



# IS VIRTUAL REALITY USEFUL FOR VISUALIZING AND ANALYZING MOLECULAR STRUCTURES?

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**RESOURCE FOR BIOCOMPUTING, VISUALIZATION AND INFORMATICS**

**UNIVERSITY OF CALIFORNIA, SAN FRANCISCO**

ACS Fall 2019 National Meeting & Exposition

# WHO WE ARE

- NIH supported research lab with long history of developing and distributing interactive molecular visualization and analysis applications
- Founded in 1969 by Bob Langridge
- Moved to UCSF in 1976
- Langridge retired in 1993, Ferrin became PI
- MIDS → Midas/MidasPlus (80's & 90's) → UCSF Chimera → ChimeraX (2017)
- All the above software supported viewing molecules in stereo



Evans & Sutherland Picture System 2  
with Bausch and Lomb mechanical shutters  
1980



Silicon Graphics O<sub>2</sub> workstation  
with Stereo Graphics eyewear  
1990



# TODAY STEREO IS ALL BUT A DEAD TECHNOLOGY

- ~~Miracube G240M Stereoscopic Computer Display~~ *No longer available*
- ~~NVIDIA 3D Vision~~ *No longer available, no driver support*
- ~~3D TVs~~ *Samsung, LG, Sony and Panasonic stopped introducing new models in 2017*
- “Old School” approaches still viable but have significant disadvantages:



Red/Cyan Anaglyph glasses



Side-by-Side images

## VR HEADSETS PROVIDE *IMMERSIVE* STEREO VIEWING AND MORE...



Oculus Rift S

- High resolution images (typically 1,440 x 1,280 each eye)
- Wide field of view (200° or more)
- Fast refresh rates (~80-90 Hz)
- Rapid tracking of head position
- Dual 6 degree-of-freedom input devices, usually with multiple auxiliary controls like push buttons and joysticks/touchpads
- Cost similar to active stereo glasses

## BUT THERE ARE SEVERAL IMPORTANT CHALLENGES

- Head tracking demands fast update rates in order to avoid severe nausea and this requires a high-end CPU, GPU and 16GB+ of memory
  - Intel i5 or i7
  - NVIDIA GTX 1070/1080, AMD Radeon RX 5700 (\$750 - \$1,000)
- 6 DOF input devices require development of new user interfaces which are time-consuming to code, test and refine
- No easy way to provide keyboard input
- Ability to support multiple users/participants is limited
- Evolving OS support – Windows 10 pretty good, Linux limited, macOS ???
- Required 3<sup>rd</sup> party software (e.g., SteamVR) still immature
- There's no standardized API among headset providers



# MATT JACOBSON'S LAB AT UCSF USES VR FOR THEIR WEEKLY GROUP MEETINGS ABOUT DRUG DESIGN

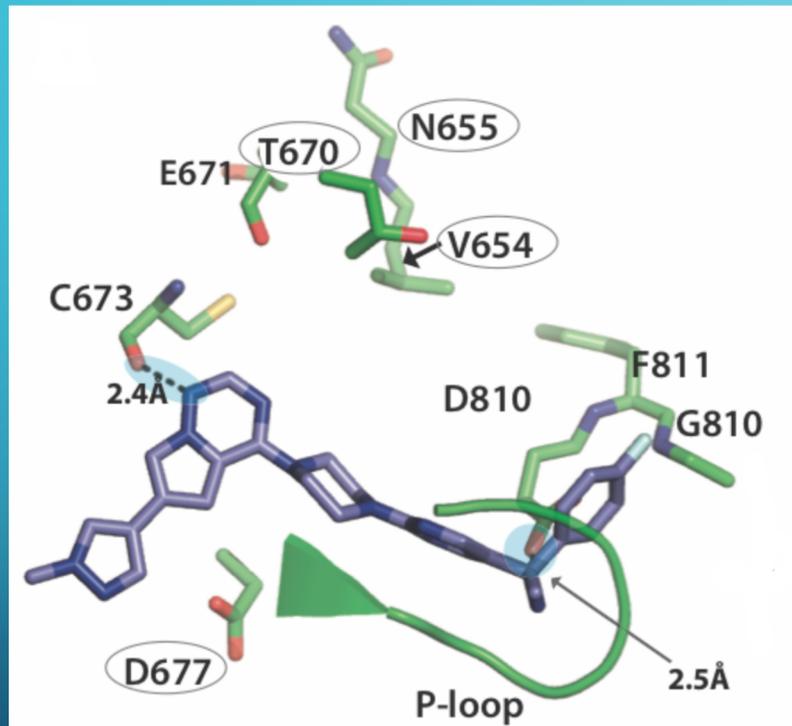
- Usually two group members use VR while others participate via video projector
- Projector shows what one of the VR users sees
- Each VR headset runs on a separate computer (a requirement of the VR driver software)
- Participants can connect to VR session remotely
  - We use remote VR meetings at UCSF with NIH and Benaroya Institute in Seattle
  - Network firewalls can block connections in high security environments



Video URL: <https://www.rbvi.ucsf.edu/chimerax/data/acs-aug2019/images/vruse.mp4>

# VR HELPED UNDERSTAND DRUG RESISTANCE IN KIT

- Some cancers commonly exhibit a mutation in receptor tyrosine kinase (KIT) protein causing over-activation and allowing cancer cell proliferation
- The cancer drugs imatinib and avapritinib block KIT signaling by binding in its ATP binding site, but some patients acquire secondary KIT mutations that make these drugs ineffective
- Several mutations that result in drug resistance were distant from the binding site yet still disrupted drug binding **BUT HOW?**
- Jacobson's lab hypothesized the drug resistance mechanism based on observations using VR
- Distant mutations were found to rigidify part of the protein which lead to different dynamics of the flexible P-loop region (coordinates phosphate transfer) in the ATP binding site



**Some KIT mutations (circles) inhibit the drug avapritinib (shown in purple) through an indirect interaction that moves the P-loop region, thereby blocking binding**

ATP-competitive inhibitors midostaurin and avapritinib have distinct resistance profiles in exon 17-mutant KIT. Apse et al., Cancer Res. 2019 Jul 3.

The screenshot shows a web browser window with the following content:

- Browser Tabs:** Chimerax Tutorial: DICOM in...,  $\mu$ -opioid receptor - Wikipedia, Predicting opioid receptor bin...
- Address Bar:** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5967713/>
- Page Header:** NCBI Resources How To Sign in to NCBI
- Search Bar:** PMC [Search]
- Journal List:** PLoS One > v.13(5); 2018 > PMC5967713
- Article Title:** Predicting opioid receptor binding affinity of pharmacologically unclassified designer substances using molecular docking
- Authors:** Christopher R. Ellis, Naomi L. Kruhlik, Marlene T. Kim, Edward G. Hawkins, Lidiya Stavitskaya
- Publication Info:** PLoS One. 2018; 13(5): e0197734. Published online 2018 May 24. PMID: 29795628
- Associated Data:** S1 Fig: Average docking score. The docking procedure (ten independent simulations and averaging the best pose) was repeated three times for the 24 opioids. This plot shows the
- Right Sidebar:** Formats (Article, PubReader, ePub (beta), PDF (5.2M), Citation), Share (Facebook, Twitter, Google+), Save items (Add to Favorites), Similar articles in PubMed, Links (Compound, Gene (nucleotide), MedGen, Nucleotide, PubMed, Taxonomy), Recent Activity
- Footer:** lysine Highlight All Match Case Whole Words Phrase not found

Video URL: <https://www.rbvi.ucsf.edu/chimerax/data/vr-demos-feb2019/opioids.mp4>

# VR EQUIPMENT: A PLETHORA OF CHOICES



HTC Vive Pro



HTC Wireless Adapter



Oculus Rift S



Microsoft HoloLens 2



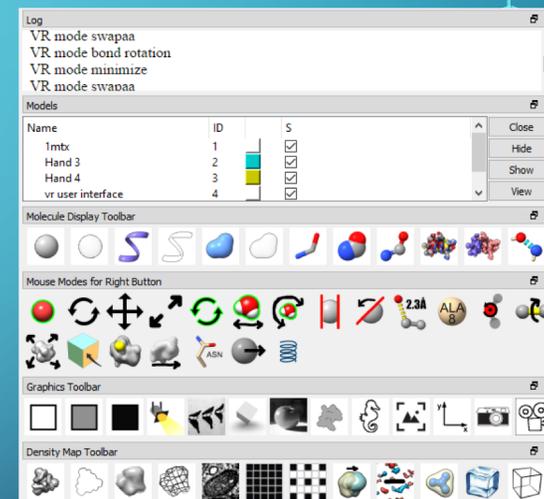
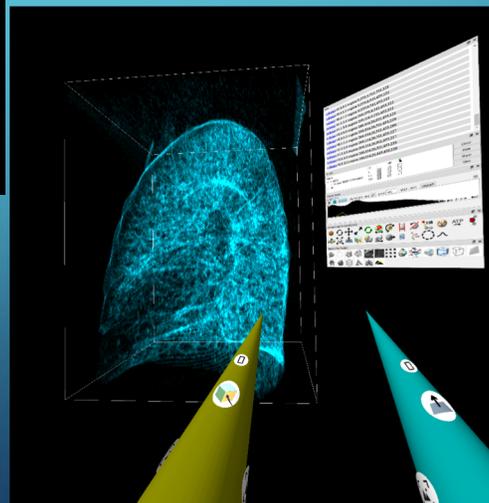
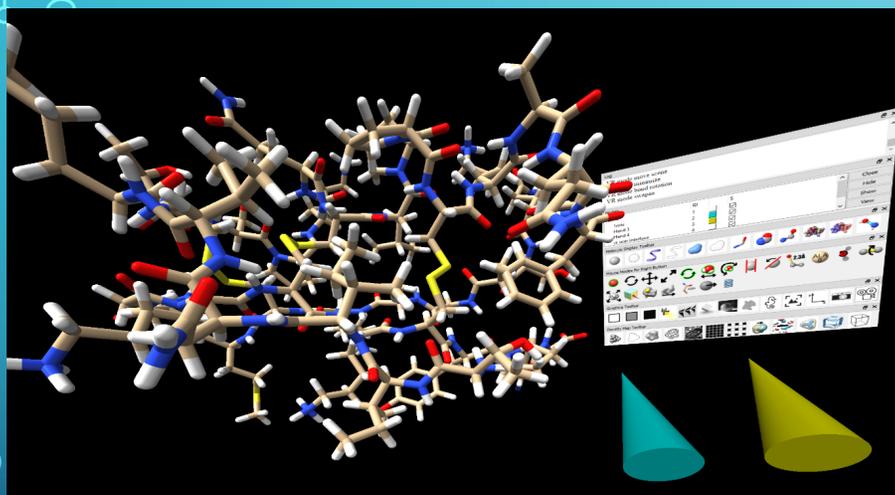
Magic Leap

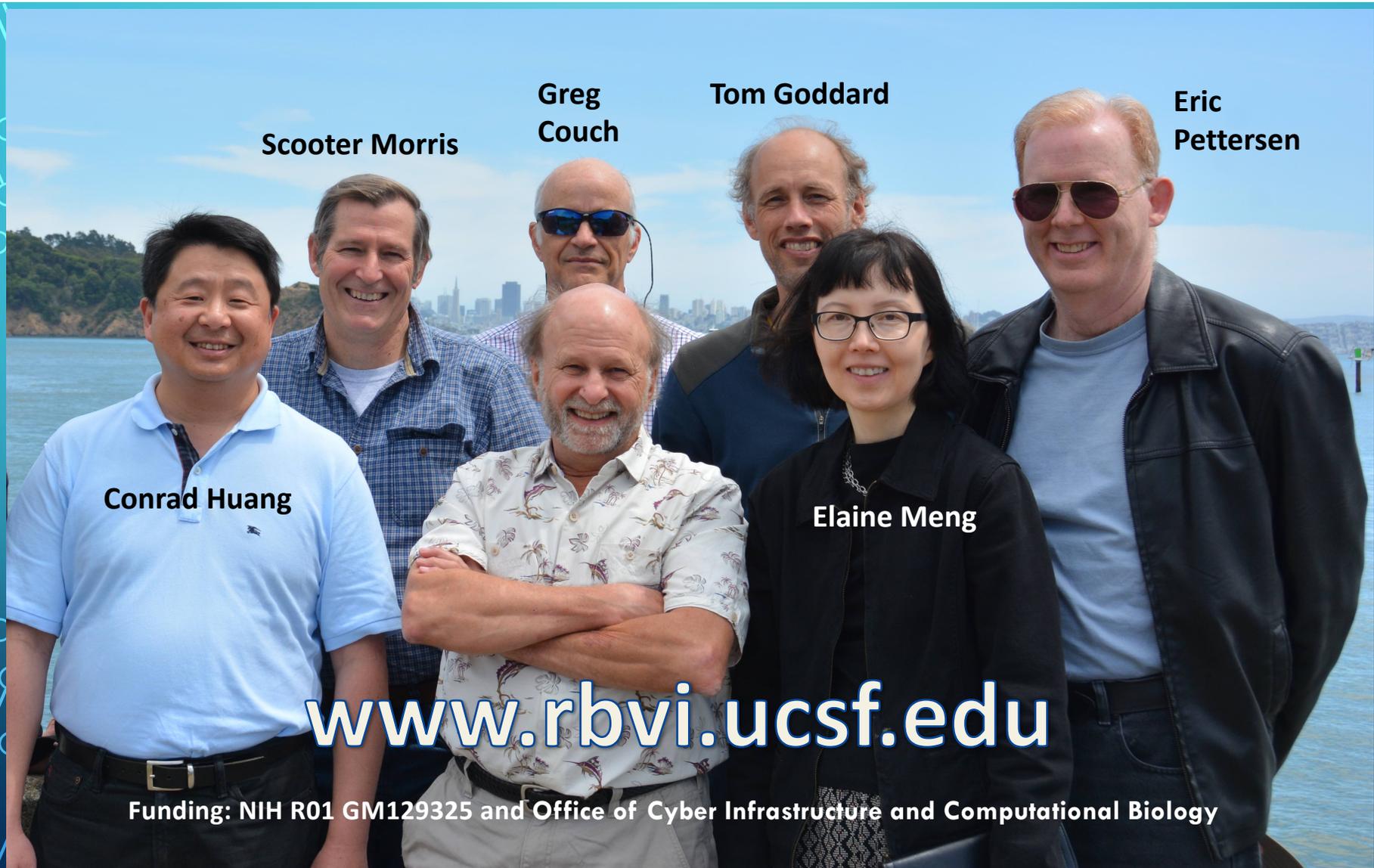


Oculus Quest

# CRITICAL TO SUCCESSFUL USE OF VR TECHNOLOGIES...

## Application-Specific User Interfaces





**Scooter Morris**

**Greg Couch**

**Tom Goddard**

**Eric Pettersen**

**Conrad Huang**

**Elaine Meng**

[www.rbvi.ucsf.edu](http://www.rbvi.ucsf.edu)

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