Virtual Reality in Drug Discovery

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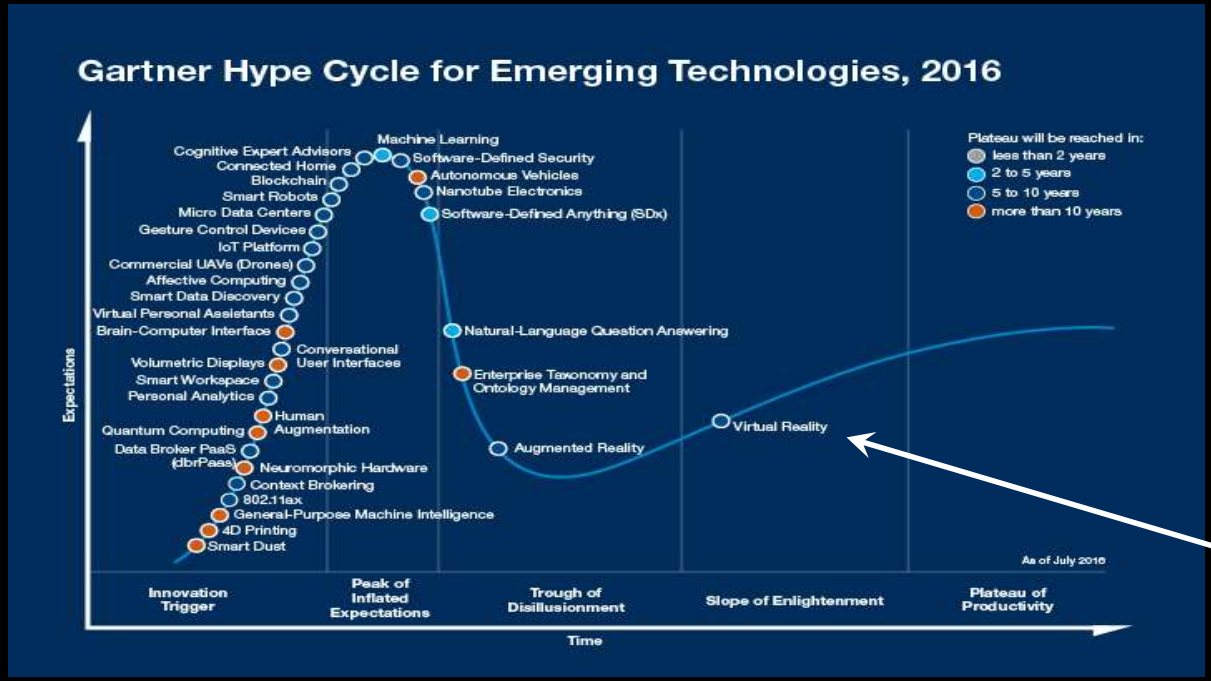
January 24th 2017, BigChem webinar

VR – What's the Fuzz?

The feeling of presence is real

Virtual Reality is not New



accessible, user-friendly, performant and relatively in-expensive
(not mainstream yet)

VR in Games

VR in Entertainment

Live-streaming from sports or music events

VR in Psychology

Itsy

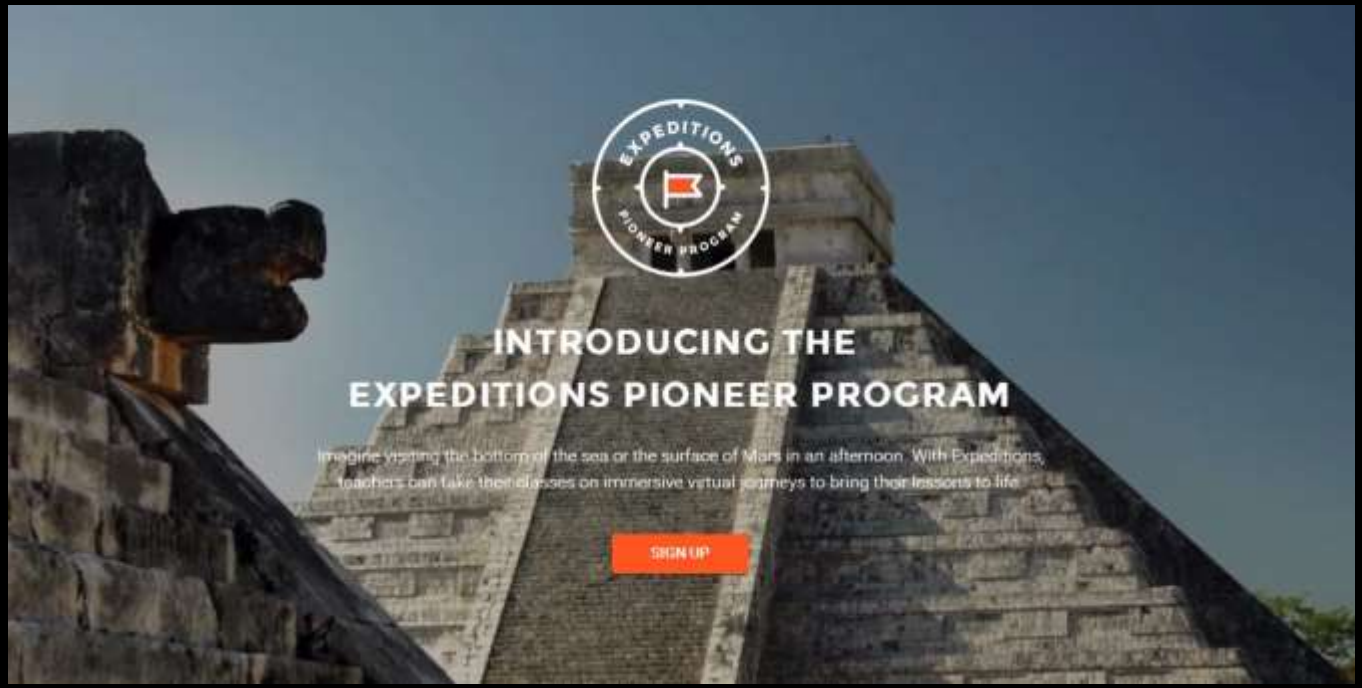
"For severe cases, it can take up to three hours to complete. Not days, not months"

Bringing change to treatment for psychological conditions by letting people face their fears and gradually let them go

VR in Architecture and Construction

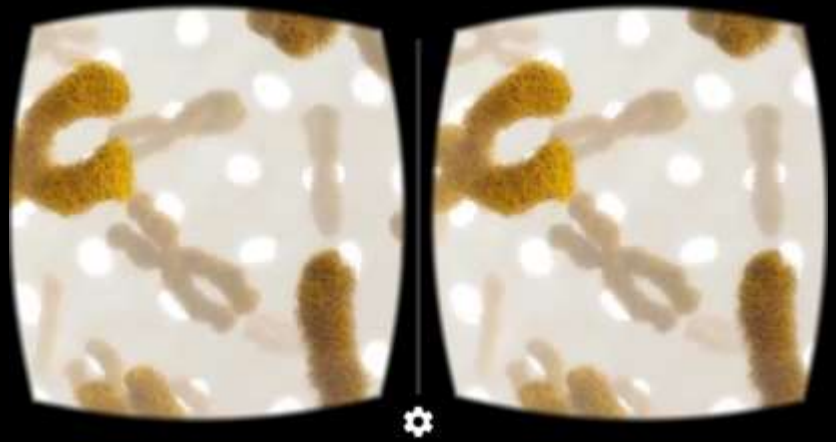
Consumers can expect homes to be viewable before they are built

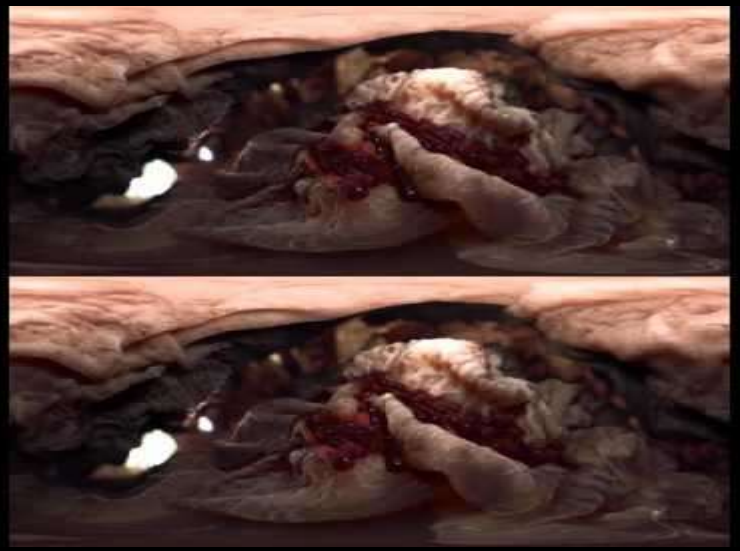
VR in Education



Taking kids where the can’t go

VR in the Human Body





Virtual Reality in Healthcare

participate in an operation through VR.

VR is Everywhere

the Medicine Maker

Reaching into a New Reality

What awaits the intrepid medicine makers who dare to venture into virtual and augmented workspaces?

28 – 37

ENTERING MOLECULES

Drug designers already use molecular visualization tools to help them with their jobs, but virtual reality can take this to a whole new level – while also making you feel like Tom Cruise.

Jonas Boström is a drug designer based in the Department of Medicinal Chemistry at AstraZeneca in Sweden. He has a Masters in Chemistry from Gothenburg University, but has always had a keen

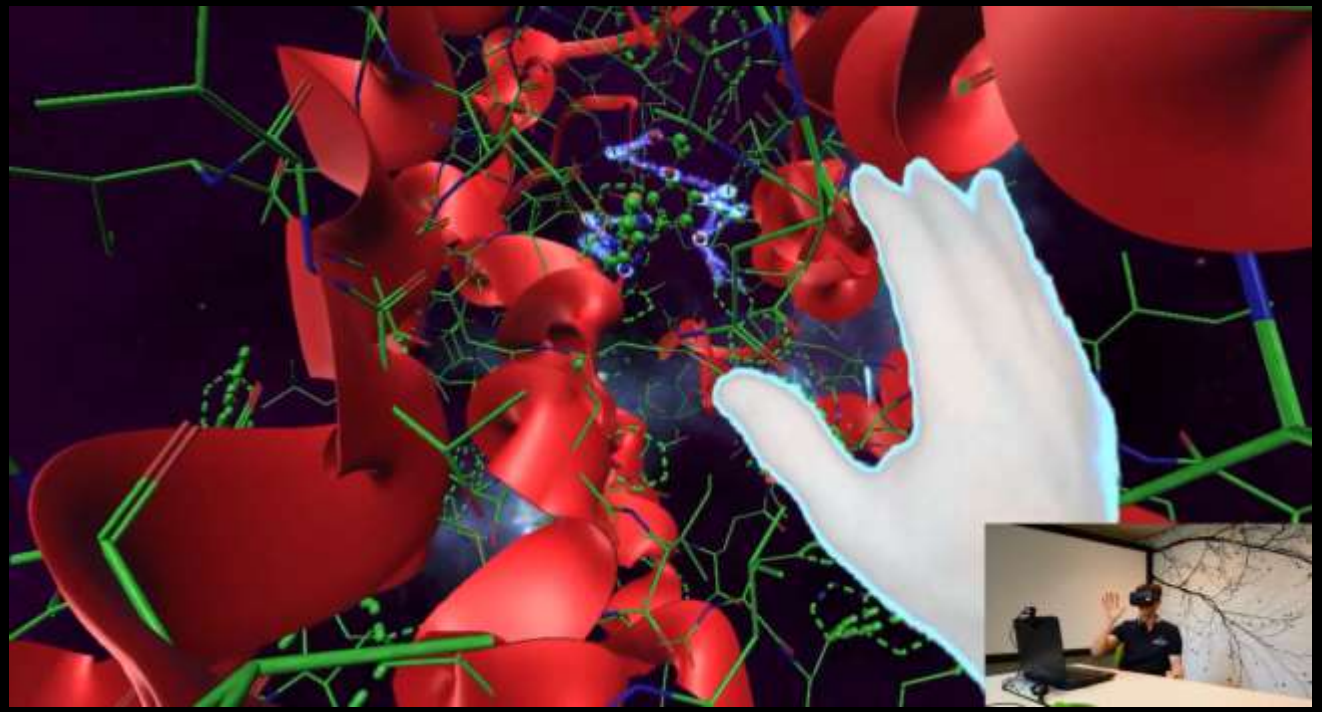
drugs such as aspirin to the famous DNA double helix are 3D objects, which drug designers work with on a daily basis. The first version of Molecular Rift was controlled with the gaming sensor Microsoft Kinect v2 (developed for the Xbox One console), but this wasn't ideal since the Kinect is designed to track a whole body rather than fine finger movements. In version two, we implemented the more advanced Leap Motion sensor, which allowed near perfect accuracy in gesture recognition.

What were the early challenges you faced?

One problem was a supposedly straightforward matter: acquiring the actual hardware. We ended up buying a used (and the last one available on the site) Microsoft Kinect v2 from Amazon in the US – and got a friend of a friend to ship it to us in Sweden. The Oculus Rift goggles were also not easy to get hold of. Technically, it was a challenge to work in a Windows environment, which can be quite

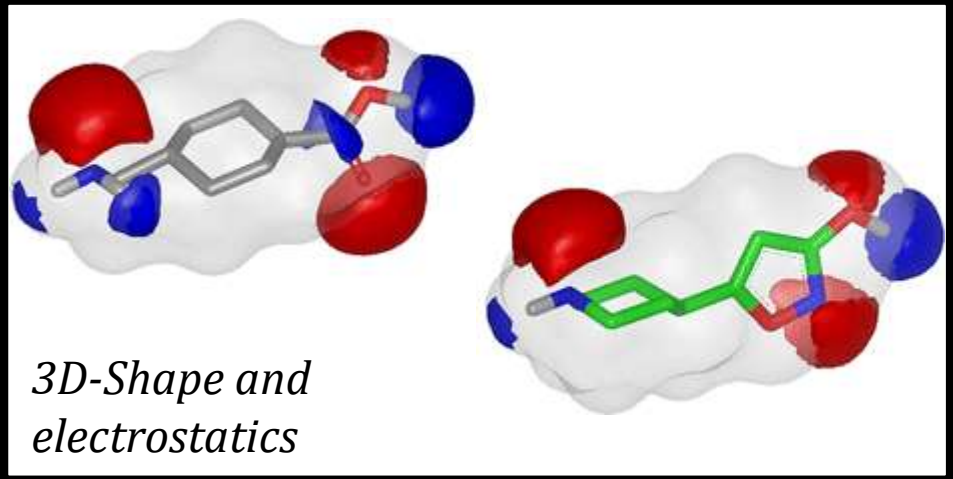
VR also in Drug Discovery @AstraZeneca

VR for Drug Designers – Molecular Rift



Computer-aided Drug Design

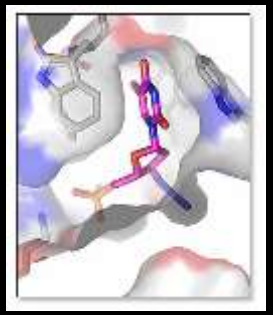
Using data to find patterns



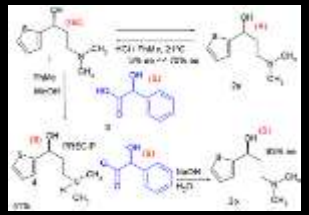
3D-Shape and electrostatics

Generate knowledge for faster and better decisions

Multi-parameter problem



Potency



Chemical synthesis

Solubility
Stability

Team

Patentability

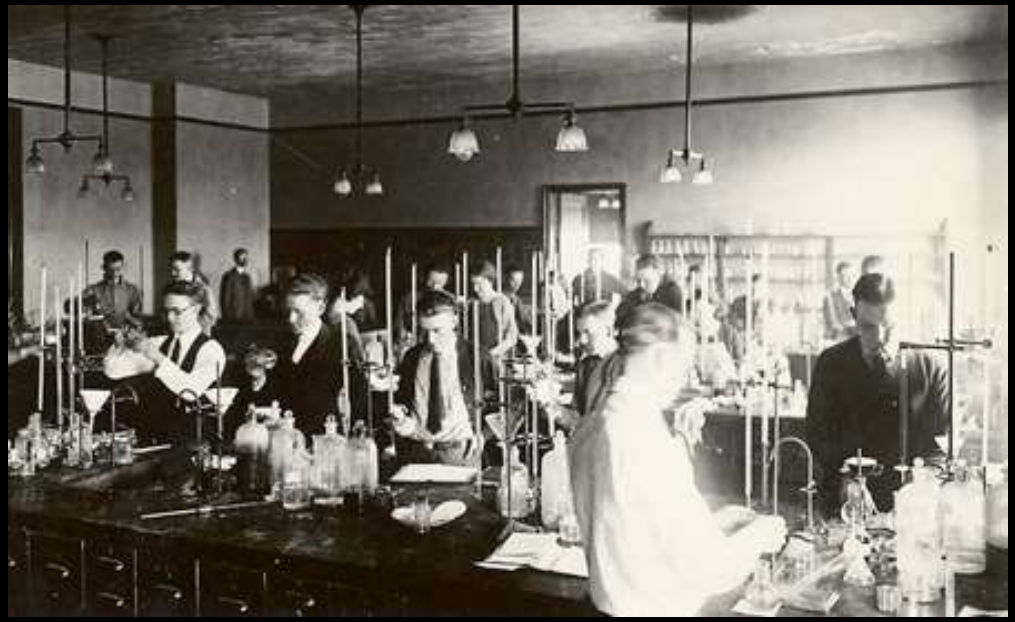
Toxicology

Permeability
Distribution
Metabolism

What we *can* make…

10^{63} molecules: R.S Bohacek *et al. Med Res Rev* 16 (1996) pp. 3–50.
10^{24} molecules: P. Ertl *JCICS* 43 (2003) 374-380.

…given enough time



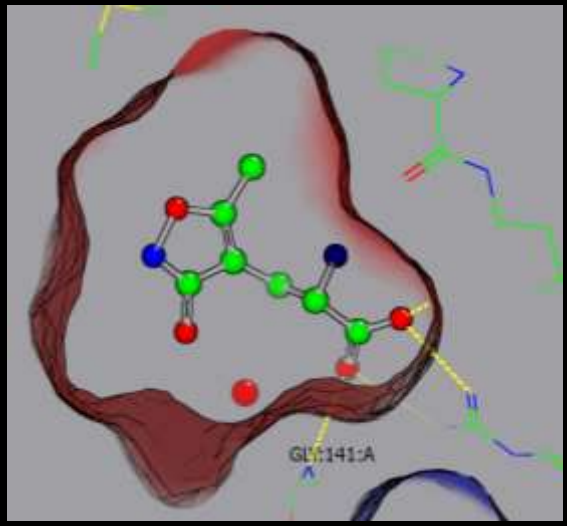
Synthesizing 10^{24} molecules would take

1 000 000 000 000 000 000 years provided…

1000 chemists makes 1000 compounds each per year

We must choose what to make

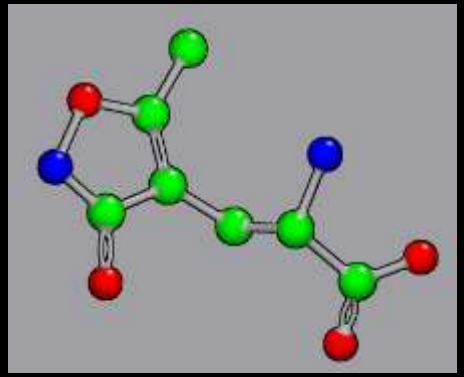
Can predict nothing
Buy more tickets
* Driven by synthesis

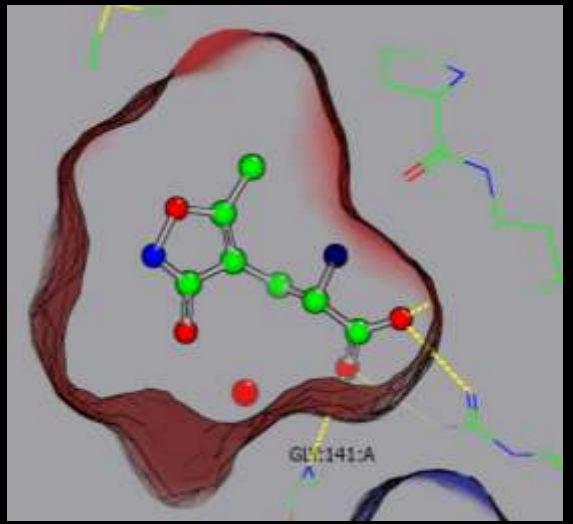


Can predict something
Place bets based on previous knowledge
* Driven by design

Molecules are 3D objects

AMPA

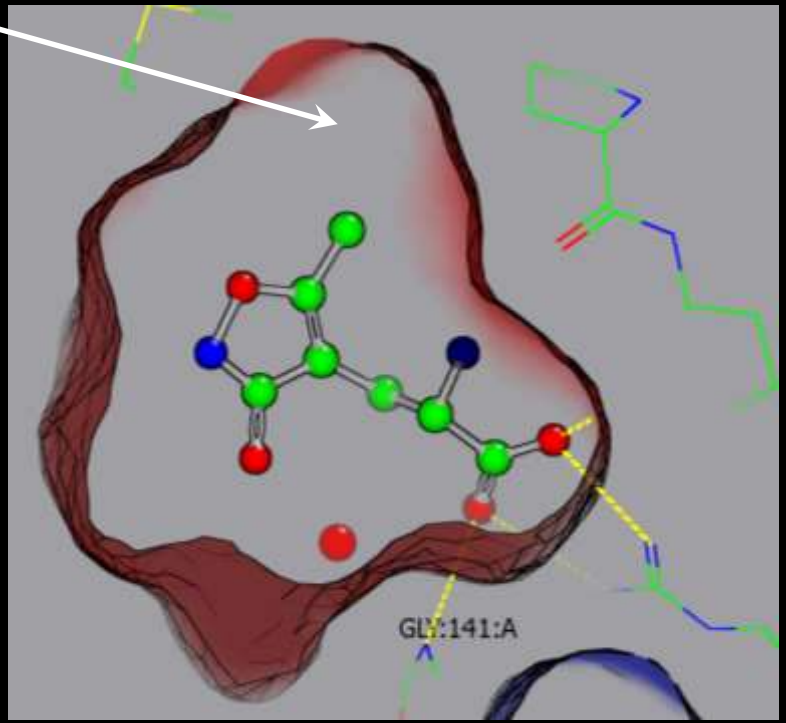




Knowledge about their 3D structure is important in most stages of drug discovery

One Simple SBDD Example

Identify empty space in binding pocket

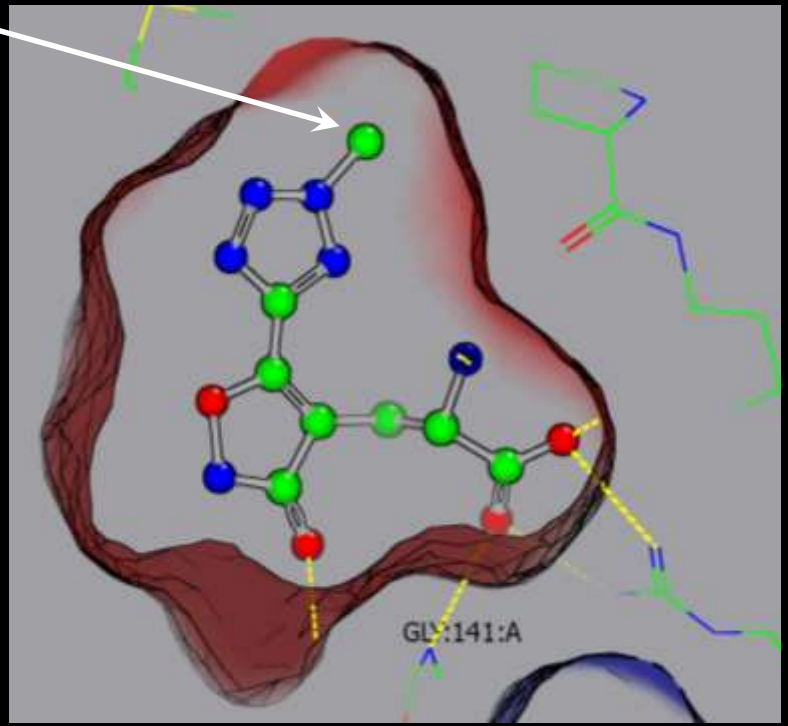


pdb: 1ftm (GLUTAMATE RECEPTOR SUBUNIT 2)

SBDD Review: Anderson, A. C., The Process of Structure-Based Drug Design. Chemistry & Biology 2003, 10, 787-797

One Simple SBDD Example

Fill empty space in binding pocket

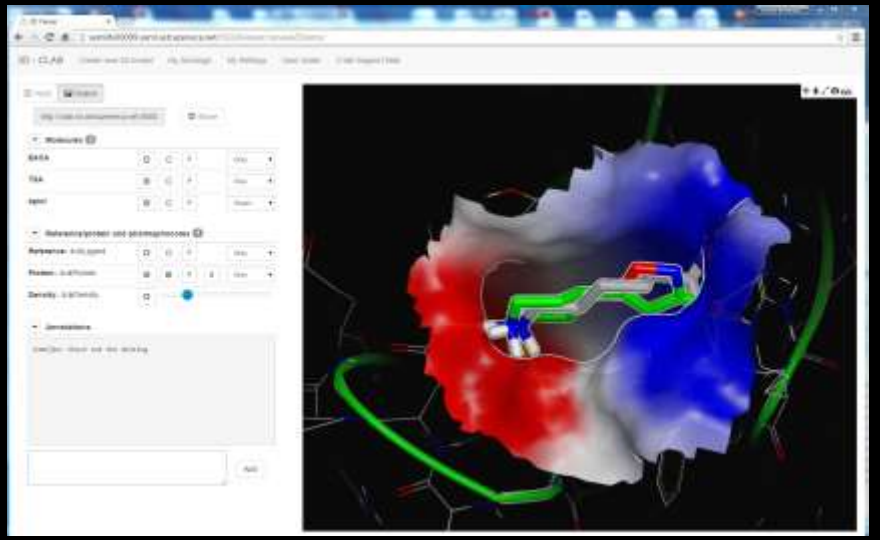


pdb: 1m5b (GLUTAMATE RECEPTOR SUBUNIT 2)

SBDD Review: Anderson, A. C., The Process of Structure-Based Drug Design. Chemistry & Biology 2003, 10, 787-797

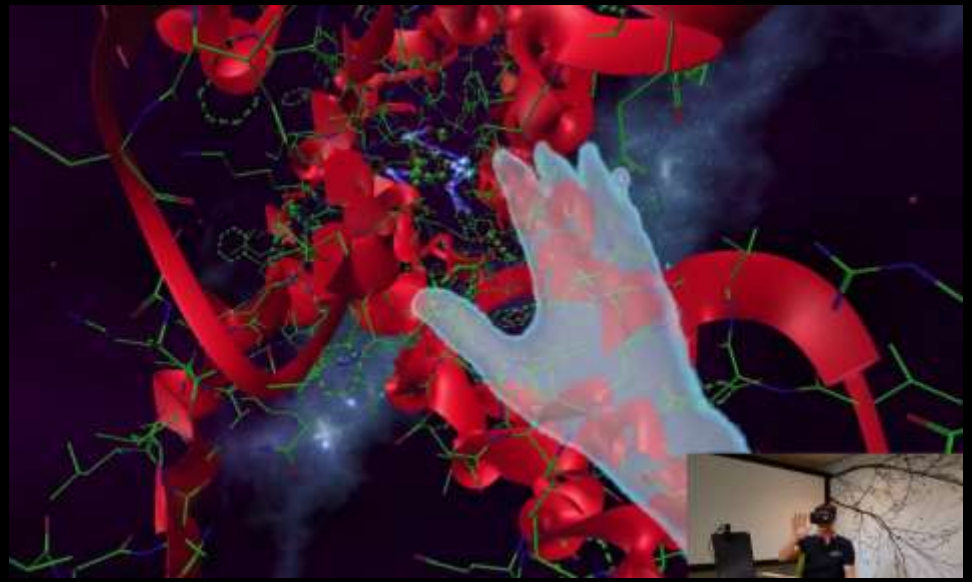
3D Molecular Tools

With the rise of efficient computers, the focus switched from physical representations to computer generated models.

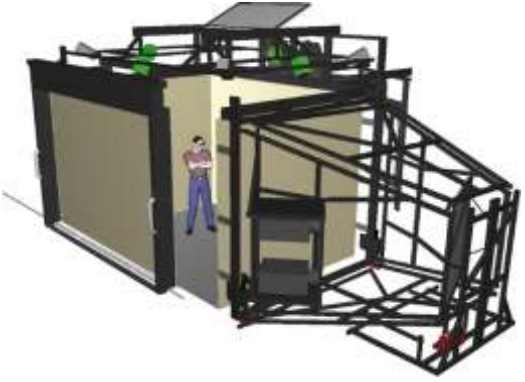


an important innovation here was the ability to display stereoscopic 3D views.

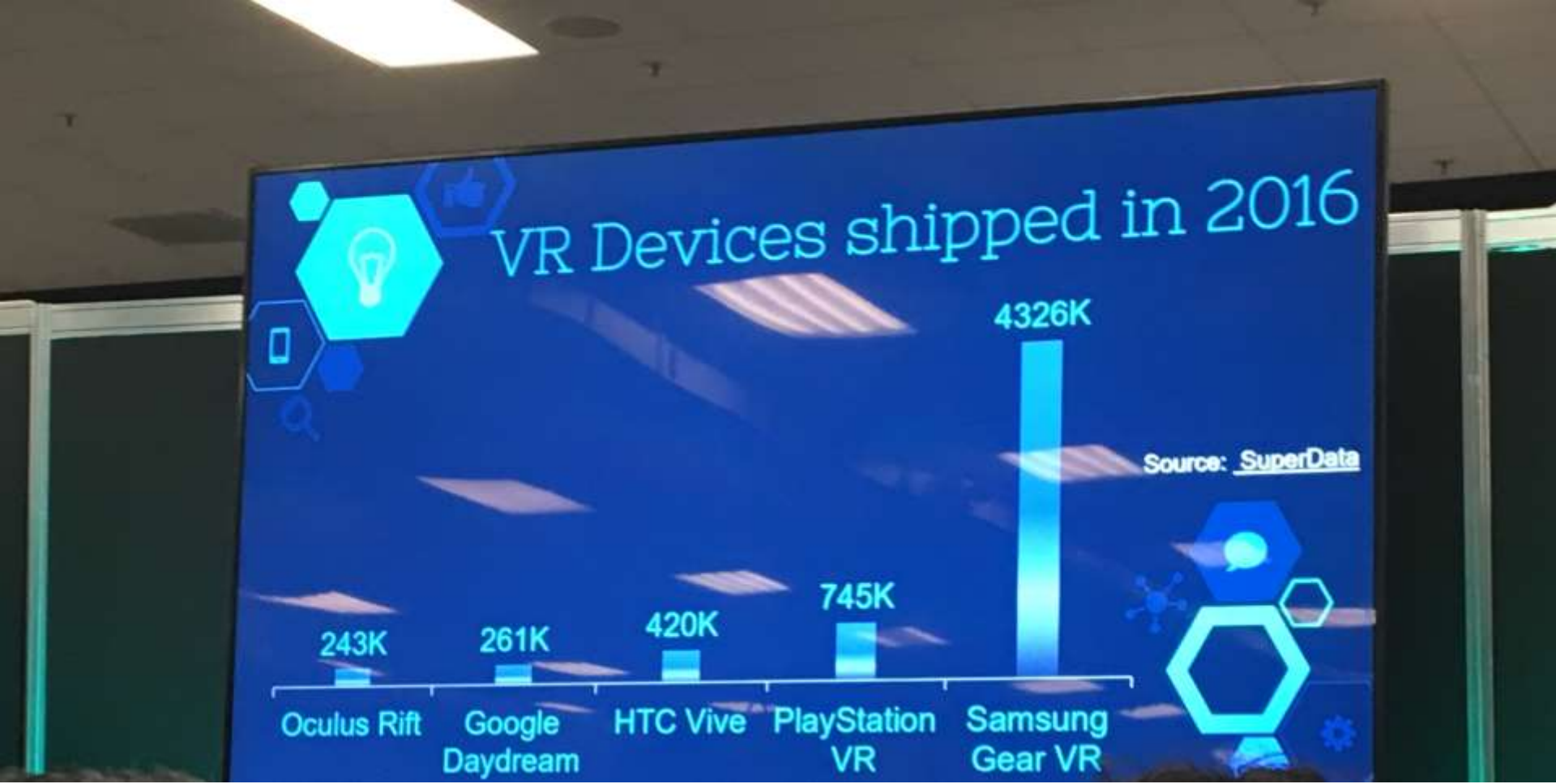
Virtual reality for Drug Designers



Virtual reality tools…

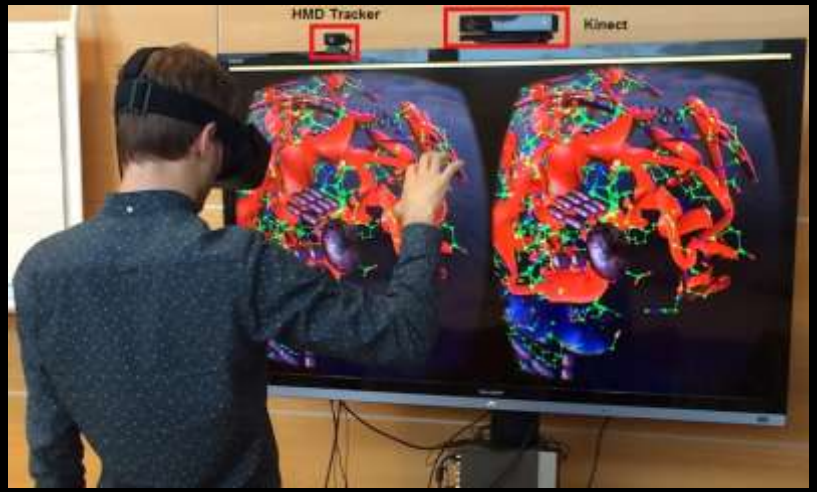


CAVEs, Head-Mounted Devices to smartphone apps using simple Google Cardboard.


VR Devices shipped in 2016
4326K
Source: SuperData
745K
420K
261K
243K
Oculus Rift
Google Daydream
HTC Vive
PlayStation VR
Samsung Gear VR

Gesture-Based Interactions

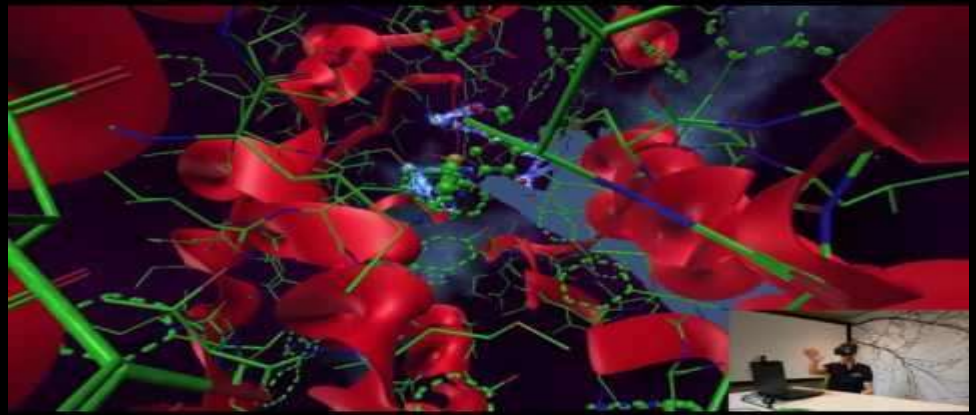
Oculus Rift

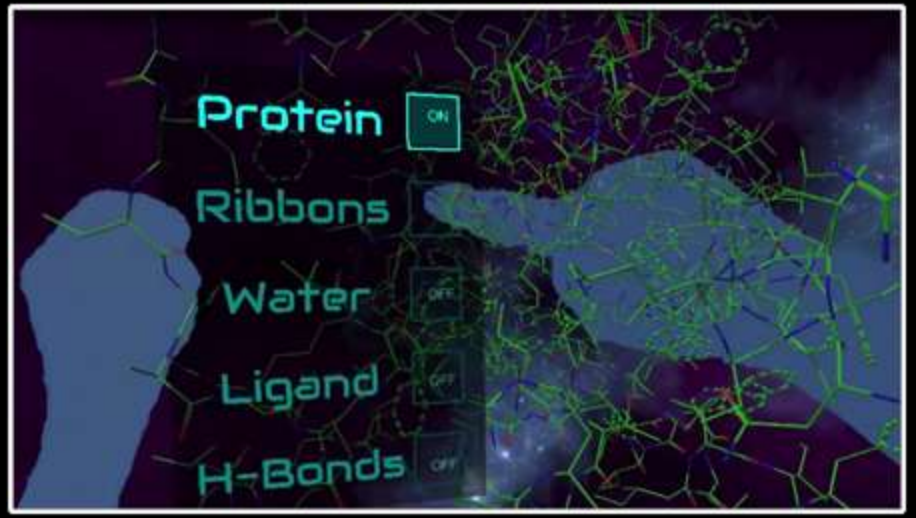


Molecular Rift v1
MS Kinect (X-box)

Molecular Rift v2
Leap Motion and controller

In-game menu





Start Menu

Graphical Representations

Built from scratch, using the game-engine Unity

Objects (atom, bonds, etc) are rendered from coordinates
parsing pdb, sdf, mol2

Small molecule representations:
lines, ball-and-stick, stick, CPK

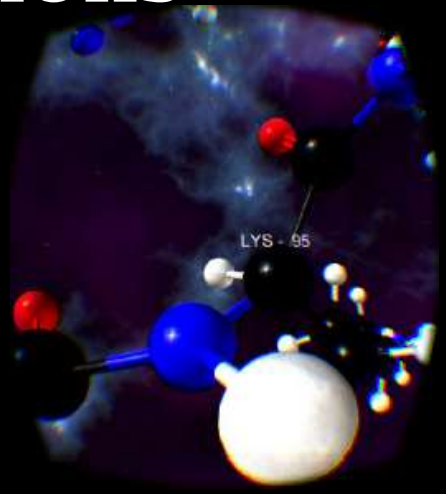
Creating protein/DNA ribbons

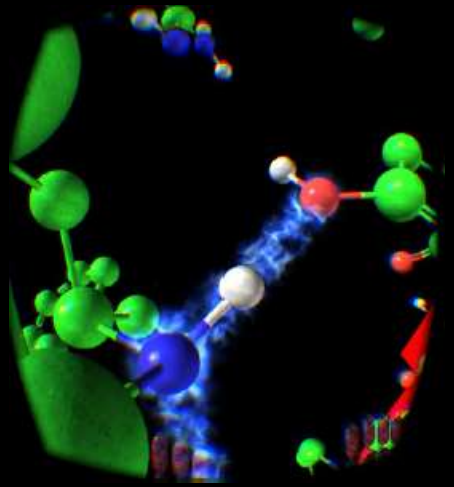
Intermolecular H-bonds

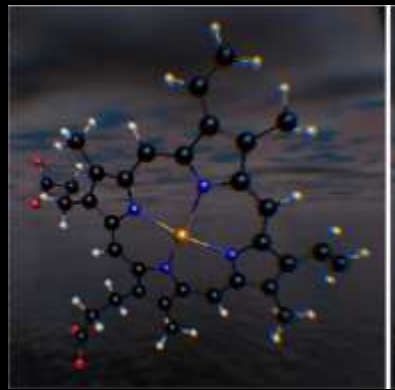
Residues can be labeled

Pharmacophore objects

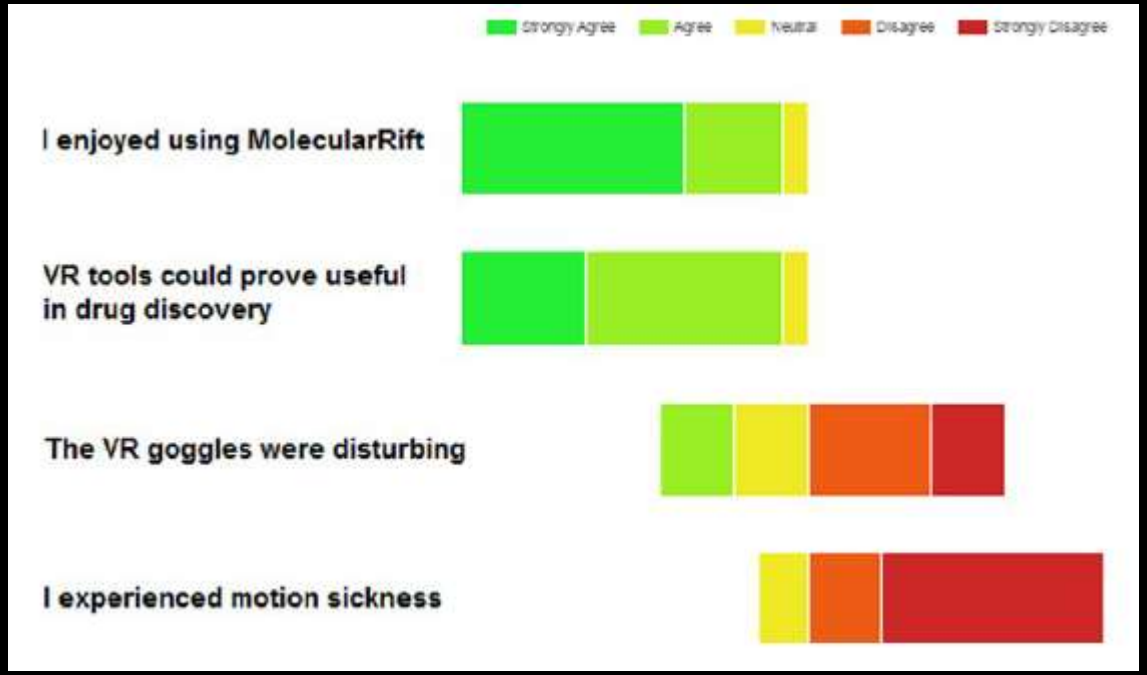
Coloring schemes







Focus groups



red is good [here]

Prominent testers

H.M. King Carl XVI Gustaf, The Sports Minister of Chile, The Executive Vice President at AstraZeneca, The Head of Business Development at EA Sports, The Crown Princess of Sweden, Swedish power elite …

Some Details

Oculus Rift goggles are used to create to the VR environment.

Gesture recognition (interaction)
- *Leap Motion (v2), MS Kinect (v1),*

Development: game engine Unity, Leap Motion SDK, Oculus Runtime, MS Kinect v2, and open source cheminformatics tool-kit integrated: openbabel.

Programming: mainly C#

Code available on GitHub
– open source under the GPLv3 license

People and papers

Magnus Norrby, Master Student
Jonatan Enström, Student
Christoph Grebner, Post-Doc

CHEMICAL INFORMATION AND MODELING

Article

Molecular Rift: Virtual Reality for Drug Designers

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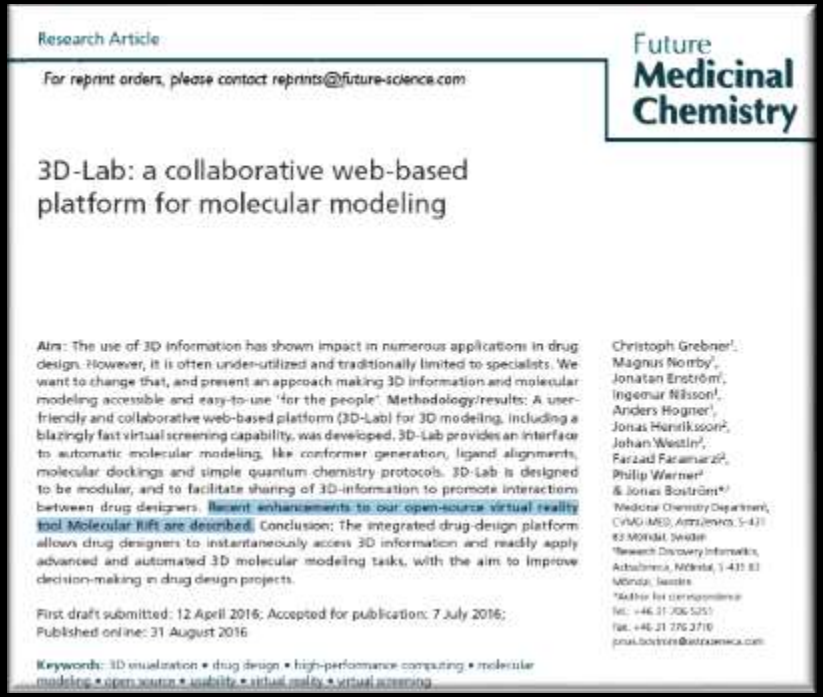
Supporting Information

ABSTRACT: Recent advances in interaction design have created new ways to use computers. One example is the ability to create enhanced 3D environments that simulate physical presence in the real world—a virtual reality. This is relevant to drug discovery since molecular models are frequently used to obtain deeper understandings of, say, ligand−protein complexes. We have developed a tool (Molecular Rift), which creates a virtual reality environment steered with hand movements. Oculus Rift, a head-mounted display, is used to create the virtual settings. The program is controlled by gesture-recognition, using the gaming sensor MS Kinect v2, eliminating the need for standard input devices. The Open Babel toolkit was integrated to provide access to powerful chemoinformatics functions. Molecular Rift was developed with a focus on usability, including iterative test-group



Research Article

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Future Medicinal Chemistry

3D-Lab: a collaborative web-based platform for molecular modeling

Aim: The use of 3D information has shown impact in numerous applications in drug design. However, it is often under-utilized and traditionally limited to specialists. We want to change that, and present an approach making 3D information and molecular modeling accessible and easy-to-use 'for the people'. **Methodology/results:** A user-friendly and collaborative web-based platform (3D-Lab) for 3D modeling, including a blazingly fast virtual screening capability, was developed. 3D-Lab provides an interface to automatic molecular modeling, like conformer generation, ligand alignments, molecular dockings and simple quantum chemistry protocols. 3D-Lab is designed to be modular, and to facilitate sharing of 3D-information to promote interactions between drug designers. Recent enhancements to our open-source virtual reality tool Molecular Rift are described. **Conclusion:** The integrated drug-design platform allows drug designers to instantaneously access 3D information and readily apply advanced and automated 3D molecular modeling tasks, with the aim to improve decision-making in drug design projects.

First draft submitted: 12 April 2016; Accepted for publication: 7 July 2016; Published online: 31 August 2016

Keywords: 3D visualization • drug design • high-performance computing • molecular modeling • open source • usability • virtual reality • virtual screening

Christoph Grebner[1], Magnus Norrby[1], Jonatan Enström[1], Ingemar Nilsson[1], Anders Hogner[1], Jonas Henriksson[2], Johan Westin[2], Farzad Faramarzi[2], Philip Werner[1] & Jonas Boström*[1]

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VR ”for the people” – smartphones

Mobile apps enables VR experiences without having to invest into extensive systems.

Does not need a high-end PC to run applications.

It’s truly mobile (no wires)

Hardware is cheap, if not ‘free’

(most people already have a smartphone).

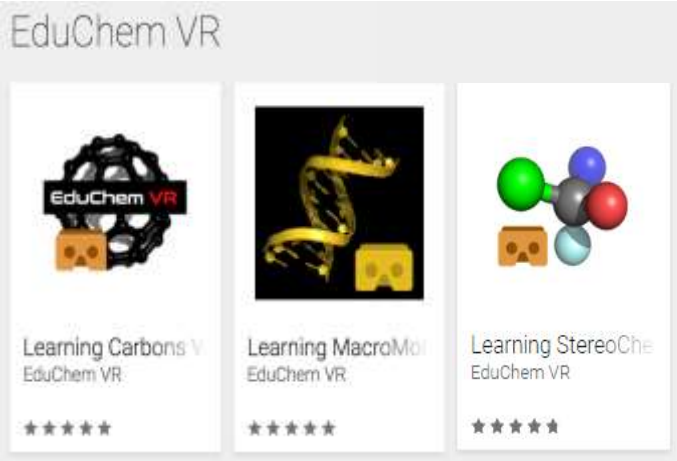
Performant

Google Daydream, Samsung GearVR

VR Smartphone apps

Cardboard VR apps (Android och iPhone): carbon forms, macromolecules and stereochemistry

Web VR platform: concepts like atom orbitals, hybridization, stereochemistry, geometries and reaction mechanisms



Cardboards
(apps and webVR)

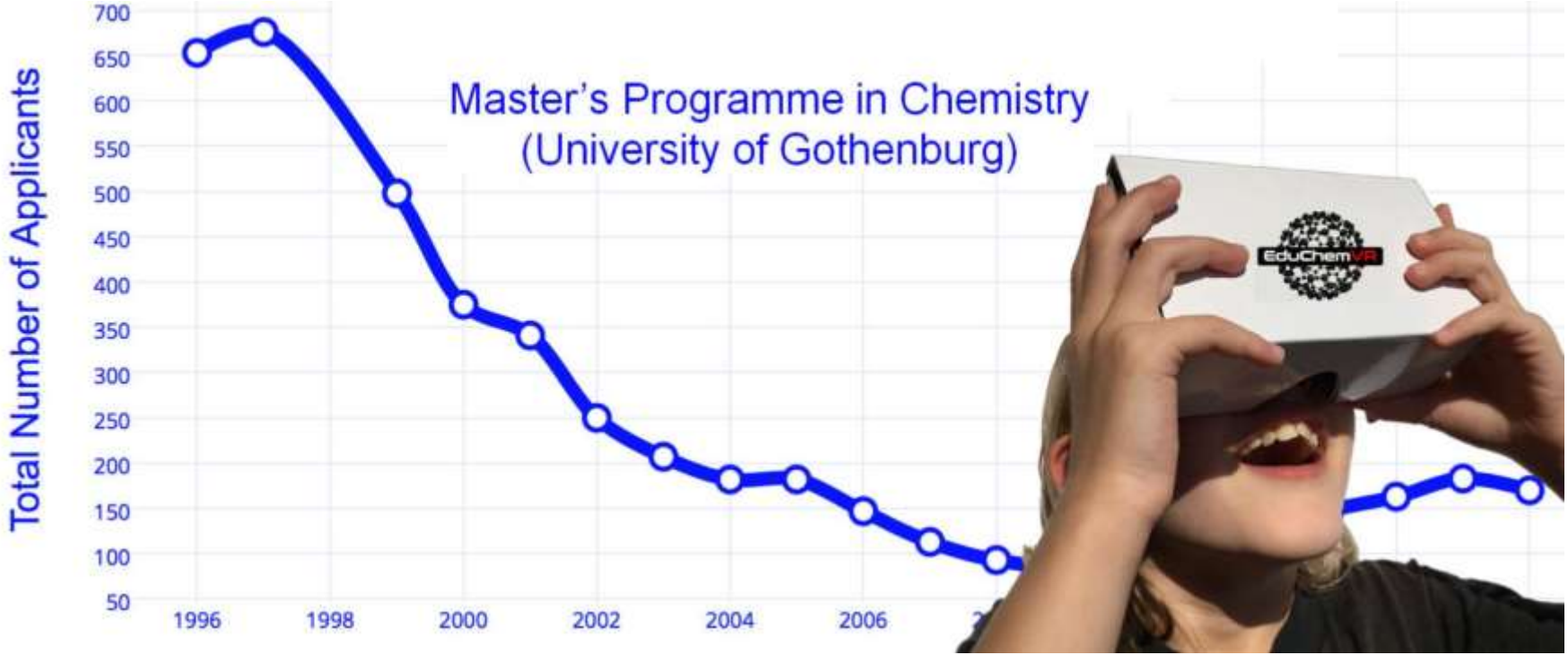
“Chemistry VR”
Samsung GearVR

“Chemistry WebVR”
in the browser

VR in Chemistry Education*

Vision is to engage more students in chemistry using virtual reality.

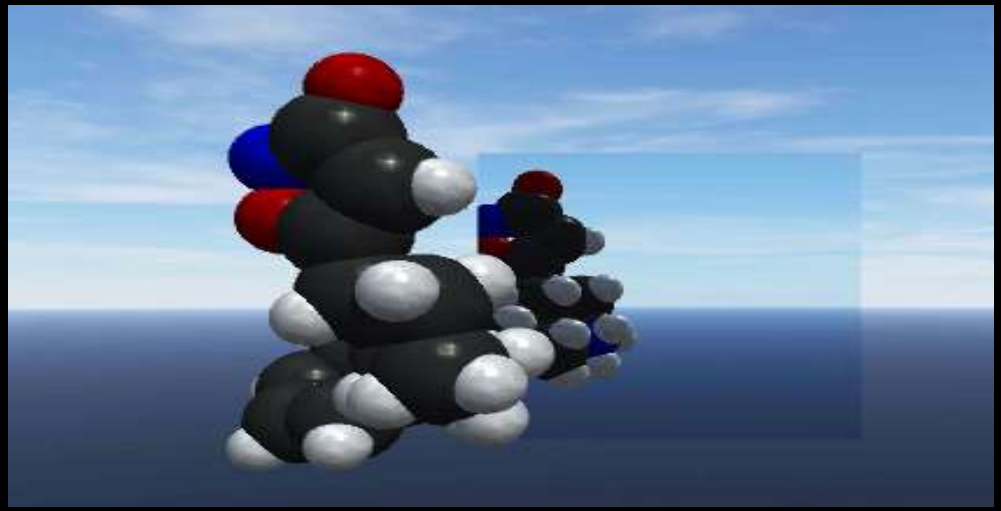
Giving us more drug designers?

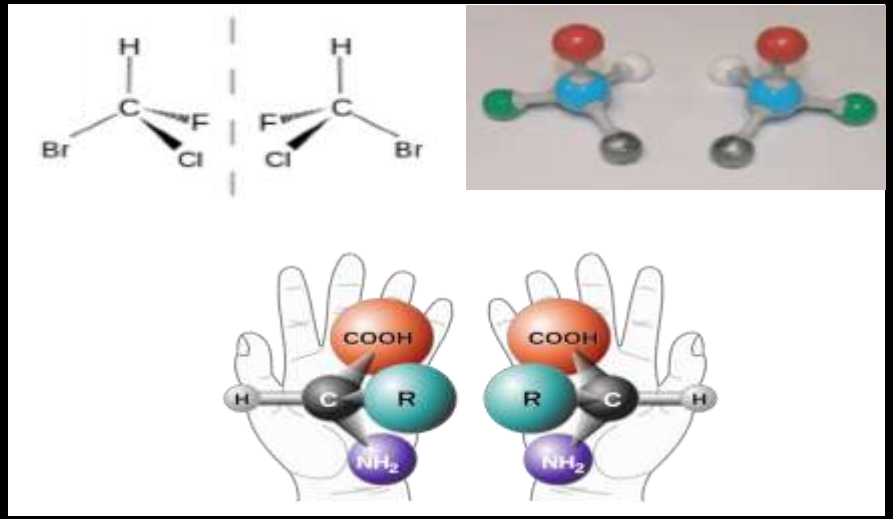


* A former student and I started a separate EdTech VR Company last year: www.educhem-vr.com

Use-Case and Benefits

Virtual Reality experience more efficient and better for learning?





"StereoChemistry is just one concept which is difficult to explain with paper&pen/white-board. It can take a day to put up such an exercise using traditional methods. With your VR apps this is instant and the technology is applicable in all our courses." Ass Prof C-J Wallentin

The Future of VR in Drug Design

Mixed/Augmented Reality?

Drug is team work -> to multi-player

”Wow!” effect not as strong

Voice recognition

There are other VR tool than ours of course
MolDRIVE/Reality Cube, VMD, UnityMol, ChemPreview, Nano-one, A/V Lab …

Nanome Inc.

Advanced Virtual Reality Tools for Scientific Research and Development

www.Nanome.ai

Virtual Reality in Drug Discovery

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