User as a bitter tastant: Immersive experience within the binding region of a bitter taste receptor

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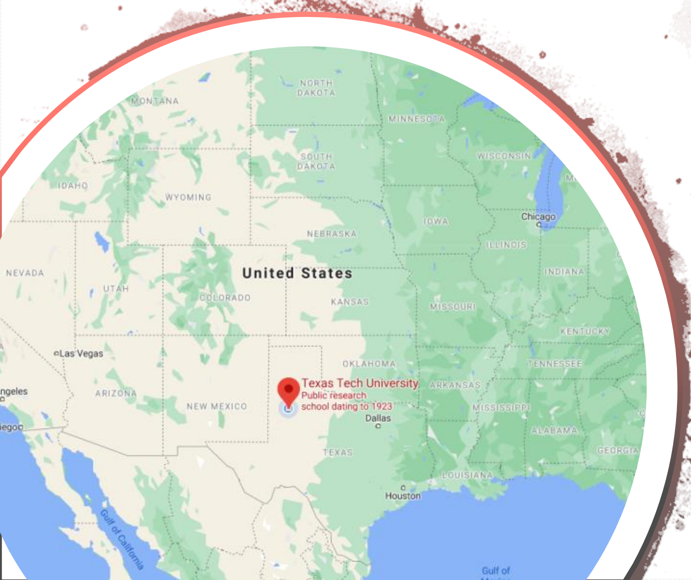

Thursday, September 17, 2020

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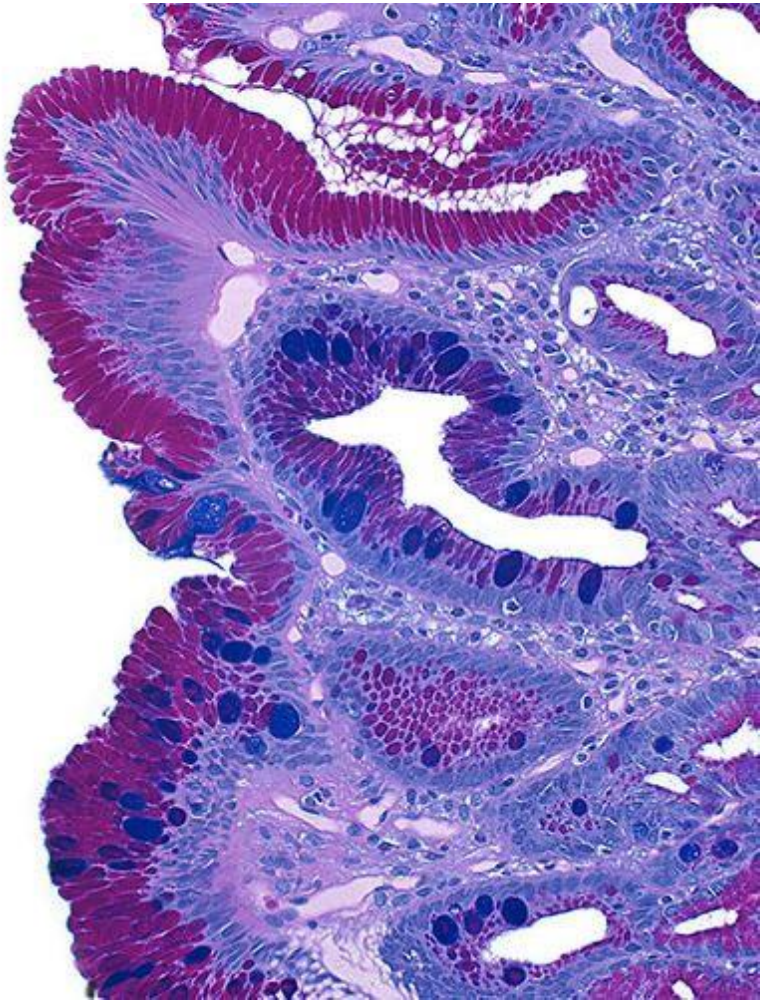


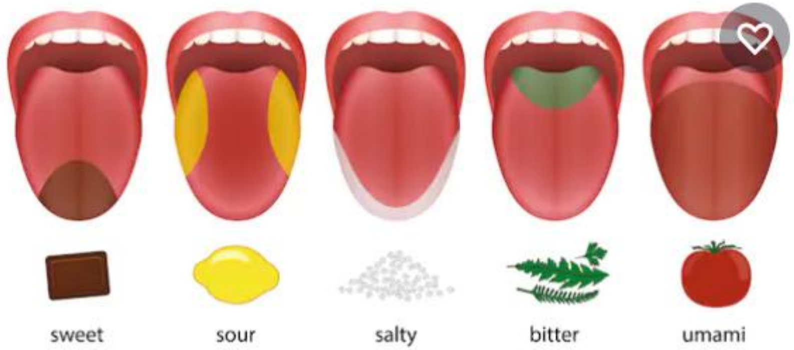
Description of the Challenge

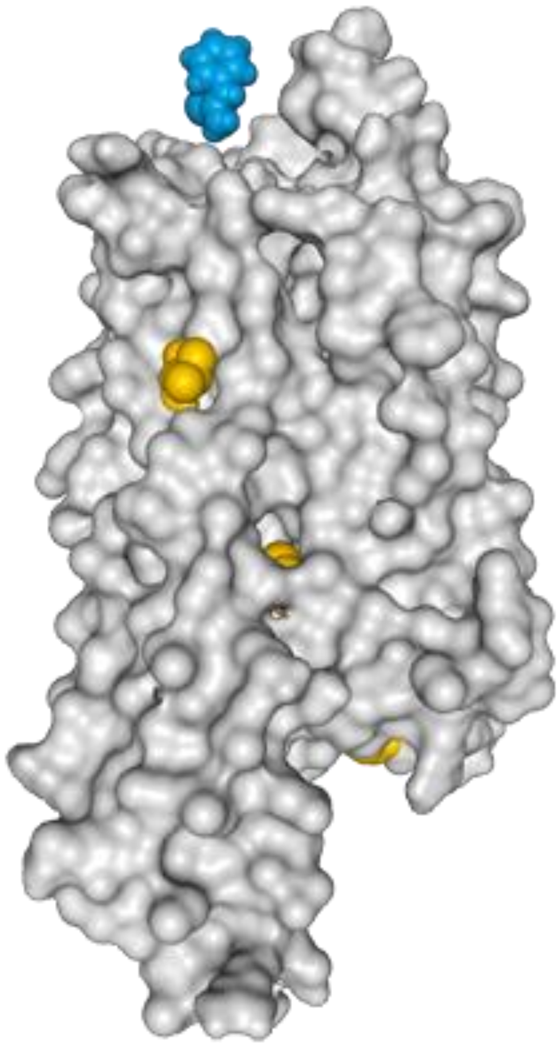
- IT-based instruction is becoming increasingly popular in the STEM disciplines.
- The primary drawback is its limited use and lack of availability, especially in disciplines far removed such from Computer Science, such as, the biosciences
  - *The mechanism of how biomolecules perform their function is a black-box*
  - *This is especially true for students who lack spatial-cognitive abilities*
- Approaches to tackle the issues
  - *Building computational structures of biomolecules*
  - *Leveraging Virtual Reality to facilitate virtual interactions with these biomolecules*

https://www.pinterest.com/pin/341569952963997840/?nic_v2=1a4nshLFB

The Perception of Taste– an Introduction

- The sense of taste allows us the ability to evaluate what we consume
  - *taste is strongly associated with smell*
  - *the hedonism associated with a good taste*
  - *thus preventing the consumption of potential toxins*
- Human can perceive five basic tastes.
  - *Sweet*
  - *Bitter*
  - *Salty*
  - *Sour*
  - *Umami*
- The sense of taste is mediated by taste receptor cells organized within taste buds





Taste receptor interactions with bitter tastants

- Very little is understood about the nature of bitter taste and how molecules that elicit the bitter taste respond interact with these receptors.
- These receptors interact with bitter tastants; this then sends a signal to the olfactory and taste sensory processing part of the brain.
- This results in the perception of bitter taste

http://svt.enseigne.ac-lyon.fr/spip/spip.php?article367

VR as a tool of instruction and research

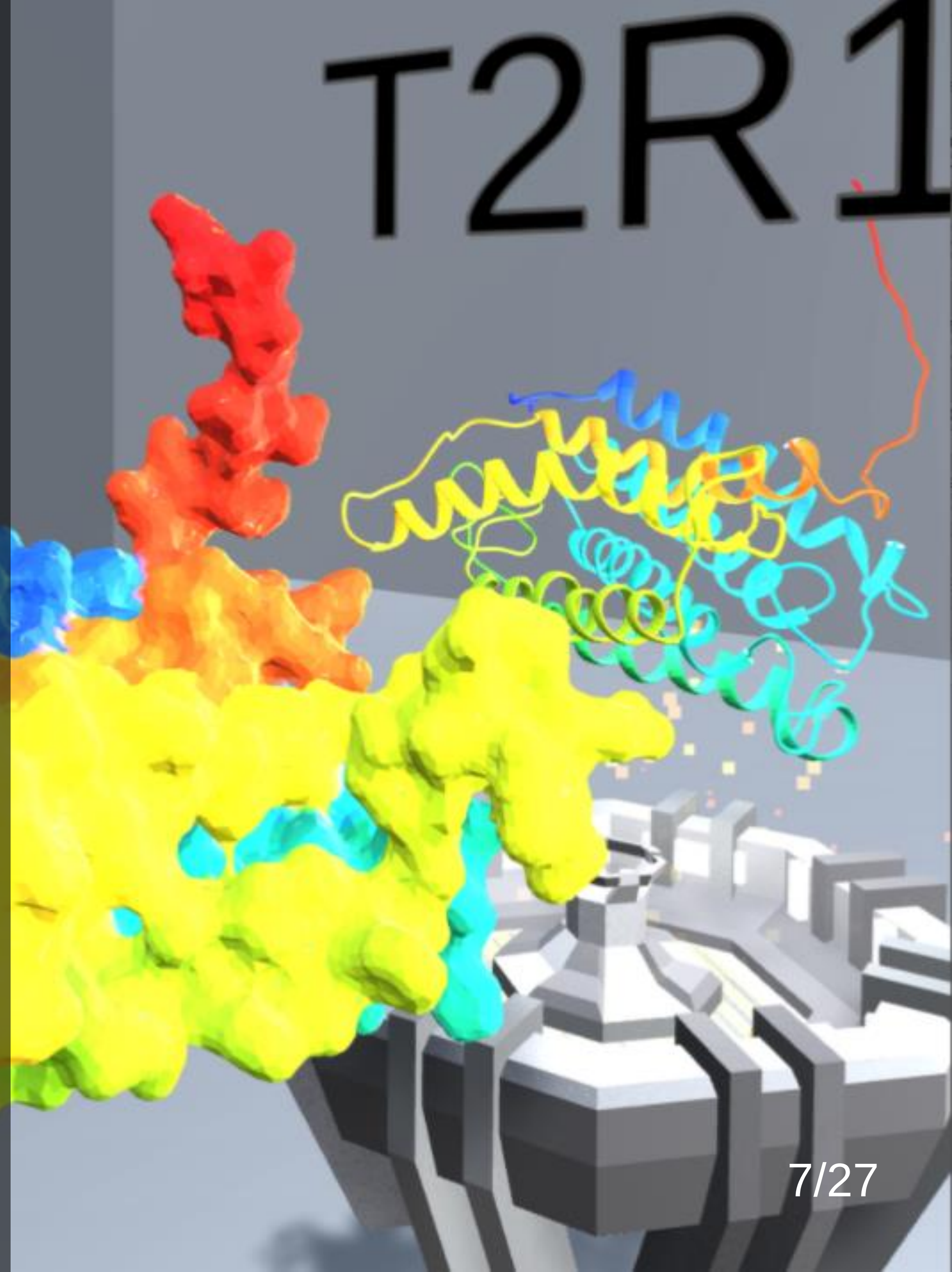
By introducing VR in the domain of the chemical senses:

Students and researchers will gain novel and mechanistic perspectives into what the bitter tastant experiences in terms of the inside of the receptor, with which interact, prior to eliciting the perception of bitter taste

Motivation

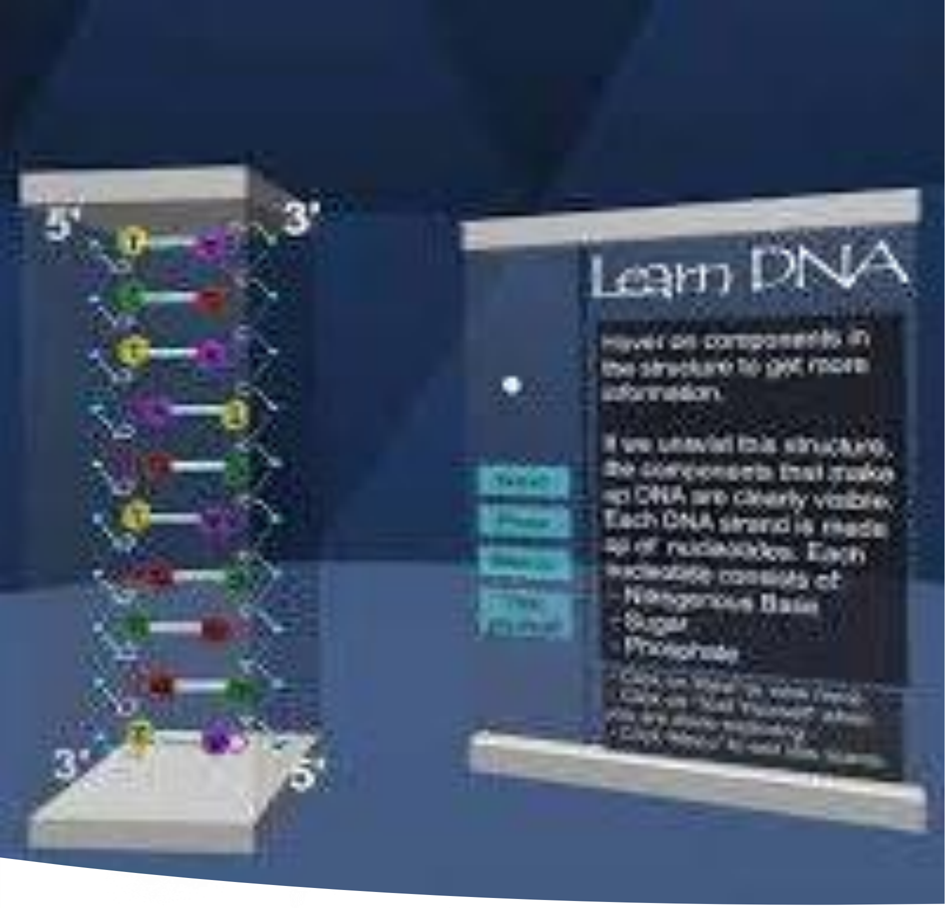
Motivated by the advancement and increasing use of VR in biological settings, and because of a lack of 3D models for taste receptor, particularly for bitter taste receptor. We made the following contributions:

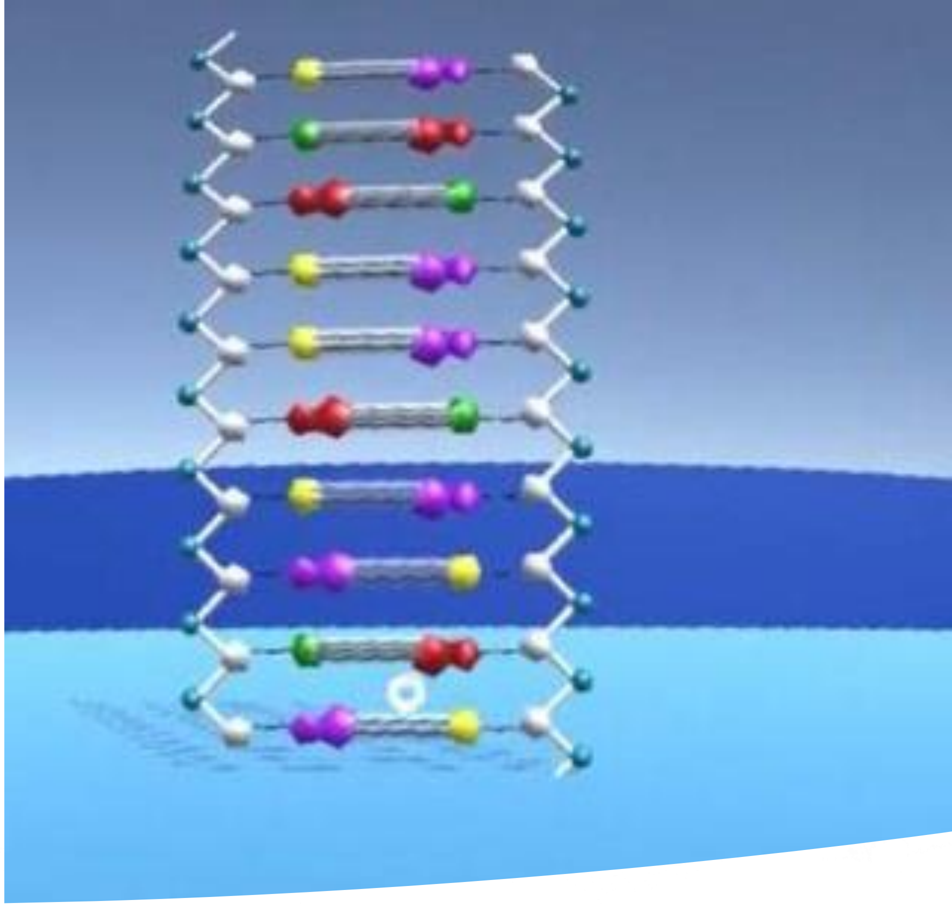
- *Developed 15 computational models of bitter taste receptors*
- *Transformed the computational models to 3D constructs leveraged for VR*
- *Incorporated the models in the VR setting*
- *Tested our system for efficacy and usability*



Related Work

- VR has been used in the biological setting to help scientists to design drug-like ligands with higher efficacy and lower toxicity (side-effects).
- Tse et al. (2001) incorporated VR to facilitate drug discovery

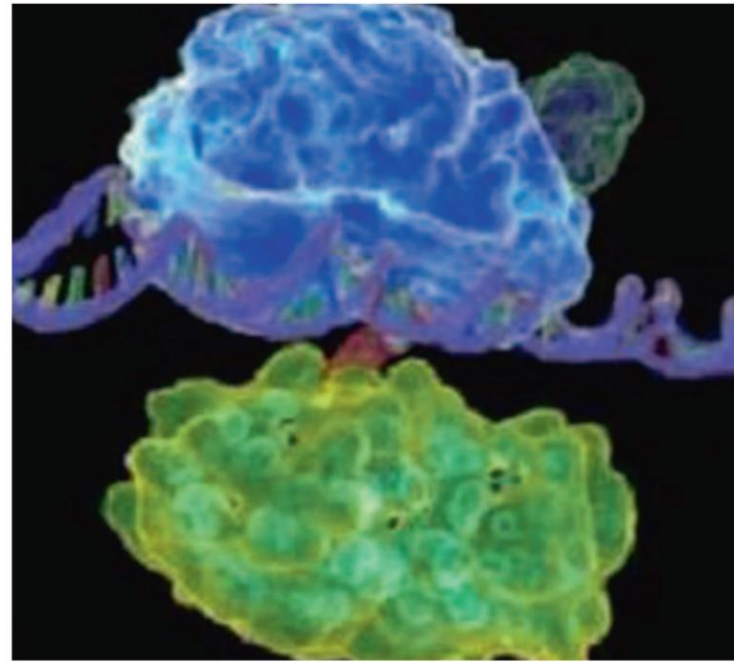




Related Work

Sharma et al. (2016) proposed an immersive VR application for teaching students to understand the complex concept of DNA structure

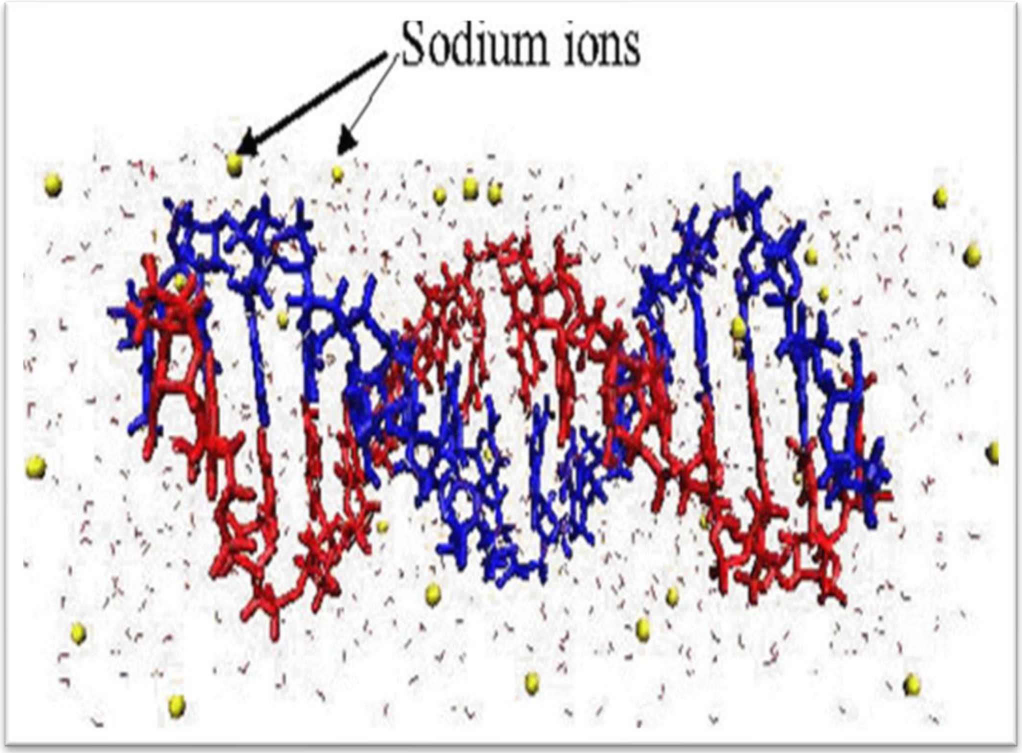
Sharma et al. (2018, April). LearnDNA: an interactive VR application for learning DNA structure. In *Proceedings of the 3rd International Workshop on Interactive and Spatial Computing* (pp. 80-87).

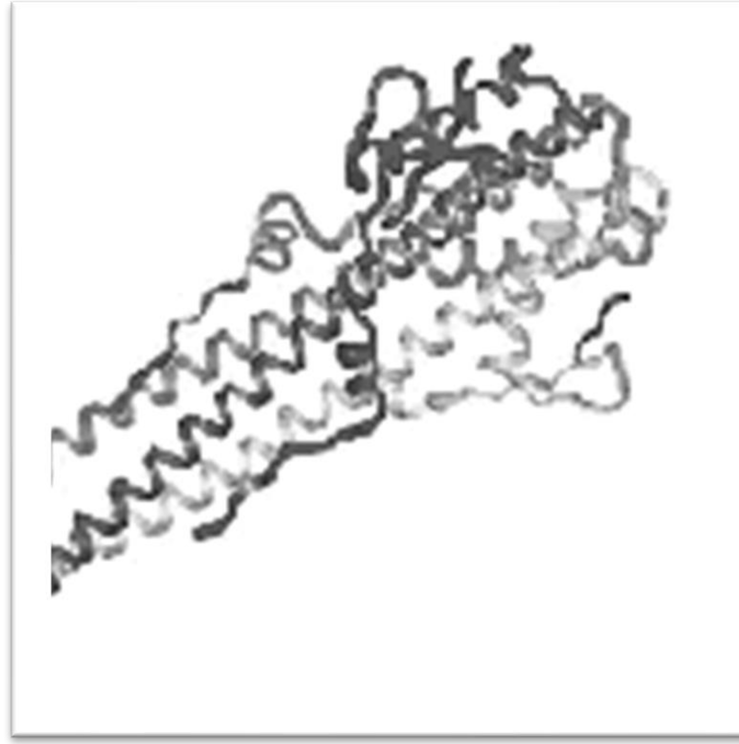


Related Work

Tan and Waugh (2013) developed 3D models of molecules and embedded them into the VR environment

Tan, S., & Waugh, R. (2013). Use of virtual-reality in teaching and learning molecular biology. In 3D immersive and interactive learning (pp. 17-43). Springer, Singapore.





Related Work

Hamdi and Ferreira (2006) presented a molecular mechanics study using molecular dynamics simulations

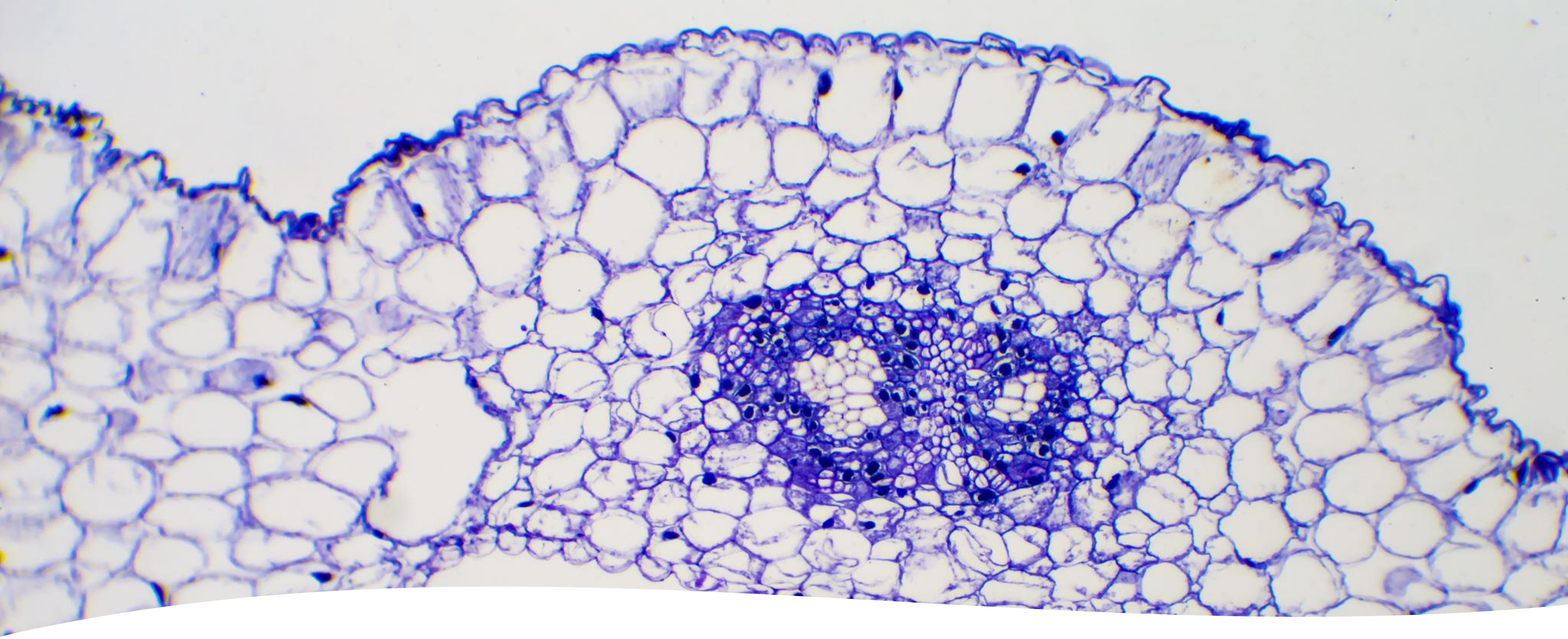
Hamdi, M., & Ferreira, A. (2006, October). DNA-based Bio-Nanorobotic Components using VR-Enhanced CAD Design. In 2006 IEEE/RSJ International Conference on Intelligent Robots and Systems (pp. 1921-1926). IEEE.

Related Work

- There is increased use of VR technologies in the biomedical sciences.

- The potential molecular elements that need to be studied, especially in the context of the domain of study, are however, vast and not covered by the current technology.

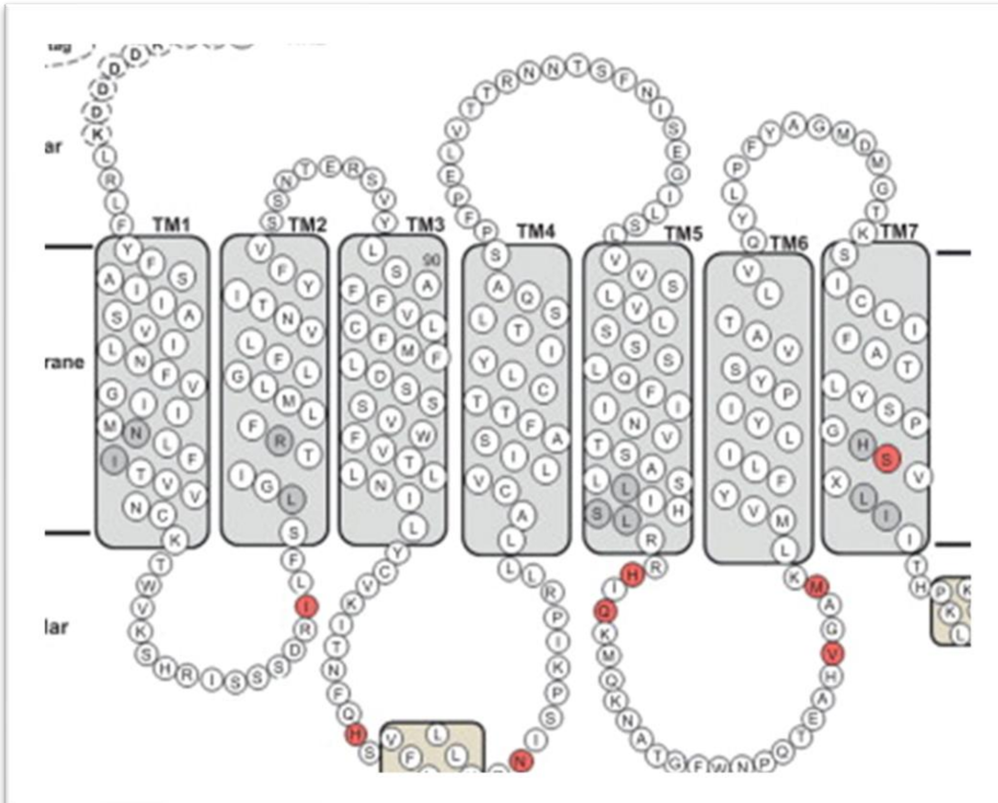
- Indeed, our work does not replace existing work but reinforces this application in the domain of education.



Materials and Methods

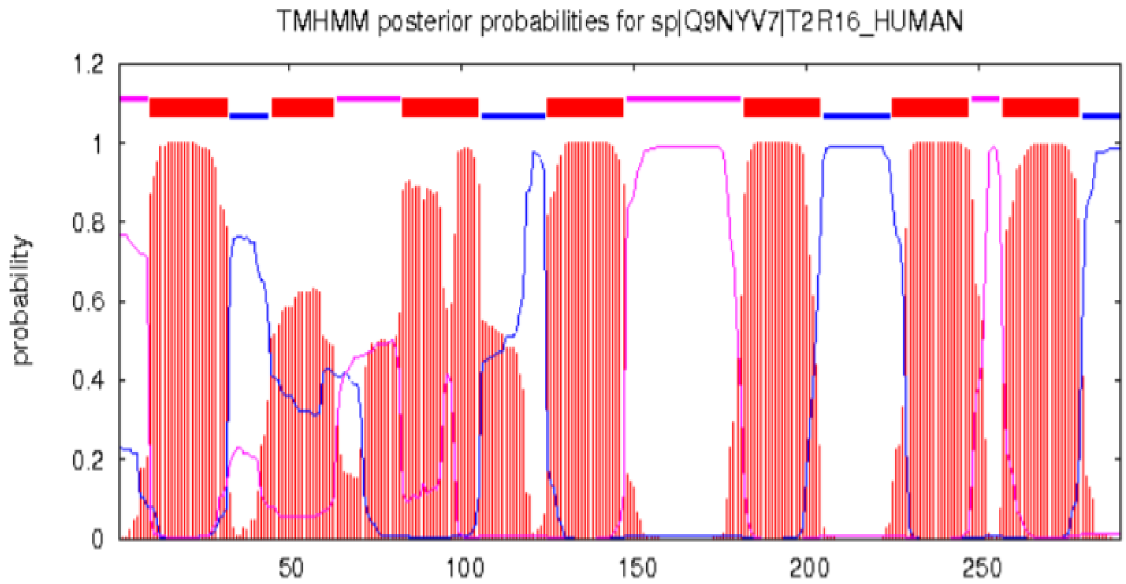
- One of the most challenging parts of our work was to produce 3D models for taste receptors
- These proteins are bound within the cell membrane and are typically difficult to purify and crystallize.
- This explains the lack of an experimentally derived structure (such as from x-ray crystallography) for these receptors

Bitter Taste Receptor Model Building



- The accompanying figure is a conceptual structure of a bitter taste receptor.
- The protein structure consists of seven helical domains, which bridge the cell wall and are embedded in the plasma membrane of the cell
- The helical regions (shown as bars) are connected by loops, which are proteins regions which do not have fixed structures

Bitter Taste Receptor Model Building



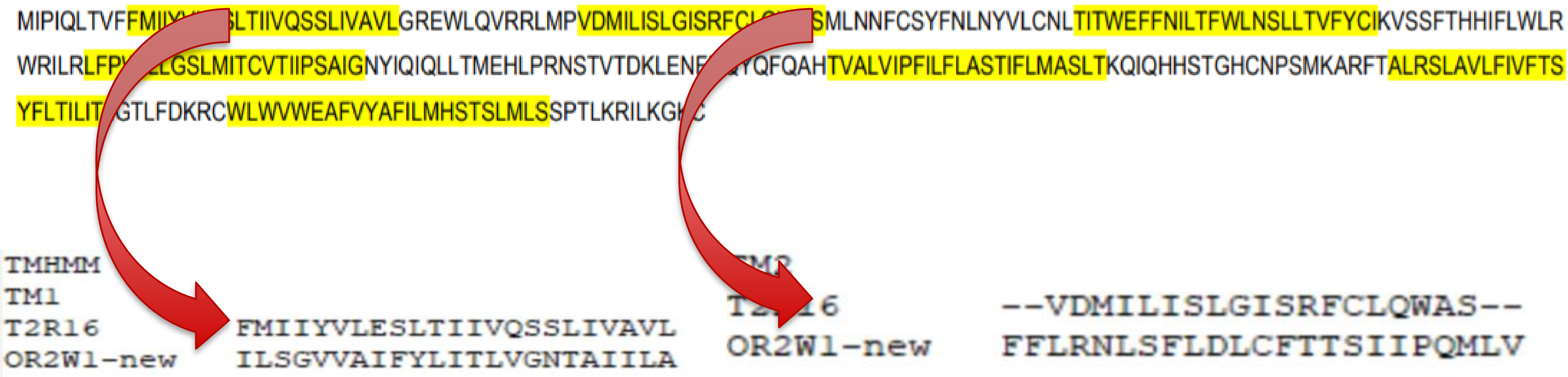
MIPIQLTVFFMIIYVLESLTIIVQSSLIVAVLGREWLQVRRLMPVDMILISLGISRFCLQWASMLNNFCSYFNLNYVLCNLTITWEFFNILTFWLNSLLTVFYCIKVSSFTHHIFLWLR

WRILRLFPWILLGSLMITCVTIIPSAIGNYIQIQLLTMEHLPRNSTVTDKLENFHQYQFQAHTVALVIPFILFLASTIFLMASLTKQIQHHSTGHCNPSMKARFTALRSLAVLFIVFTS

YFLTILITIIGTLFDKRCWLWVWEAFVYAFILMHSTSLMLSSPTLKRILKGKC

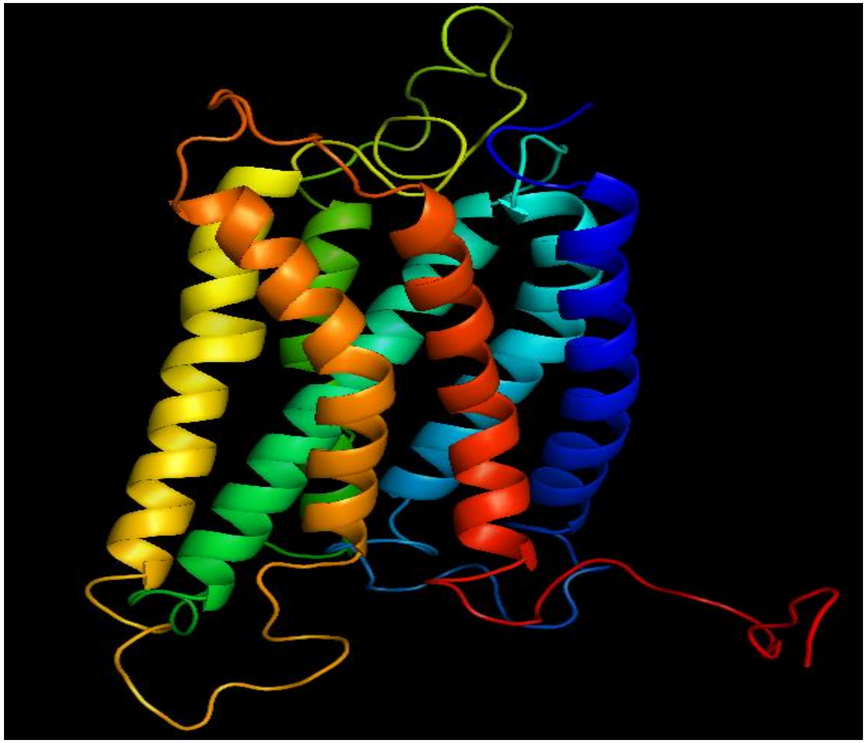
- Hidden Markov Models was used to identify the transmembrane (TM) helical regions. These are identified by the red bars. The blue and red think lines are the loops that connect the helices
- The yellow highlighted regions where the helices lie in the protein sequence

Bitter Taste Receptor Model Building



- The helical regions were aligned with the helical regions obtained from a previously created computational model of an olfactory receptor, Or2W1. This served as the template for building the taste receptor model
- Bitter taste and olfactory receptors have the same structure—that of a G-Protein Coupled Receptor
- The program Modeler (https://salilab.org/modeller/) was used to create the model of the taste receptor

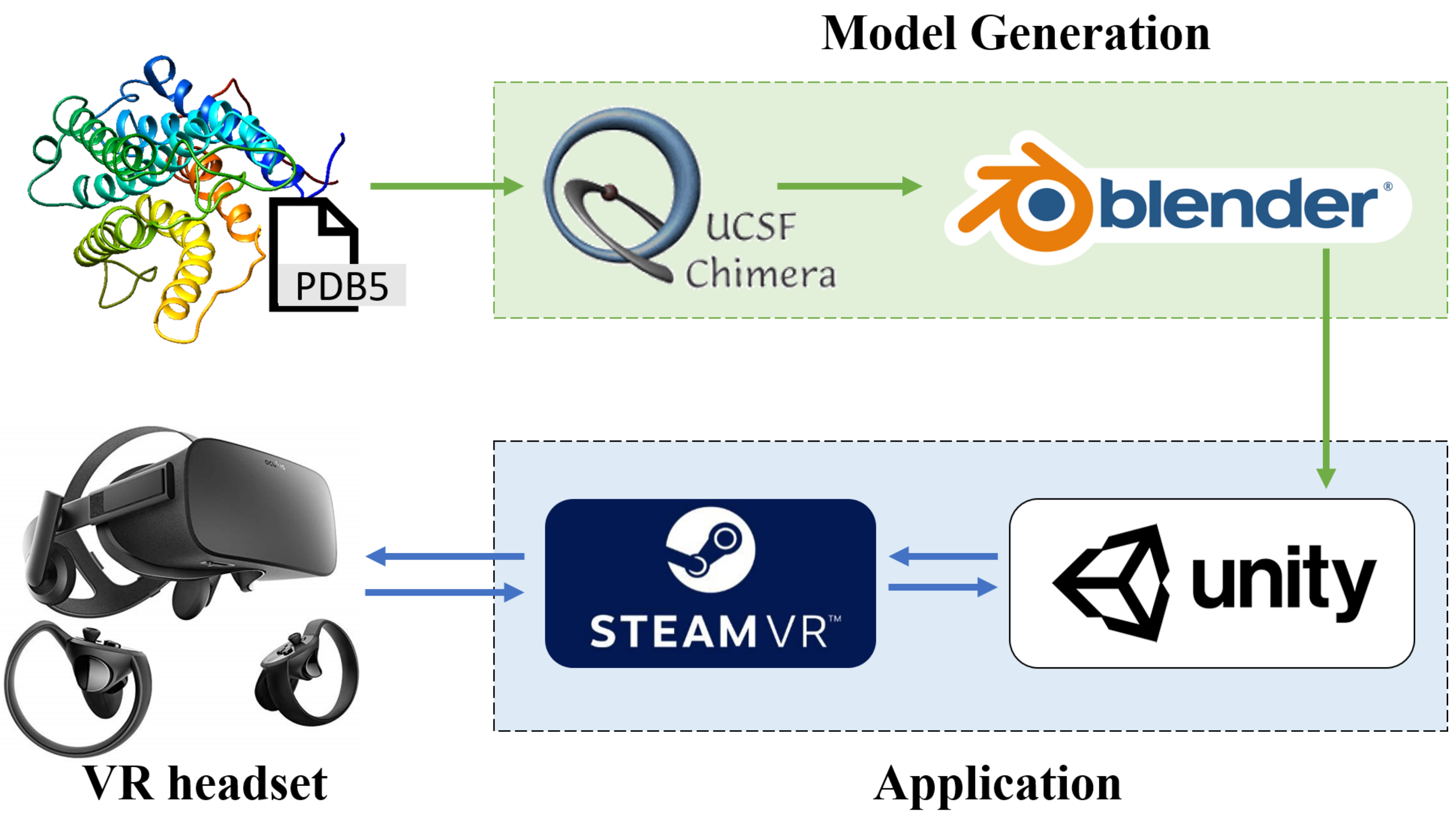
Bitter Taste Receptor Model Building



- The resulting structural model of the bitter taste receptor
- 14 more such computational models were created

Lokubandara, A. Computational Studies of Bitter Taste Receptors, M.S. Thesis, Texas Tech University, 2018

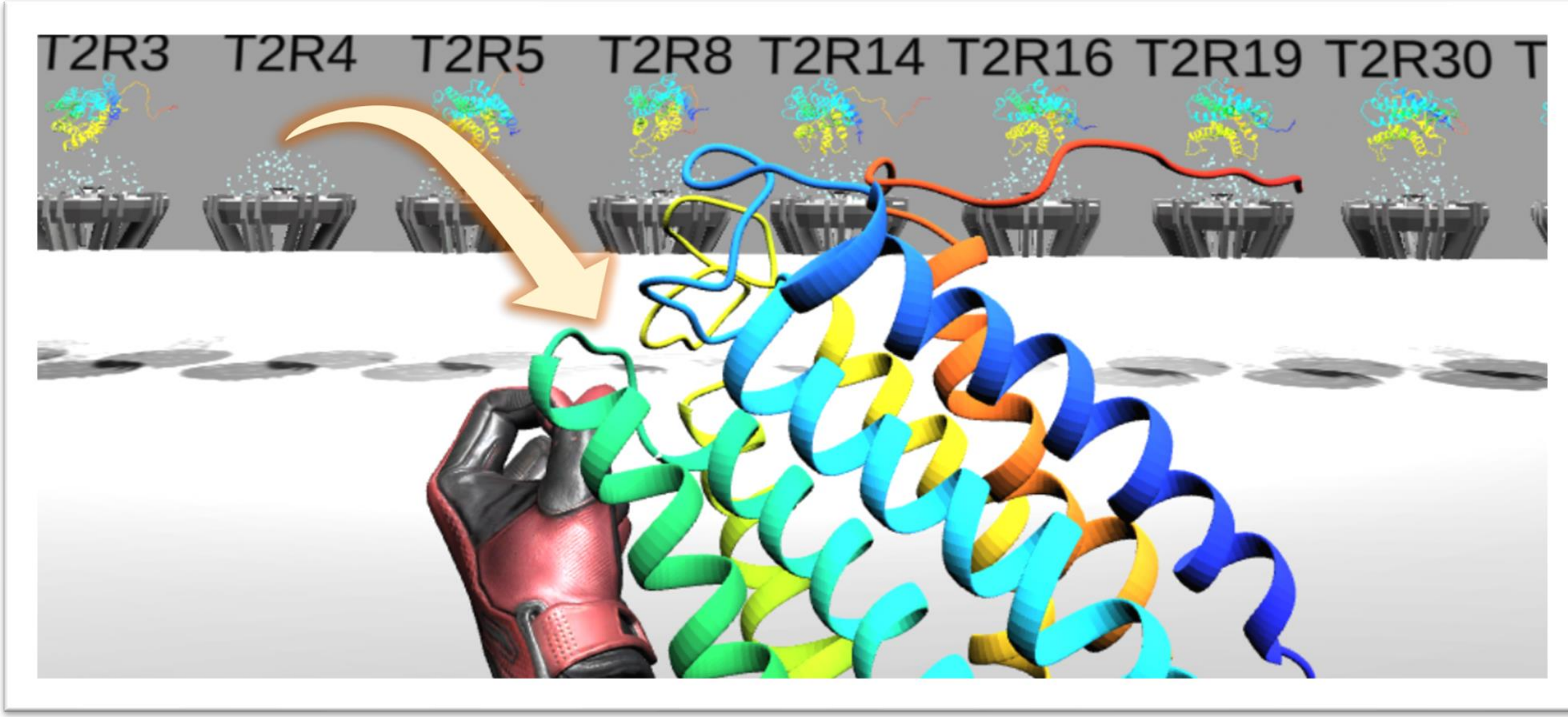
Model Generation and Experiment Setup



Model Generation and Experiment Setup

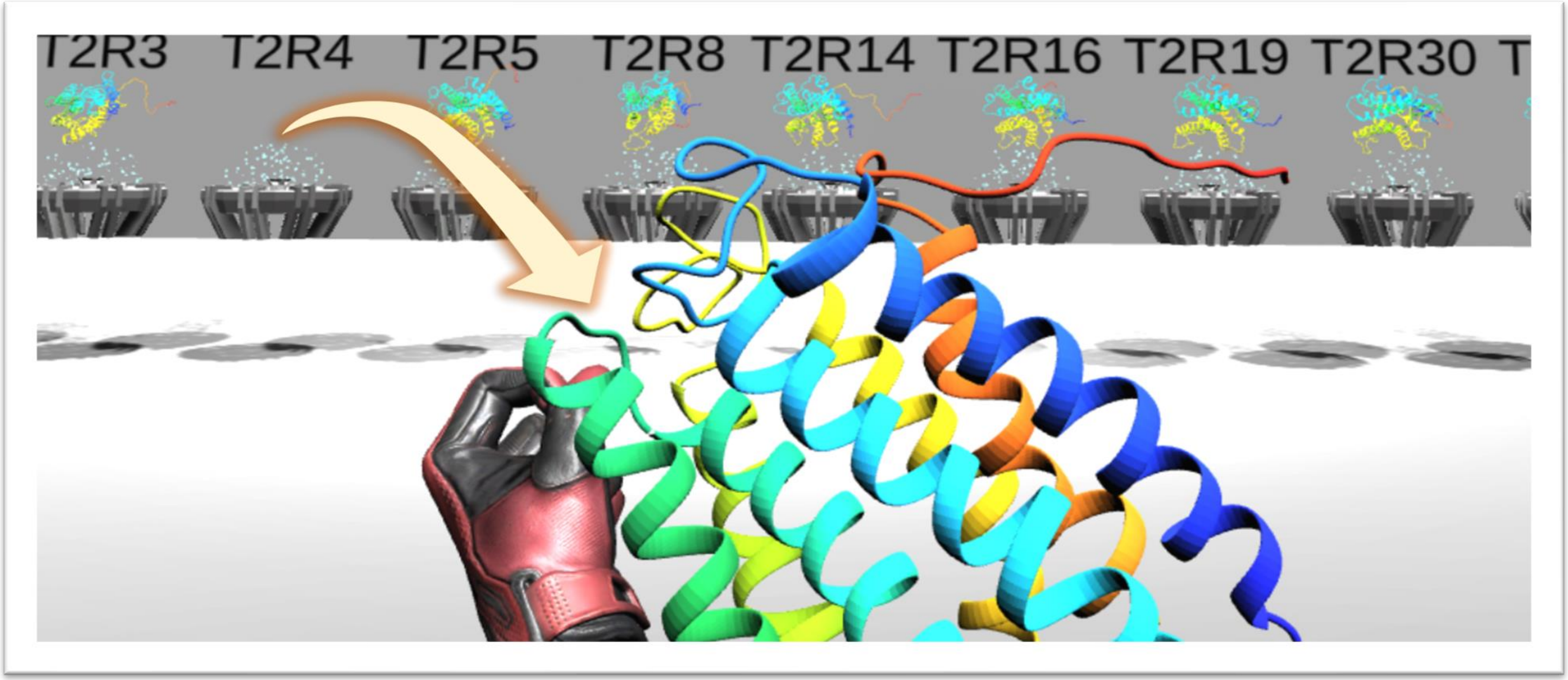
VR application requirements:

- **R1**: Learners can see the molecule from different perspectives or differently stated; the bitter taste receptor can be observed from the inside-out view in an immersive setting
- **R2**: Users can identify and recognizing the characteristics of different complex molecules
- **R3**: And finally, as being immersed in the VR environment, users should be able to sense the feedback from the virtual world



VR application design:

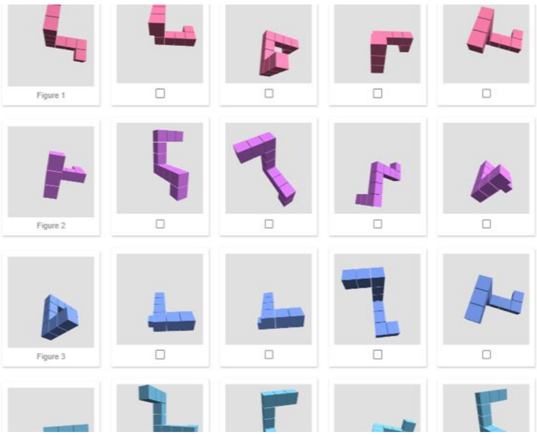
- R1: using virtual hands to grasp the molecule and examine it from different angles
- R2: two controllers enables users to grasp two receptors at the same time for comparison and finding the similarity and differences among them
- R3: three types of feedback: sound, visual, and vibration



- Two main evaluation techniques: empirical and heuristic
- Nielsen recommended that 3-5 evaluators are enough for the justification since much additional information cannot be gained by using larger numbers of evaluators
- We used five domain expert-users

Nielsen, J. (1995). How to conduct a heuristic evaluation. *Nielsen Norman Group*, *1*, 1-8.

User Study



Qualitative research questions

- **Q1**: Does the VR applications allows users to perform tasks that they are intended to do?
- **Q2**: Does the VR application provide expected response?
- **Q3**: Which components need to be improved to enhance the user experience?

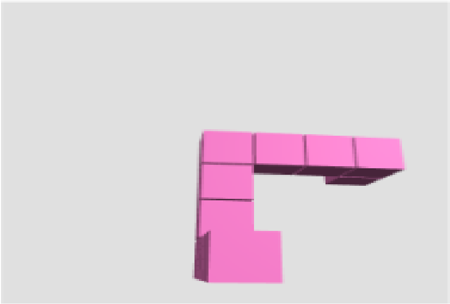


Figure 1

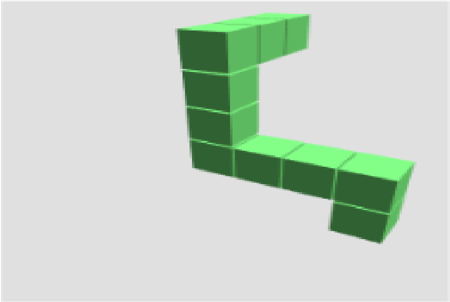


Figure 2

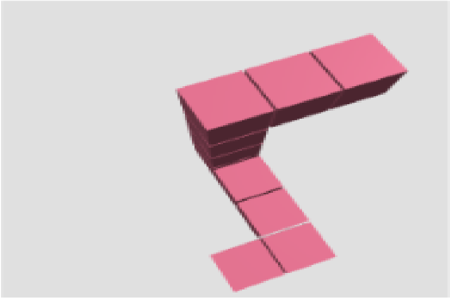
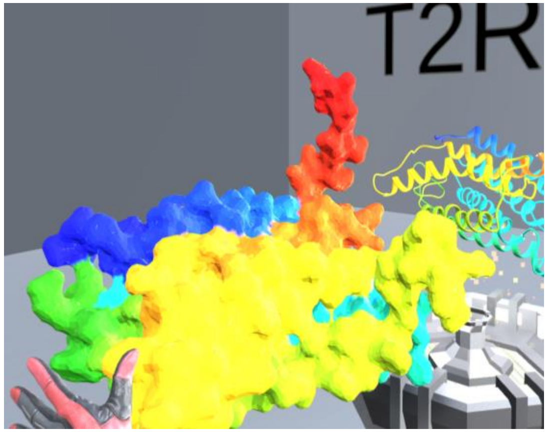


Figure 3

Procedures

- Mental rotation test for addressing spatial cognitive ability
- Users were provided with training on how to use VR headset and controllers
- After familiarizing themselves with the VR devices, participants took part in the experiments

User Study



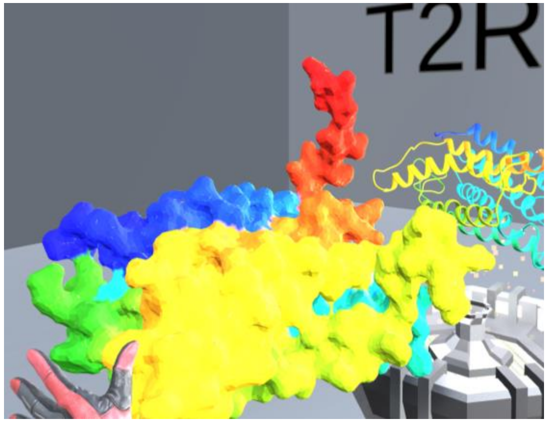
Results

- 5 participants passed the mental test with the same score (the number of correct answers) as well as were able to perform the intended actions in the VR environment

- They pointed out two limitations:
  - *text-labels for the receptors always faced in one direction, making it difficult to read when moving in the VR environment*
  - *grasping the taste receptor from the inside view is sometimes challenging due to the size changes of the 3D objects*

- We received additional feedback to improve user experience, namely, to introduce a volumetric view of the bitter taste receptors

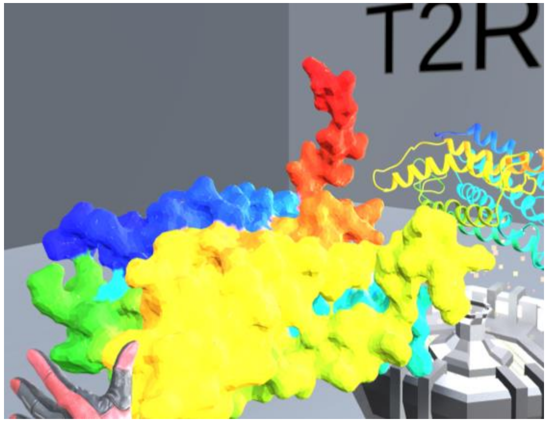
User Study



We addressed the issues raised by the users

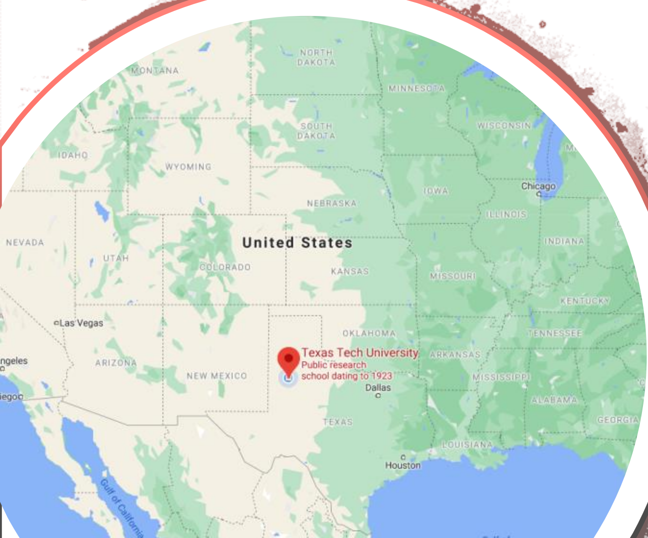
- Issue (1) can be overcome by setting the text to point toward the VR headset
- Issue (2) is technically challenging, and it can be mitigated by incorporating more accurate hand controllers such as GloveOne
- We responded to feedback requesting a volumetric view of a receptor by upgrading this feature

Conclusion



- We presents the VR app for an immersive experience of receptor-ligand interactions from the perspective of the bitter taste.
- 15 computational models of bitter taste receptors were developed and transcribed into 3D models
- We evaluated the usability of the VR application with 5 domain experts.
- Implications from the user study revealed that 3D visual representations of the genes and transcriptomes could be used in the medical application to understand their functionalities as well as support the drug design.
- Our 3D models can be adapted to the classroom where young learners can play a role of the bitter tastant and try to find the binding region of a bitter taste receptor within an immersive microscopic environment that can trigger their motivation, learning, and additional scientific perspectives.

THANK YOU!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