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

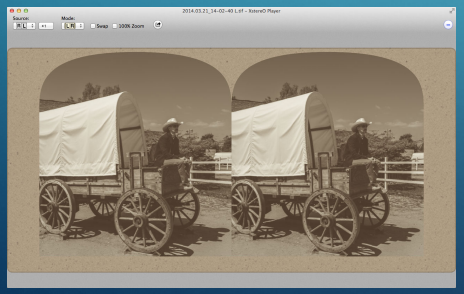
Silicon Graphics O_2 workstation
with Stereo Graphics eyewear
1990

Christie Digital Mirage video projector
with RealD CrystalEyes eyewear
2005

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…

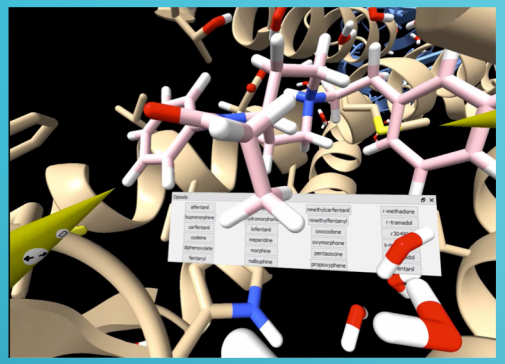
Oculus Rift S

- 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

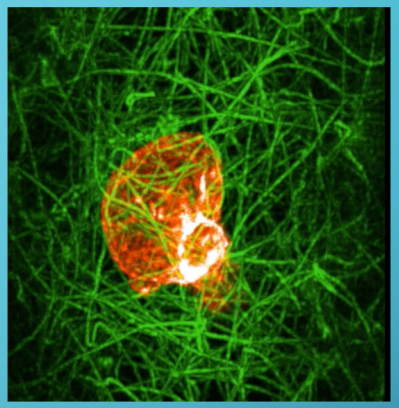
BUT THERE ARE SEVERAL IMPORTANT CHALLENGES

- 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 3rd party software (e.g., SteamVR) still immature
- There's no standardized API among headset providers

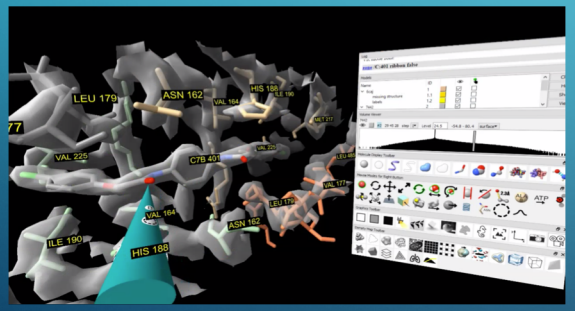
VR AT THE RBVI



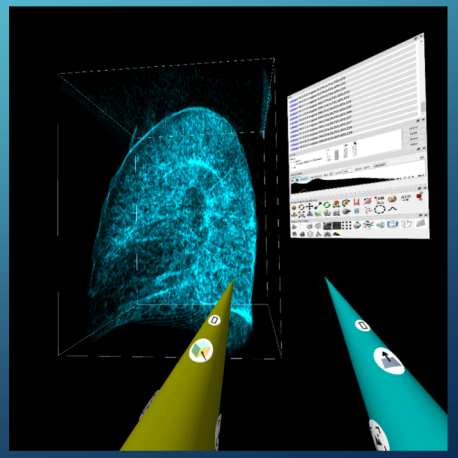
Computational Docking



Light Sheet Microscopy



cryoEM



Medical CT Imaging

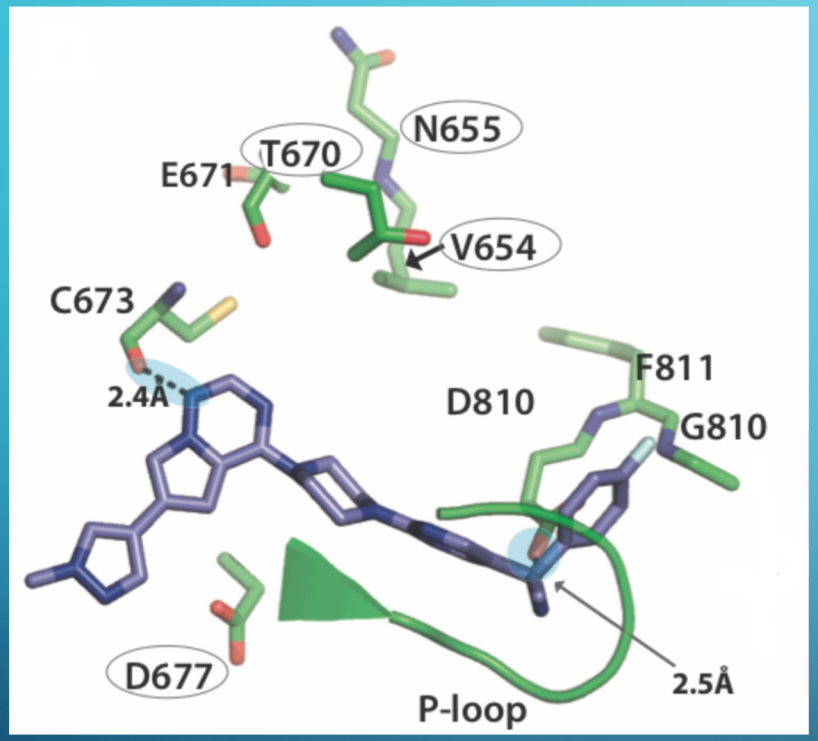
MATT JACOBSON'S LAB AT UCSF USES VR FOR THEIR WEEKLY GROUP MEETINGS ABOUT DRUG DESIGN

- 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

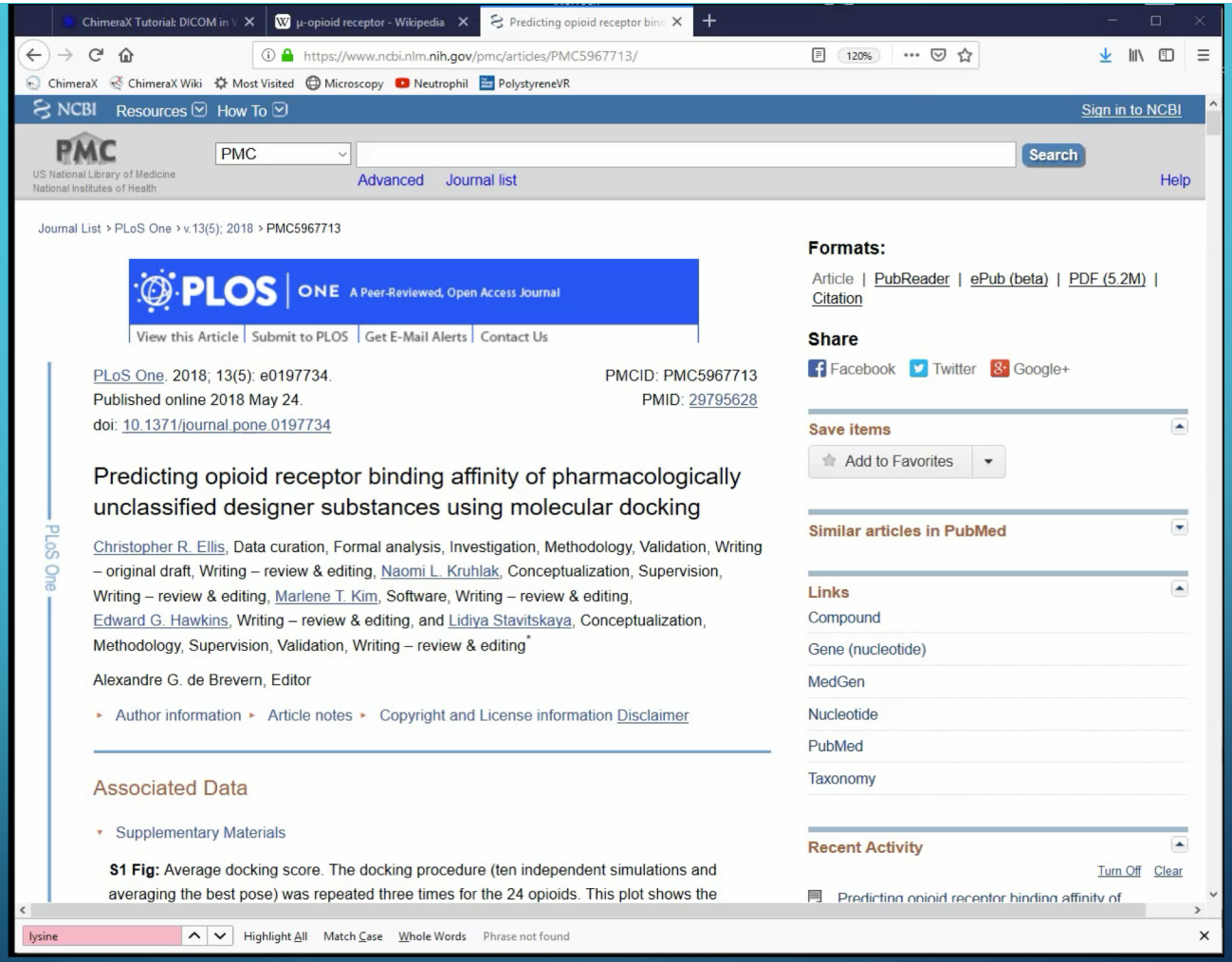
VR HELPED UNDERSTAND DRUG RESISTANCE IN KIT

- Some cancers commonly exhibit a mutation in receptor tyrosine kinase (KIT) protein causing over-activation and allowing cancer cell proliferation
- The cancer drugs midostaurin 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. Apsel et al., Cancer Res. 2019 Jul 3.



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

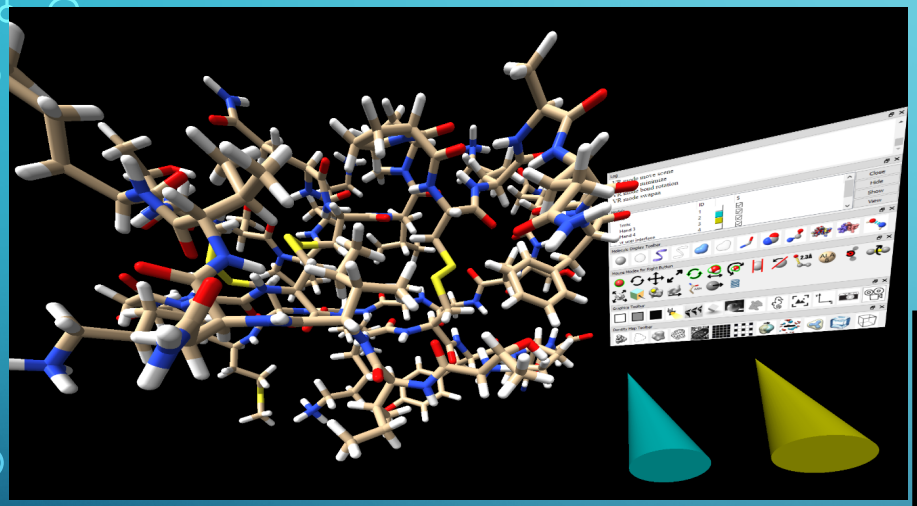
Microsoft Hololens 2

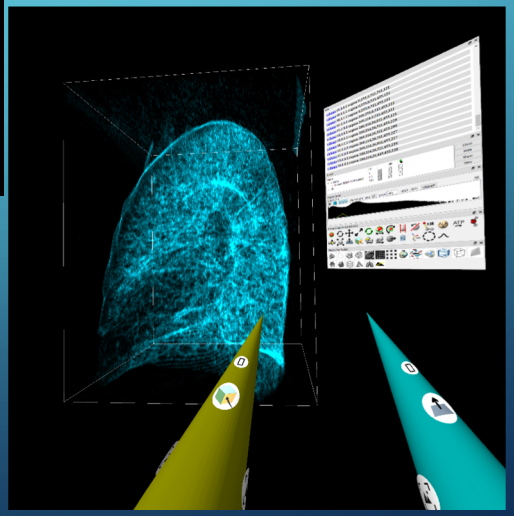
Magic Leap

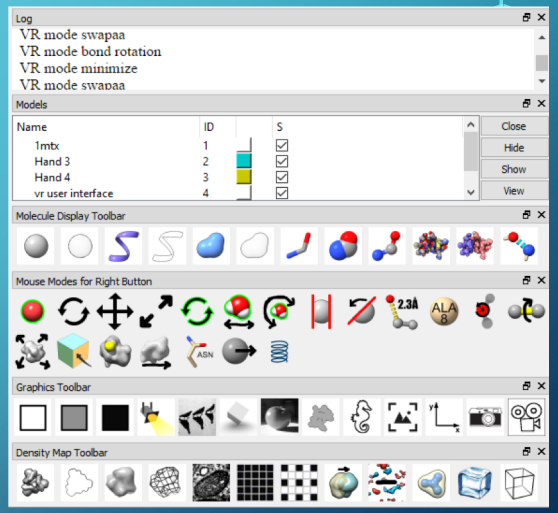
Oculus Quest

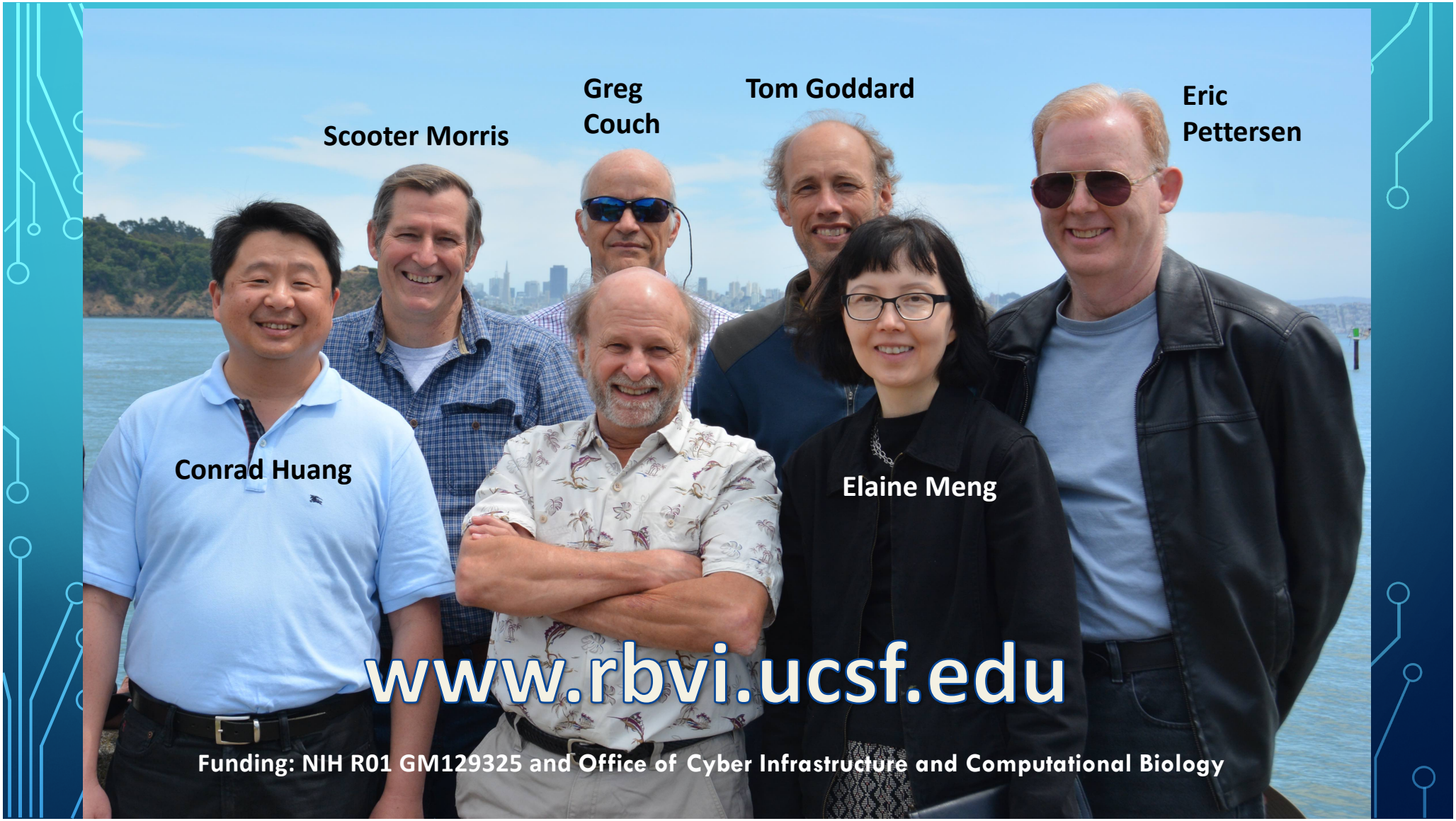
CRITICAL TO SUCCESSFUL USE OF VR TECHNOLOGIES…

Application-Specific User Interfaces









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