



**qbio**  
quantitative  
biology



The background of the main title area features a dark blue gradient with a faint grid pattern. Overlaid are several mathematical symbols and equations in a lighter blue color, including a differential equation  $\frac{du}{dt} = \frac{a_1}{1 + u^2}$ . There are also small, semi-transparent blue circular dots scattered across the background.

**QBIO MASTER PROGRAM**  
quantitative biology in practice

## LAB1 - POSTER PRESENTATIONS

Emmanuel.Margeat ([Margeat@cbs.cnrs.fr](mailto:Margeat@cbs.cnrs.fr))

# LAB 1 – POSTER PRESENTATIONS



- When and where will you do a poster presentation ?
- Preparing the poster
- Preparing your speech
- Practical examples

# LAB 1 – POSTER PRESENTATIONS



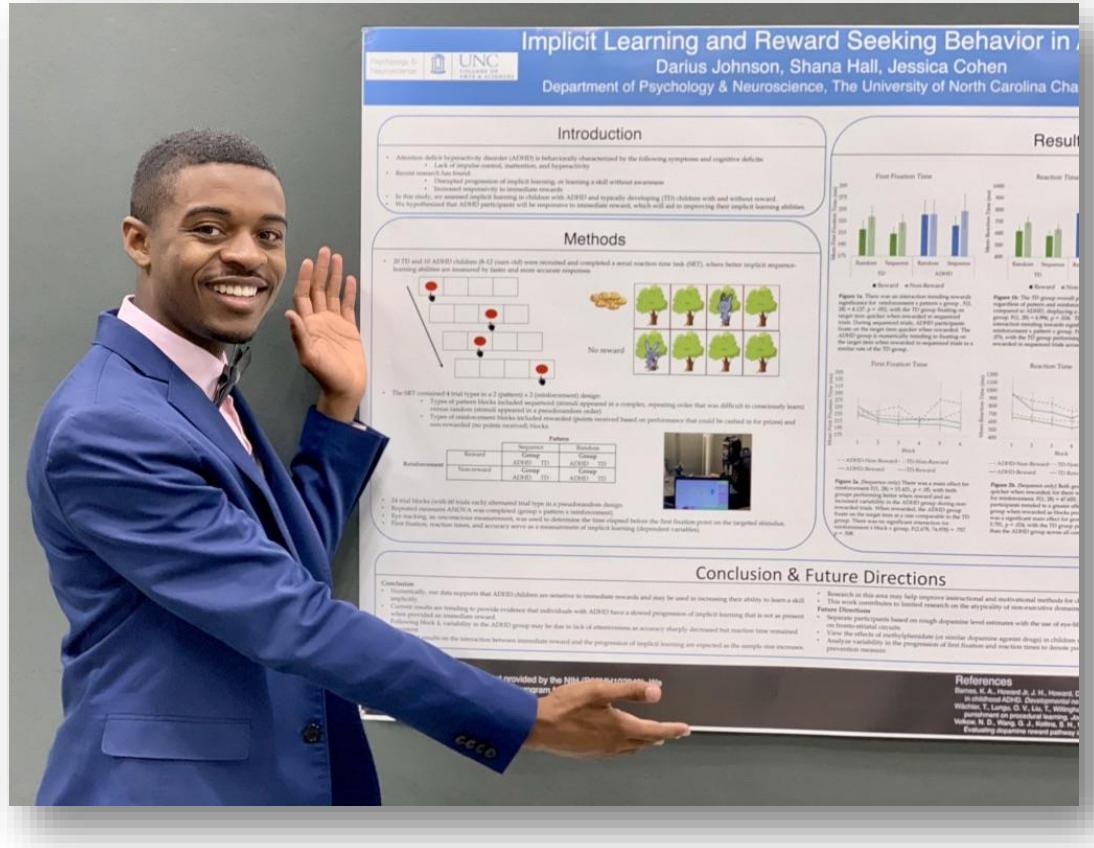
- When and where will you do a poster presentation ?
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# When and where will you do a poster presentation ?



A typical poster presentation in a (very large) scientific meeting

# When and where will you do a poster presentation ?



An effective poster operates on multiple levels ...

- Summary of your work
- Advertisement of your work
  - Reference of your work
  - Conversation starter

An effective poster is not just a standard research paper stuck to a board.

A poster uses a different, visual grammar.

**It shows, not tells**

**Know Your Audience !!**

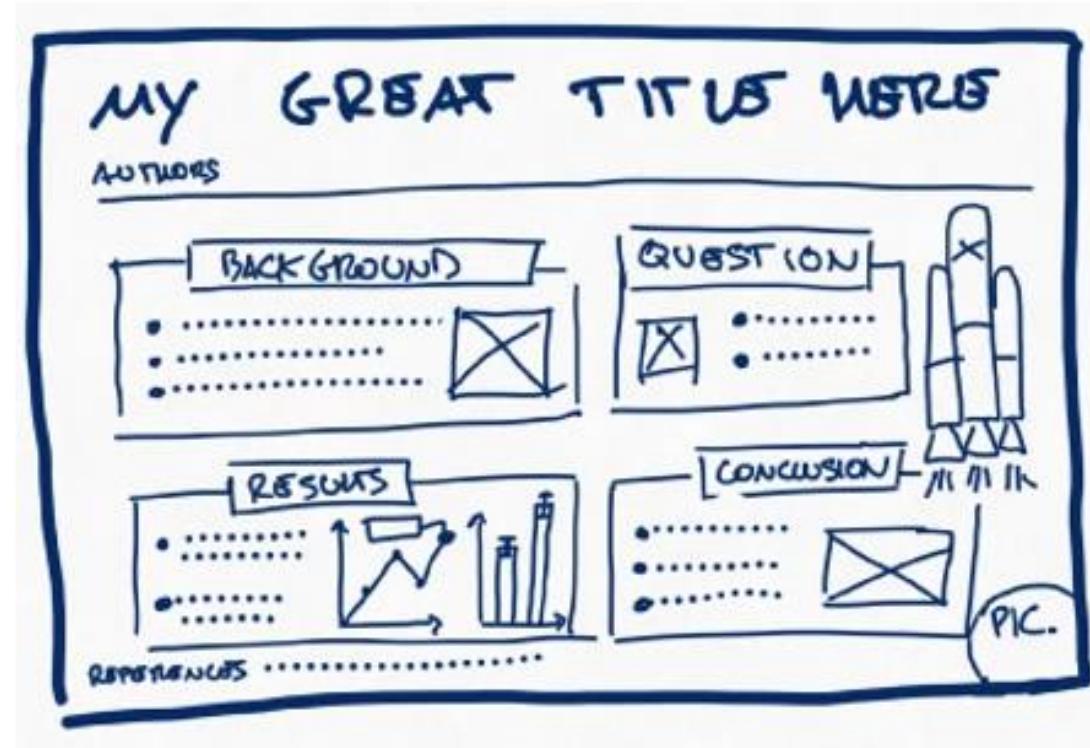
- When and where will you do a poster presentation ?
- **Preparing the poster**
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# Content

## MANDATORY :

- Title section
- Authors names and affiliations, contact
- Introduction / Aims and objectives
- Methods
- Results
- Discussion / Conclusion
- Acknowledgments / Sponsors
- References

YOU CAN ADD : abstract or summary



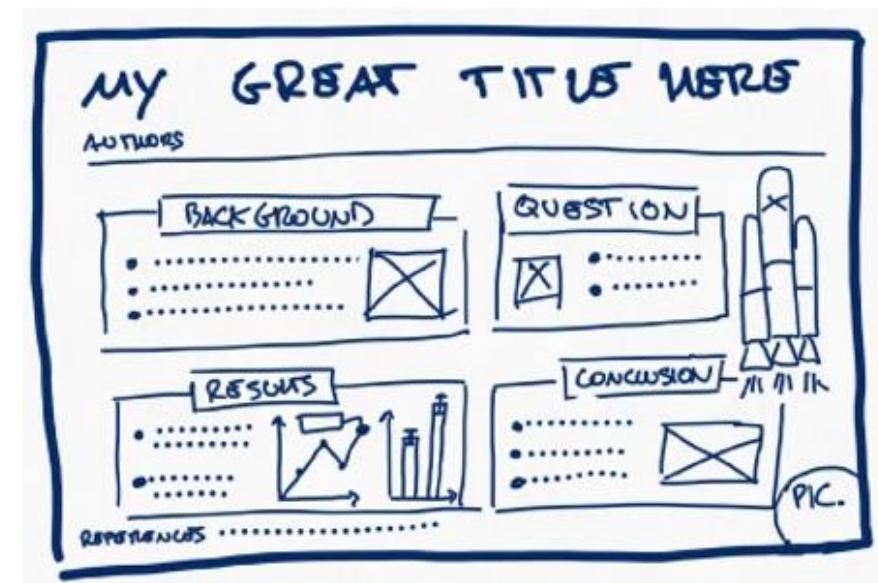
- Start with a sketch of the layout
- Dimensions, orientation
- Pick a software

# Title

- Manuscript titles are often long and complex, as they describe the basic findings of the research paper
- ... but your poster title can be more creative. The goal is to catch a viewer's attention !

Paper title :  
Solubilization and stabilization of several class-C G-protein receptors using circularized nanodiscs produced using total extracts from E. Coli

Poster title :  
**GPCR stabilization with circular nanodiscs**



# Authors names and affiliations

- Full names of all authors (incl. First name, not just the initial)
- Underline the presenter (you)
- Affiliations
- Contact
- Picture if you want

Emmanuel Margeat<sup>1</sup>, The-Other Student<sup>1</sup>, My Collaborator<sup>2</sup>, My Boss<sup>1</sup>

<sup>1</sup> Centre de Biologie Structurale, CNRS, Montpellier, France

<sup>2</sup> The other amazing lab, INSERM, Palavas, France

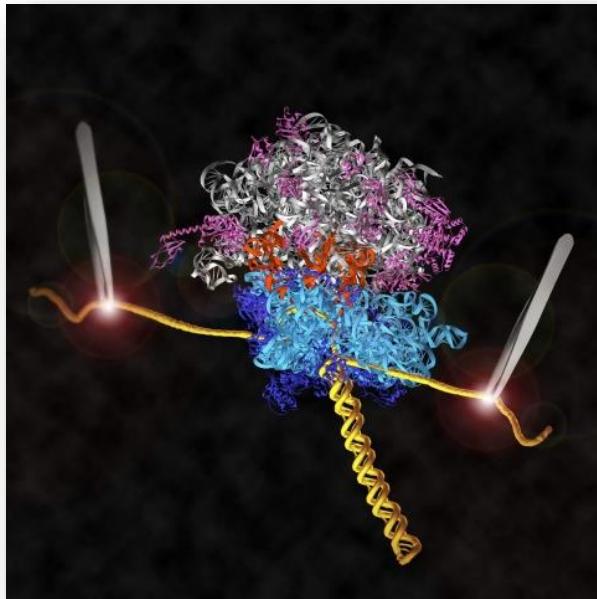
Contact : emmanuel.margeat@umontpellier.fr



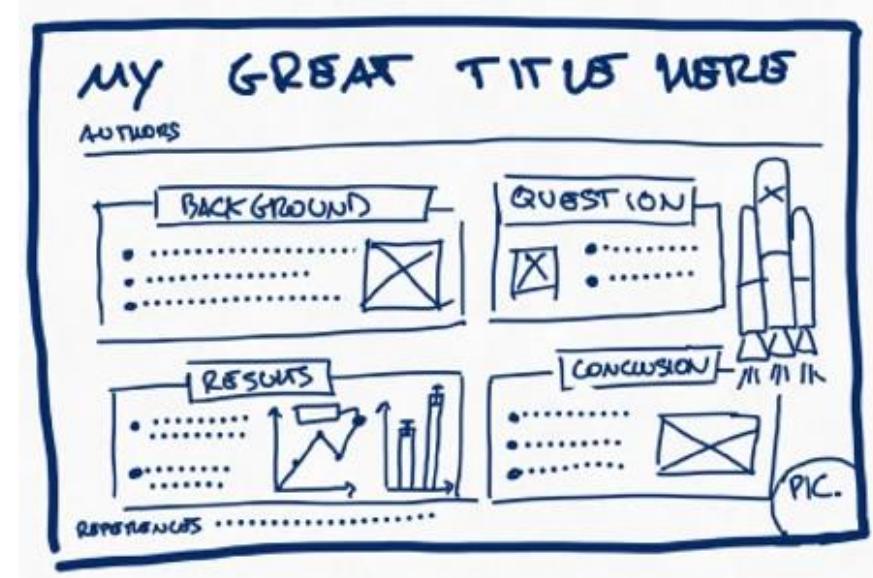
# Introduction, Aims and Objectives

- Target here someone who is not necessarily in your field
- Get your viewer *interested* in the issue or question
- Use the absolute minimum of background information, definitions, and acronyms
- Pitch an interesting, *novel* hypothesis
- Describe (briefly) the experimental approach that can test your hypothesis.

A nice image can draw people in !



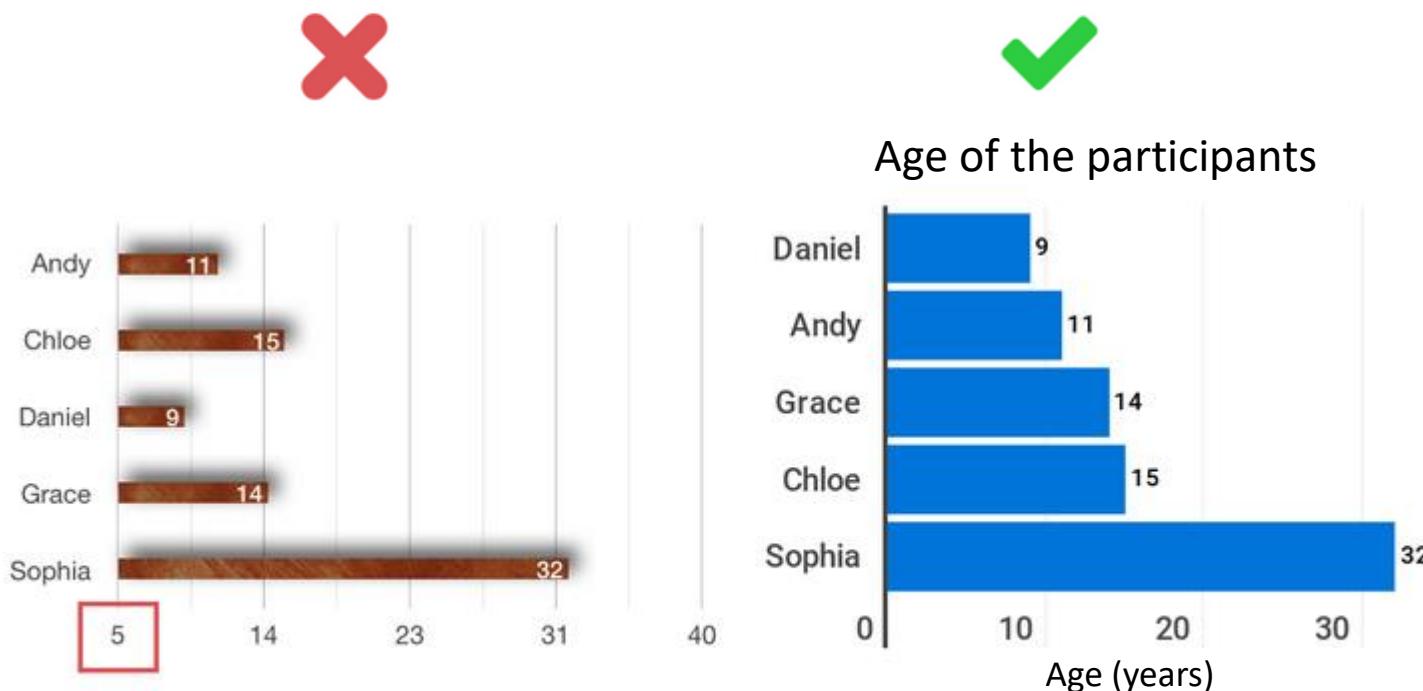
Courtney Hodges (UC Berkeley) and Laura Lancaster (UC Santa Cruz), Bustamante lab



# Results

- This is where the action is !
- Remember – you don't need to include every experiment you've ever done.
- Just describe the results that help address the main question/hypothesis.

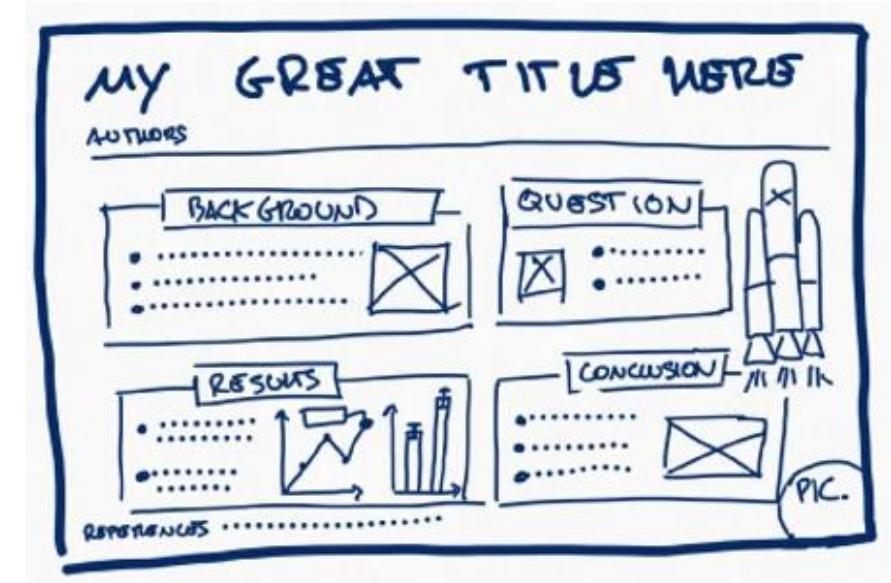
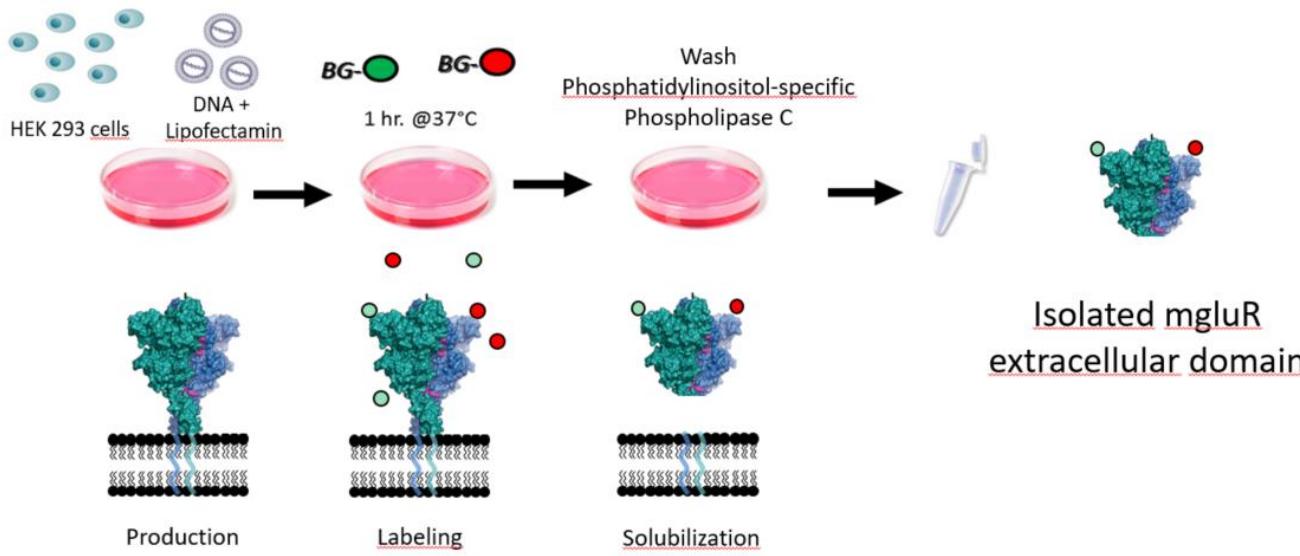
**Figures, Images, Data representation are central here**



# Methods

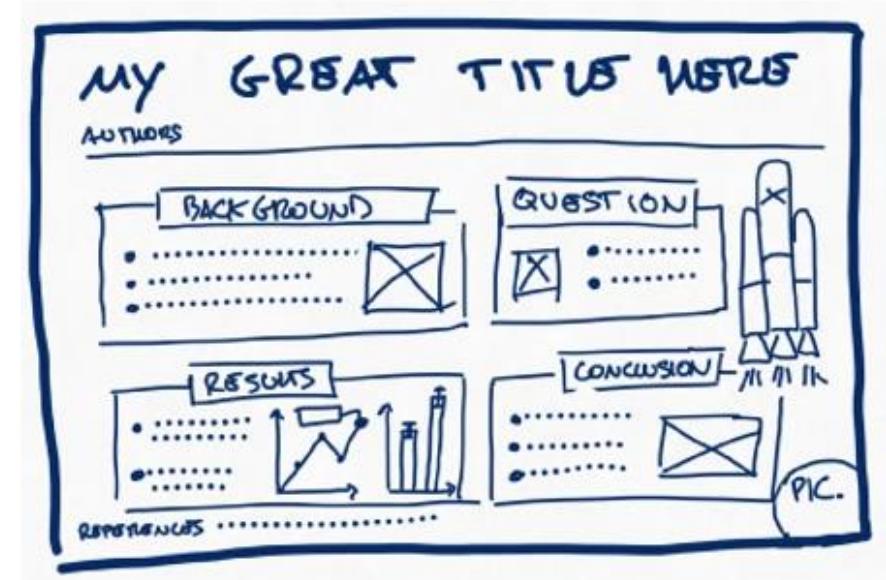
- Use this section to help the viewer understand your experimental approach to the question.
- You don't need to detail every last step – save that for the paper you publish!

Again, a diagram or figure works great here.



# Conclusion / Discussion

- remind readers of the importance/relevance of your work
- Use 2-4 bullet points to summarize the meaning or implications of your results
- Did this address the objectives of the project ?
- Mention any alternative explanation for results or unanticipated results
- What are the potential outcomes ?



# Layout and Format

- Top to bottom and from left to right.
- Common alternative layout : conclusions in the centre of the poster and supporting work radiating out from it
- No long and detailed sections of text. Bullet points are more effective and maintain the reader's interest.
- White-space is important, and will make the poster more readable.
- Printing on paper



# Style

- Ensure that your font size is large enough to be legible from at least one-two meters away (e.g. 18-24 for the text and 24 - 36 for titles).
- Don't use CAPITAL LETTERS even in Title AS THEY ARE MORE DIFFICULT TO READ
- Try to use one or two font types at most. Too many font types can look messy and confusing,
- Choose fonts that are easy on the eye, such as Times Roman or Arial.

# Text sizes:

Title: 85 point

Authors : 36pt

Sub-headings: 36pt

Body text: 24pt

Captions: 18pt

Your Ingenious Teaser Right Here to Woo Them Down to the Body  
The name of the poster is 24pt regular

**Conclusions first: 44 pt bold**  
Always put the most important part - your conclusions - first! Place your conclusions in the upper left hand corner of your poster.  
Prepare your material from the reader's perspective. What was done, by who and your conclusion has to be understood within a couple of second's reading! Use active voice when writing the text. Textsize: 34 pt regular

**Introduction**  
Posters are primarily visual presentations. Your poster should be dominated by self-explanatory illustrations such as graphs and pictures while the amount of text should be kept to the minimum.

**Your aim**  
Your poster is an advertisement for your research and as such it needs to be eye-catching and straight to the point. You only have seconds, or at best a few minutes to attract the attention of the visitor to a poster session. Keep your message short and clear

**Your message**  
Keep your message clear and your text concise. Decide what is relevant for this poster and try to get your message across to your target group.

**Layout, photos and print**  
Contact [Mediashop](#) at University Library for help with layout and image enhancement. For printouts and professional photographers contact [Bilmakarna](#). For more information: [www.bilmakarna.kth.se](http://www.bilmakarna.kth.se)

**Tips:**  
The best font for text blocks that are as short as they should be on a poster is a Sans Serif typeface family. Therefore, use sans serif fonts such as Arial or [Mundo sans](#) rather than serif fonts like Times or Courier.  
AVOID CAPITAL LETTERS IN TEXTS THAT ARE LONGER THAN ONE LINE, SINCE THEY ARE MORE DIFFICULT TO READ.

**Handouts**  
If you succeed in getting the reader's attention, provide her/him with more detailed information in the form of handouts or printed articles. Include references on your handout instead of your poster.

It is always nice to put in a picture and write some few short notes of what's going on in the future. Put handouts, business cards, nearby - on a table or in an envelope hung with the poster.

Illustration of a brain  
Textsize: 24pt regular

Always write a descriptive caption 22pt regular

Karolinska Institutet  
Forskningsinstitutet för hälsa, service och  
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# LAB 1 – POSTER PRESENTATIONS



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# Preparing your speech

- Introduce yourself
- You should have a short and a long version of your speech
  - The short one should be 1 minute / 3-4 sentences, covering
    1. What is your research topic?
    2. What have you found?
    3. Why is that important?
  - If you have caughted your audience attention, you can switch to the long version (+5 minutes) that covers :
    - Background information about your research, How did this lead you to your research question, what were you hoping to find out and why?
    - How did you get from your research question to your conclusion? What techniques did you use and why ? Were there any interesting twists ?
    - What are the conclusion of your work ? How does this open new avenues ?
- Be prepared for questions
- Practice !

# LAB 1 – POSTER PRESENTATIONS



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# REFINEMENT OF ATOMIC MODELS OF HIV-1 CA OLIGOMERS

JUAN R. PERILLA<sup>†</sup>, GONGPU ZHAO<sup>\*</sup>, DANIELLE CHANDLER<sup>†</sup>,

ANGELA GRONENBORN<sup>\*</sup>, PEIJUN ZHANG<sup>\*</sup> AND KLAUS J. SCHULTE<sup>†</sup>

<sup>†</sup>BECKMAN INSTITUTE FOR ADVANCED SCIENCE AND TECHNOLOGY, UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

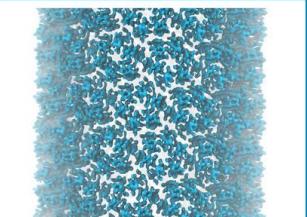
<sup>\*</sup>DEPARTMENT OF STRUCTURAL BIOLOGY, UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE



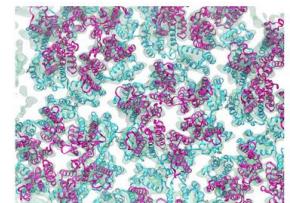
## INTRODUCTION

Native capsids are made of higher-order structures of HIV-1 CA, involving thousands of CA proteins, but arranged in a lattice involving only two types of oligomers: hexamers and pentamers. High-resolution structures for the oligomers are available, but not in native conformations, thus they lack the intrinsic curvature. By using MDFF combined with cryo-EM data, we present a new structure of the hexameric form of HIV-1 CA. The MDFF-derived model accurately captures the inter- and intra-hexameric interactions. Using the MDFF-derived model of the hexameric form of HIV CA, we have also been able to model new interactions between pentamers and hexamers.

## MDFF

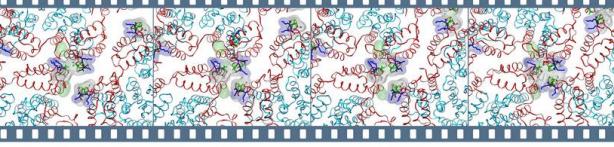


The hexameric structure 3H47 is used as the starting point, missing residues are built by homology modeling using Modeller, and are optimized via MD while constraining the solved residues. Dimers are modelled after the NMR structure 2KOD. Initial rigid body docking to the cryo-EM map is performed by using SITUS with a resulting cross correlation coefficient of 0.75.



Molecular dynamics flexible fitting (MDFF) incorporates the EM density map as a potential in a way that high density areas in the grid correspond to energy minima. MDFF yields a structure with a CCC of 0.96.

## STRUCTURAL REFINEMENT

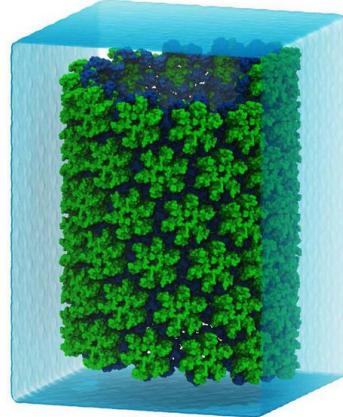


The MDFF-derived structure was allowed to equilibrate for 20ns. During equilibration the 7-hexamers were stabilized

by the formation of hydrogen bonds, and by the presence of a hydrophobic core at the three-fold symmetry axis.

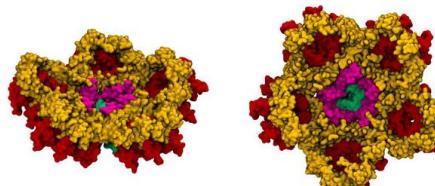
## CYLINDRICAL MODEL

A total of 71 MDFF-derived hexamers were docked to the cryo-EM cylindrical map, solvated and ionized by NaCl (1M). The resulting system consisting of  $15 \times 10^6$  atoms, was equilibrated for 100ns using the **NSF BlueWaters supercomputer**.



## PENTAMER MODEL

Using the MDFF-derived model, and the pentameric structure 3P05. We were able to construct an all-atom pentamer-hexamer model. The system was equilibrated for 200ns.



# The effects of sub-anesthetic doses of the non-competitive NMDA receptor antagonist ketamine on reconsolidation and expression of fear memory in Sprague Dawley rats



Delcellier, K.<sup>1,2</sup>, Cayer, C.<sup>1,2</sup>, Kent, P.<sup>1</sup> and Merali, Z.<sup>1,2</sup>

<sup>1</sup>Institute of Mental Health Research, <sup>2</sup>University of Ottawa School of Psychology

## Introduction

-Ketamine, a non-competitive NMDA receptor antagonist, has historically been used as a sedative in veterinary and human medicine.

-Recent reports suggest that it displays anti-depressant as well as anxiolytic effects at sub-anesthetic doses. Several non-competitive NMDA receptor antagonists that have been shown to disrupt fear memory processes, however surprisingly little work has been done on the effects of ketamine in this domain.

-The objective of this study was to investigate the effects of ketamine on reconsolidation and expression of fear memory in Sprague-Dawley rats.

## Methods

**Subjects:** Male Sprague-Dawley rats (275-300 g) were maintained on a 12h light/dark cycle and given ad libitum access to food and water.

**Drugs:** Ketamine, dissolved in saline was administered intraperitoneally at doses 1, 3 or 10 mg/kg. The control (vehicle) animals received an equivalent volume of saline alone.

**Procedure:**  
**Acquisition:** Rats were placed in conditioning chambers (Gulbeam Instruments) where they received either 1.0 footshock (1.0 mA; 1s duration) on a random schedule (contextual training) or 20 pairings of a 20-s tone with a 1.0 mA (1-s) continuous footshock delivered during the final second of the 20-s tone (cued training).

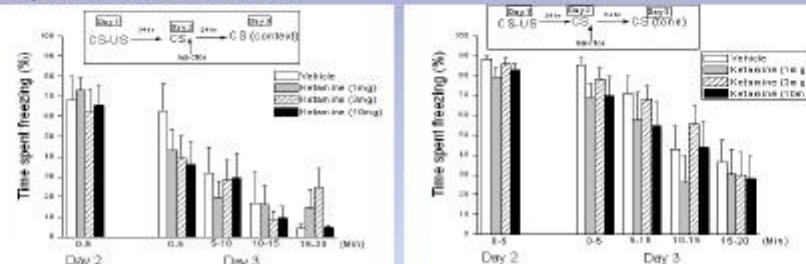
**Experiment 1 (expression):** 24 h after acquisition training, rats were randomly injected with one of the 3 doses of ketamine 20 min before testing. Contextual fear expression was assessed over 20 min by placing the rats back into the conditioning chamber where they had previously been shocked and freezing behavior monitored. To assess fear expression in the cued condition, rats were transferred to a novel environment and presented with the cue (tone previously paired with footshock). A total of 15 tones (each 20 s in duration) were presented at 1 min intervals.

**Experiment 2 (reconsolidation):** 24 hr after acquisition training rats were presented with the CS (either context or cue, as described previously) without the US for 5 min (reactivation). Immediately thereafter, rats were injected with one of three doses of ketamine or saline and returned to their home cage. The following day (Day 2), rats were tested for contextual or cued fear expression as described in Experiment 1.

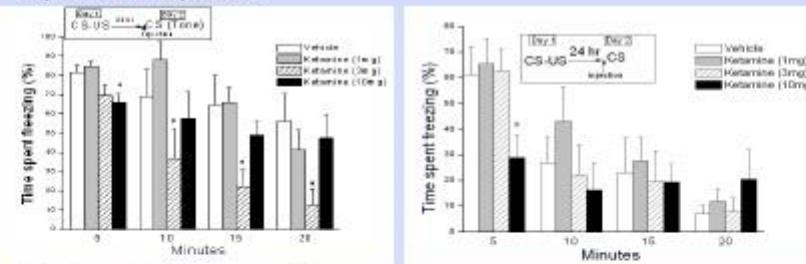
**Experiment 3 (locomotor activity):** rats were injected with one of two doses of ketamine (3 or 10mg/kg) or saline 20 minutes before testing. Locomotor activity was assessed over 30 minutes in the testing arena for the Open-Field test.

## Results

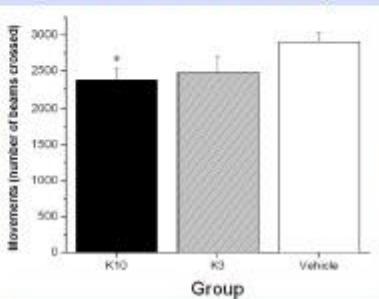
### Experiment 1: Reconsolidation



### Experiment 2: Expression



### Experiment 3: Locomotor activity



## Conclusions

-Ketamine did not disrupt reconsolidation, which is contrary to previous research on other non-competitive NMDA receptor antagonists using CER.

-Higher doses (3 and 10 mg/kg) of ketamine were shown to disrupt the expression of fear memory in both contextual and cued conditions.

-High dose (10mg/kg) of ketamine was shown to lower locomotor activity, leading to believe that its use would not be causing an increase in activity and therefore would not be interfering with the freezing behavior.

-The results of this study appear to indicate that ketamine is indeed implicated in the disruption fear memory processes, although there seems to be some differences with results previously reported on other non-competitive NMDA receptor antagonists using the same paradigm. Results such as these lead to the possibility of ketamine using a different mechanism.

## Acknowledgements

I would like to thank everyone from Dr. Zul Merali's laboratory for all of the assistance and wonderful help they have given me throughout the year. I would like to especially thank Christian Cayer and Jonathan James for their most appreciated help in data collection and the invaluable guidance they have given me, as well as Pamela Kent, who has been an incredible source of support and knowledge throughout this experience.

## Future research

-Future research into ketamine's effect on fear memory processes should focus on the possibility of its implication in a different mechanism in the amygdala, as well as its effects on fear memory acquisition.

-Implications of such studies could eventually lead to novel treatments for anxiety disorders, such as PTSD.

# Structural determinants of binding of the human bile acid transporter SLC10A2 (ASBT)



Viktoria Gamsjäger<sup>1</sup>, Claire Colas<sup>1</sup>, Gerhard F. Ecker<sup>1</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, University of Vienna , Althanstrasse 14, 1090 Vienna, Austria

**RESOLUTE**  
Research Empowerment on Solute Carriers

## Introduction

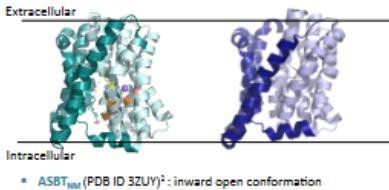
The human apical sodium-dependent bile acid transporter (hASBT, SLC10A2) is a membrane protein that is responsible for the uptake of bile acids across the enterocytes apical membrane. hASBT is a key drug target for the treatment of hypercholesterolemia. Additionally, hASBT is an interesting target for prodrugs.

Here we describe the interactions of this transporter with its ligands using computational methods. Our results improve our understanding on how substrate specificity is determined in hASBT, providing guiding rules for the development of new compounds targeting this pharmacologically important transporter.

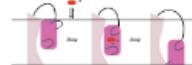
## Goals

- To determine the specificity determinants of binding
- => Understanding the transporter's interaction with substrates and inhibitors at a molecular level
- Discovering new compounds
- => Used as chemical tools to understand function, or new scaffolds for the design of new drugs

## Prokaryotic transporters ASBT<sub>NM</sub> and ASBT<sub>yf</sub>



- X-Ray structures of homologues in 2 conformations (ASBT<sub>yf</sub> and ASBT<sub>NM</sub>)
- 22-26% sequence identity with human hASBT
- Elevator mechanism of transport<sup>3</sup>



## Homology modeling



- Generation of a 3D model of a protein with an unknown structure ('target') based on an experimentally determined structure of a homolog protein ('template').
- The protocol generally includes several steps (c.f. flow chart) ranging from template selection to model validation.
- The process is iterative until a suitable model is obtained.

## Substrate selectivity

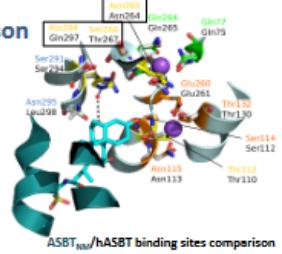


- Large discrepancy of affinities despite a similar scaffold
- Grouping of bile acids depending on their hydroxylation profile and substitutions

## Binding sites comparison

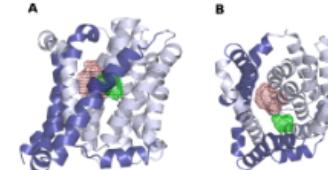
- Mutagenesis studies on the template characterized essential residues for binding
- Hydrogen bond network with a water molecule
- Residues constituting the binding sites are conserved

=> Hypothesis : the substrate selectivity occurs in the outward open conformation



ASBT<sub>NM</sub>/hASBT binding sites comparison

## Outward open models reveal an horizontal orientation



Binding pockets in the outward open conformation

## Future directions

Rationalize the substrate specificities of ASBT in the outward open conformation:

- => to reveal important residues involved in binding and transport
- => to identify conformation-specific compounds by virtual screening

## Conclusions

- Our study reveals that the binding sites in the inward open conformation are conserved
- We suggest that selectivity occurs in the outward open conformation

1. Hu et al. Crystal structure of a bacterial homologue of the bile acid sodium symporter Asbt. *Nature* 478: 408 (2011)  
2. Zhou et al. Structural basis of the alternating-access mechanism in a bile acid transporter. *Nature* 505: 509-513 (2013)

3. Colas et al. SLC Transporters: Structure, Function, and Drug Discovery *MedChemComm* 7(6):1069-1081 (2016)  
4. Geyer et al. The solute carrier family SLC10: more than family of a bile acid transporters regarding function and phylogenetic relationships *Arch Pharmacol* 372: 413-431 (2006)



# PIGS IN SPACE: EFFECT OF ZERO GRAVITY AND AD LIBITUM FEEDING ON WEIGHT GAIN IN CAVIA PORCELLUS



SPACE-EXES

## ABSTRACT:

One ignored benefit of space travel is a potential elimination of obesity, a chronic problem for a growing majority in many parts of the world. In theory, when an individual is in a condition of zero gravity, weight is eliminated. Indeed, in space one could conceivably follow ad libitum feeding and never even gain an gram, and the only side effect would be the need to upgrade one's stretchy pants ("exercise pants"). But because many diet schemes start as very good theories only to be found to be rather harmful, we tested our predictions with a long-term experiment in a colony of Guinea pigs (*Cavia porcellus*) maintained on the International Space Station. Individuals were housed separately and given unlimited amounts of high-calorie food pellets. Fresh fruits and vegetables were not available in space so were not offered. Every 30 days, each Guinea pig was weighed. After 5 years, we found that individuals, on average, weighed nothing. In addition to weighing nothing, no weight appeared to be gained over the duration of the protocol. If space continues to be gravity-free, and we believe that assumption is sound, we believe that sending the overweight — and those at risk for overweight — to space would be a lasting cure.



## INTRODUCTION:

The current obesity epidemic started in the early 1960s with the invention and proliferation of elastane and related stretchy fibers, which released wearers from the rigid constraints of clothes and permitted monthly weight gain without the need to buy new outfitts. Indeed, exercise today for hundreds of million people involve only the act of wearing stretchy pants in public, presumably because the constrictive pressure forces fat molecules to adopt a more compact tertiary structure (Xavier 1965).

Luckily, at the same time that fabrics became stretchy, the race to the moon between the United States and Russia yielded a useful fact: gravity in outer space is minimal to nonexistent. When gravity is zero, objects cease to have weight. Indeed, early astronauts and cosmonauts had to secure themselves to their ships with seat belts and sticky boots. The potential application to weight loss was noted immediately, but at the time travel to space was prohibitively expensive and thus the issue was not seriously pursued. Now, however, multiple companies are developing cheap extra-orbital travel options for normal consumers, and potential travelers are also creating new ways to pay for products and services that they cannot actually afford. Together, these factors open the possibility that moving to space could cure overweight syndrome quickly and permanently for a large number of humans.

We studied this potential by following weight gain in Guinea pigs, known on Earth as fond of ad libitum feeding. Guinea pigs were long envisioned to be the "Guinea pigs" of space research, too, so they seemed like the obvious choice. Studies on humans are of course desirable, but we feel this current study will be critical in acquiring the attention of granting agencies.

## CONCLUSIONS:

Our view that weight and weight gain would be zero in space was confirmed. Although we have not replicated this experiment on larger animals or primates, we are confident that our result would be mirrored in other model organisms. We are currently in the process of obtaining necessary human trial permissions, and should have our planned experiment initiated within 80 years, pending expedited review by local and Federal IRBs.

## ACKNOWLEDGEMENTS:

I am grateful for generous support from the National Research Foundation, Black Hole Diet Plans, and the High Fructose Sugar Association. Transport flights were funded by SPACE-EXES, the consortium of wives divorced from insanely wealthy space-flight startups. I am also grateful for comments on early drafts by Mariana Athletic Club, Corpus Christi, USA. Finally, sincere thanks to the Cuy Foundation for generously donating animal care after the conclusion of the study.

## LITERATURE CITED:

- NASA. 1982. Project STS-XX: Guinea Pigs. Leaked internal memo.  
Sekulić, S.R., D. D. Lukač, and N. M. Naumović. 2005. The Fetus Cannot Exercise Like An Astronaut: Gravity Loading Is Necessary For The Physiological Development During Second Half Of Pregnancy. Medical Hypotheses. 64:221-228.  
Xavier, M. 1965. Elastane Purchases Accelerate Weight Gain In Case-control Study. Journal of Obesity. 2:23-40.

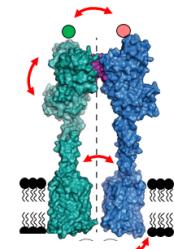
# Structural dynamics of single metabotropic glutamate receptors dimers



Robert Quast<sup>1</sup>, Anne-Marinette Cao<sup>1</sup>, Fataneh Fatemi<sup>1</sup>, Linnea Olofsson<sup>1</sup>, Philippe Rondard<sup>2</sup>, Jean Philippe Pin<sup>2</sup>, Emmanuel Margeat<sup>1</sup>.

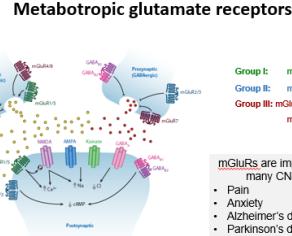
<sup>1</sup> Centre de Biochimie Structurale, CNRS UMR 5048, INSERM U1054, Université de Montpellier, Montpellier, France  
<sup>2</sup> Institut de Génétique Fonctionnelle, CNRS, INSERM, Université de Montpellier, Montpellier, France  
 Contact : margeat@cbs.cnrs.fr

Centre de Biochimie Structurale  
 Montpellier, France



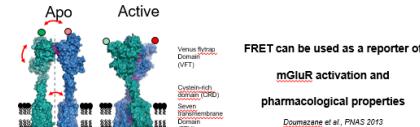
The activation mechanisms of GPCRs, where an external signal is propagated across the membrane through conformational rearrangements, have been extensively studied over the last decades by various biochemical, structural and biophysical methods. These have led to the conclusion that GPCR activation cannot be sufficiently explained by a simple on/off transition from an inactive to a distinct active state. Instead, it is rather a highly dynamic process where the equilibrium between multiple coexisting conformational states is altered by interacting molecules such as proteins, lipids, ions and others. Therefore, methods to monitor solubilized full-length receptor dimers.

these conformational changes, preferentially at the single molecule level, are needed. Here, using single molecule Förster resonance energy transfer (smFRET) we are studying the structural dynamics that occur during activation of metabotropic glutamate receptors (mGluRs) in response to ligands. We have previously shown that isolated ligand binding domains oscillate between an active/open and an inactive/closed state in a time range of ~100 µs and that orthosteric ligands shift the equilibrium depending on their efficacy. We have now extended these observations to detergent-solubilized full-length receptor dimers.

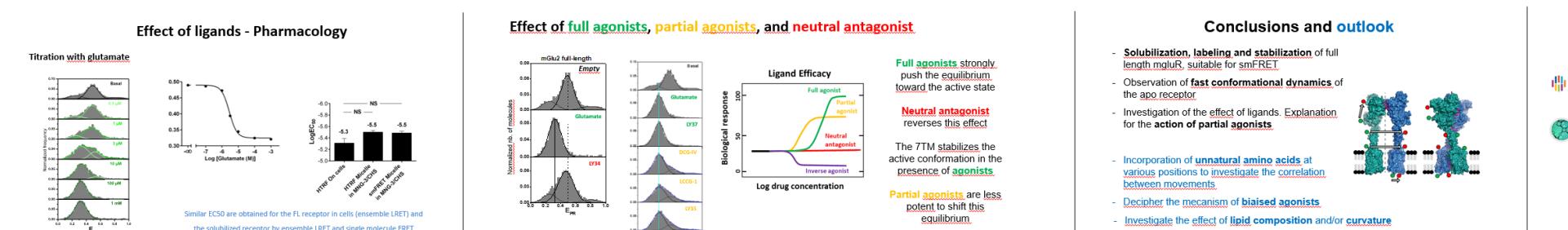
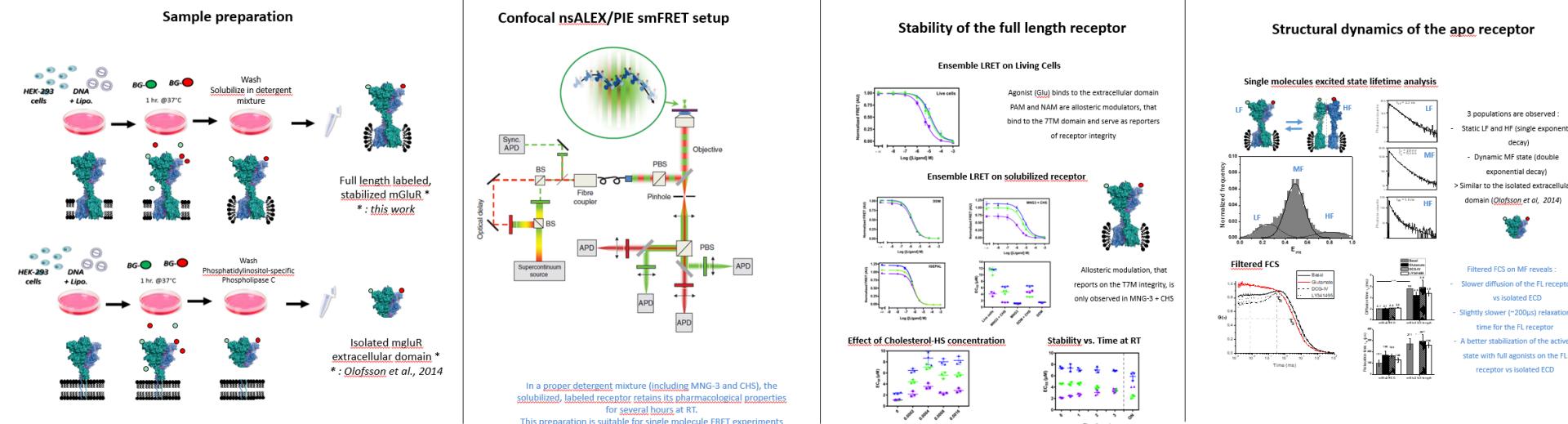


- mGluRs are important targets for many CNS disorders:
- Pain
  - Anxiety
  - Alzheimer's disease
  - Parkinson's disease
  - Depression
  - Schizophrenia

## Conformational changes associated with activation



FRET can be used as a reporter of mGluR activation and pharmacological properties  
 Doucet et al., PNAS 2013





# Molecular Dynamics Simulation of Viral Glycan Binding Activity of Porcine/Human Lung Surfactant Protein D

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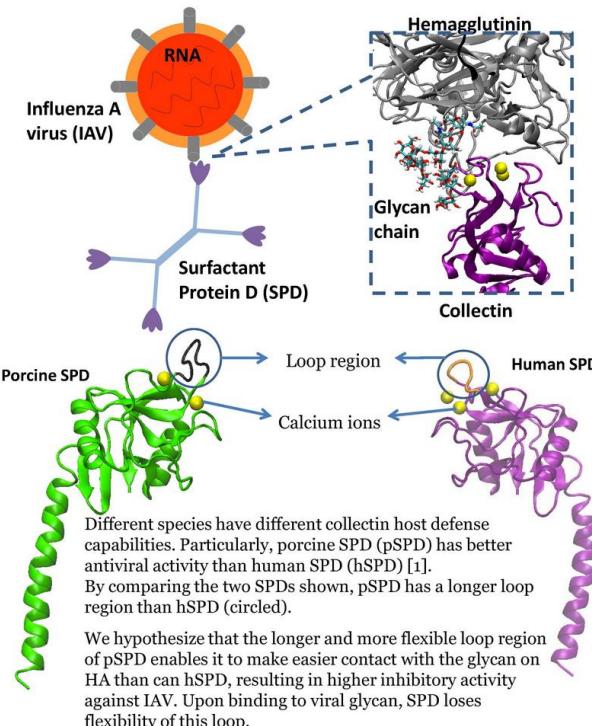
<sup>1</sup>Department of Physics, and <sup>2</sup>Beckman Institute, University of Illinois at Urbana-Champaign; <sup>3</sup>Department of Physiology and Biophysics, Boston University

## Abstract

Lung collectin surfactant protein D (SPD) is a pulmonary host defense protein that contributes to innate, front-line defense against influenza A virus (IAV) and other inhaled pathogens. Collectins recognize viral glycans on the globular head of hemagglutinin (HA) on the IAV surface and initiate events leading to pathogen neutralization. Thus, effective pulmonary host defense requires fast recognition of IAV HA by collectins. In order to assist development of new approaches to collectin-based antiviral therapeutics, we investigated the mechanism underlying SPD recognition of IAV HA using molecular dynamics simulations. Comparing the binding likelihoods of SPDs of human and swine on different IAV HA proteins, we showed that swine's SPD has a higher binding likelihood towards the glycans of HA proteins.

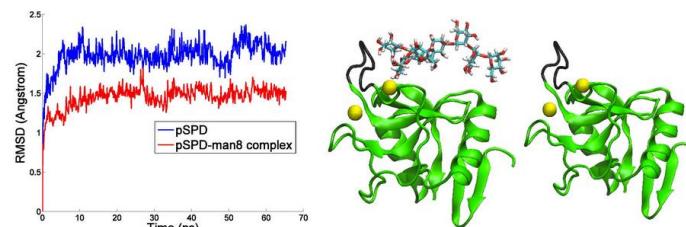
## Introduction

Influenza is an infectious disease that continues to cause severe illness and deaths annually worldwide. To infect a host cell, HA on the surface of IAV's viral envelope, binds and subsequently fuses the IAV membrane to the host cell membrane. The collectin protein of SPD binds to the glycan chain of HA, which leads to functional inhibition of HA and reduction in virulence of IAV.



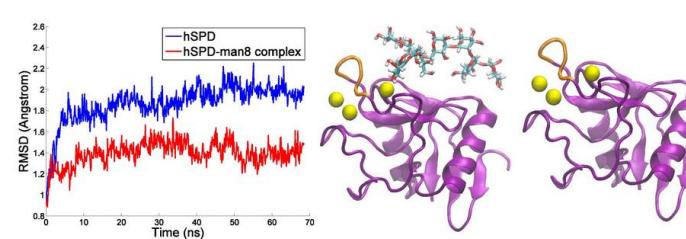
This computational work compares the flexibility of the loop region of porcine and human SPDs. It also shows reduction of flexibility upon glycan binding.

## Porcine SPD (pSPD)-Glycan Interaction



Based on an rmsd calculation between the globular head of pSPD, simulations of pSPD-man8 complex and free pSPD revealed that the pSPD-man8 complex fluctuates less and therefore is conformationally more stable than pSPD alone.

## Human SPD (hSPD)-Glycan Interaction



Calculations show that rmsd values for free hSPD are larger than for a hSPD-man8 complex.

The results of pSPD and hSPD are consistent with the hypothesis that glycan binding reduces the flexibility of SPD.

## Simulation Methods

Protein	Glycan	Time (ns)
pSPD	Mannose-8	65
pSPD	None	65
hSPD	Mannose-8	68
hSPD	None	68

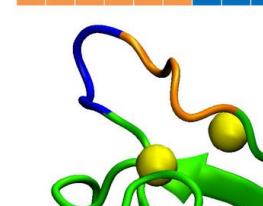
The pSPD-mannose-8 (man8) complex was determined by molecular docking with Glide using the pSPD crystal structure as the receptor for the man8 model. hSPD-man8 complex was obtained from overlay of the pSPD and hSPD crystal structures to align the docked man8 of the pSPD conformation in the lectin site of hSPD. The protein structures of pSPD and hSPD without man8 were generated by removing the mannose residues via VMD.

The simulations were performed using NAMD 2.8 [2] with CHARMM27 for proteins, CHARMM36 for carbohydrates and TIP3P water model. Na<sup>+</sup> and Cl<sup>-</sup> ions were added to neutralize the system. The complexes were simulated in NVT ensemble at temperature of 310K using a Langevin-Brownian thermostat and pressure of 1 atm via the Langevin Nosé-Hoover method.

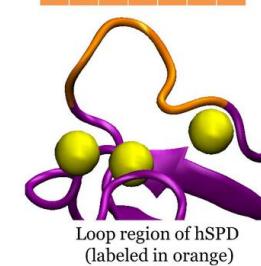
## Flexibility Comparison of the Loop Region of the SPDs

Compared with the amino acid sequence of hSPD, pSPD has an insertion of three amino acids (329S,330G,331A) at the loop region close to collectin binding site. This insertion has been suggested to be functionally important [3]. We term this 3-residue-longer loop a 'lip' as we hypothesize this lip increases the likelihood of capturing the glycan chain of HA.

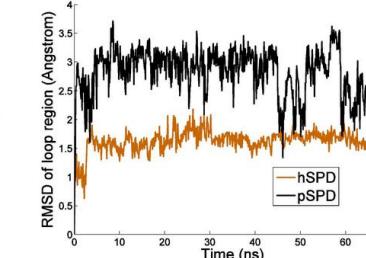
N N N G G S S G A E



N D D G G S E



Loop region of pSPD (labeled in orange) with the three-residue-insertion (labeled in blue)



Rmsd of the loop regions of free pSPD and hSPD are calculated. The lip of pSPD has higher rmsd values than hSPD almost throughout the simulation.

The three-residue-insertion introduces more flexibility to pSPD and increases the likelihood of binding to HA glycan of IAV.

## Future Work

This comparative study between pSPD and hSPD allows one to understand the effect of amino acid insertion on the binding affinity of SPD.

Starting from docked structures between crystallized proteins of different strains of IAV and species of SPD, MD simulations will be performed to investigate the interaction between SPD and glycan of HA and identify the most stable docking configuration of the SPD-HA complex.

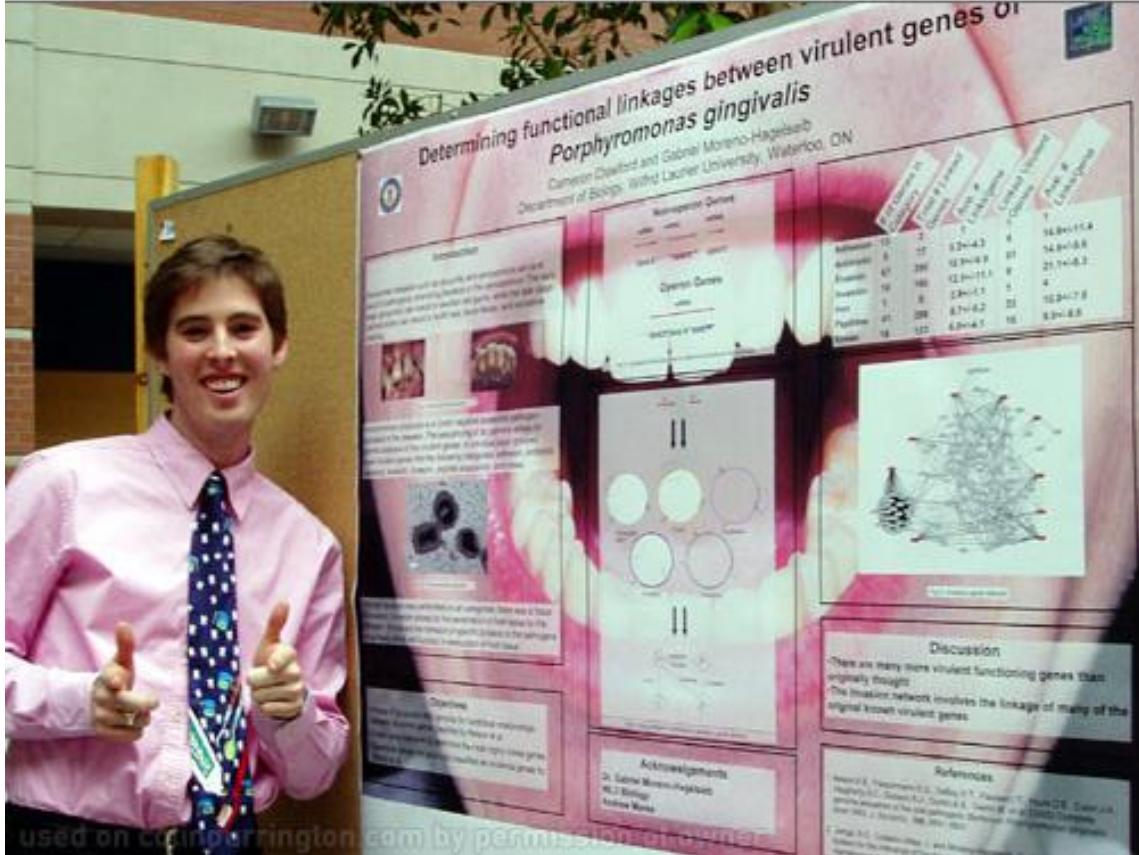
## Acknowledgement

This work was supported by grants from NIH P41-RR005969, NIH AI 083222 (to B.A.S.) and NSF PHY0822613. The authors gratefully acknowledge the use of the parallel computing resource provided by the Computational Science and Engineering (CSE) Program at the University of Illinois. All figures were produced by using VMD [4].

## References

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- [4] W. Humphrey, et al, *J. Mol. Graphics* (1996) **14**:33-38

For the next session (Mon February 7)



GOOD LUCK