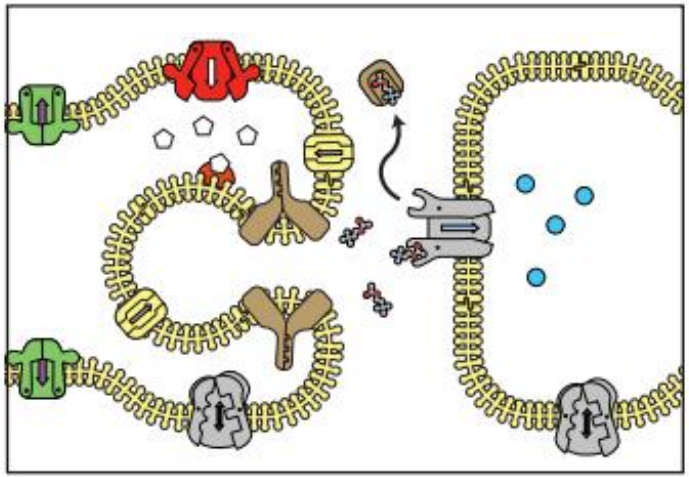
sequences differed at 18 nucleotide positions, two of them being non-synonymous. In the YAO strain, one mutation that resulted in the replacement of a valine residue by

Nature, 243, 136-137, 2003

Part III: Modeling Neurotransmission – A Cholinergic Synapse



Step 5 - The acetylcholine receptor opens to allow sodium ions to follow their concentration gradient into the postsynaptic cell. Depolarization of the postsynaptic cell occurs and an action potential may be generated in the post synaptic cell. Note: the receptor also allows passage of Ca^{2+} and K^{+}.



Step 6 - The enzyme acetylcholinesterase breaks the neurotransmitter down into acetic acid and choline.

Don't tell your students this story….

...in 15 minutes

Instead, pose a series of challenges, or questions

- *What are some possible mechanisms of insecticide resistance?*
- *How might you analyze the acetylcholinesterase enzyme found in insecticide resistant mosquitoes?*
- *How might we prevent the emergence of insecticide resistant mosquitoes?*

Thank you for attending!

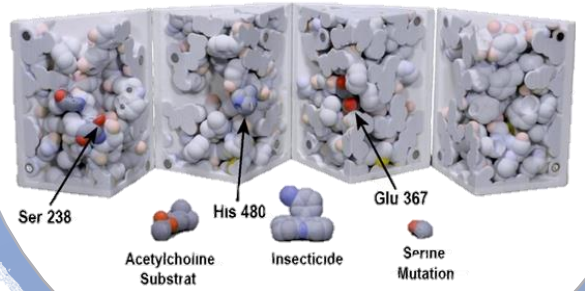
Apply for a Summer Course

cbm.msoe.edu

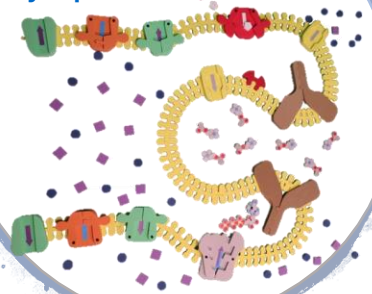
Stock Up Sale
Buy 4 or more for 25% off, 3 for 20%, 2 for 15%

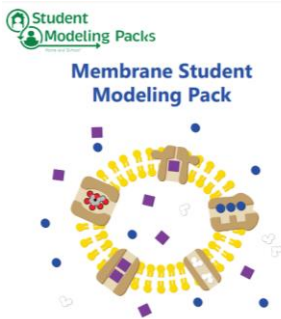
Enzymes in Action Kit©

Acetylcholinesterase Active Site Cube©



Synapse Construction Kit©





Invite your colleagues to register!

Proteins & the Protein Folding Problem

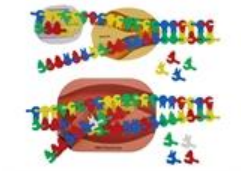
Proteins – Now that Everything has Changed

Wednesday, February 17, 2021 at 6:00 PM Central

Chromosomes & DNA

Making Connections Between DNA and Chromosomes!

Wednesday, February 24, 2021 at 6:00 PM Central



Genome Editing, I

CRISPR – As an Adaptive Immune System in Bacteria

Wednesday, March 10, 2021 at 6:00 PM Central

https://www.3dmoleculardesigns.com/Webinars4.htm