Summer Research Program (SRP)

EPFL
School of Life Sciences
Impact Report 2024

School of Life Sciences

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School of Life Sciences

A word from the program directors

Since the establishment of the Summer Research Program (SRP) in 2006, more than 400 international students have had the opportunity to visit EPFL and, for a brief 2-month period become a part of its ecosystem. 2024 was a record year for us, receiving over 1000 applications from scholars worldwide. We believe that this level of interest speaks to the academic merits of the program and the stellar reputation of EPFL research. Through a careful selection process, 21 exceptional students representing 15 countries were invited to join host labs at the School of Life Sciences over this past summer.

SRP features a comprehensive professional development program. In addition to expanding their practical skills through participation in research projects and access to state-of-the-art infrastructure on campus, SRP scholars also attend workshops on career development, scientific integrity, leadership, and ecology. Their training is complemented with regular social events, such as international potlucks, beach BBQs and visits to the breathtaking alpine villages. Through these experiences, SRP participants discover Switzerland, connect with their peers, both scientifically and culturally, forge long-lasting friendships and build bridges of understanding.

The final event in the program is a closing symposium, where our students present their research projects to the EPFL scientific community at large. This past summer, over 100 collaborators and visitors joined together to celebrate the hard work put in by these young researchers and their supervisors, contributing to a very successful conclusion of 2024 activities.

As the 20th anniversary of the SRP approaches, we are hard at work assembling another dynamic program to catalyze the personal and professional growth in these future scientists.

Aleksandar Antanasijevic

Gioele La Manno

Summer Research Program

This summer, our laboratories welcomed 21 outstanding future researchers representing 15 different nationalities. The SRP strives to discover and nurture talent and potential worldwide, from all backgrounds.

Benefits to the Students

The participants:

- Gain hands-on interdisciplinary research experience.
- Put classroom learning into action to solve current research problems.
- Improve critical thinking skills by evaluating scientific information, designing experiments and testing hypotheses.
- Experience the excitement and challenges of scientific research gaining insight into what a research career entails.
- Present their research to the local scientific community during lab meetings and at the closing symposium.
- Prepare for future independent research projects and advanced research in graduate school.

Selection criteria

Fellowships are awarded on a competitive basis, applicants are required to have completed two years of undergraduate study in a life sciences program, be in the top 5% of their class, demonstrate a strong potential and have a keen interest in a life sciences career.

Facts

Over the last 19 years, SRP has grown to be a truly international program.

- 16% of the participants return to the EPFL to continue their studies in some capacity.
- 482 students were selected from over 10’267 applicants.
- A living stipend is provided and the majority of travel expenses are covered by program sponsors and the School of Life Sciences.
- Housing in Lausanne for the duration of the stay is provided.
- The working language is English.

School of Life Sciences

Hands-on research experience

SRP Students dive into eight weeks of hands-on research, each matched to a lab that suits their background and interests. As part of a research team, under the mentorship of lab heads or group members, they work on specific projects within our five institutes. They explore interdisciplinary questions in neuroscience, global health, bioengineering, and cancer research.

Visits and Cultural Activities

Students visit research hubs like Campus Biotech in Geneva and the Agora Cancer Research Center in Lausanne, experiencing the importance of collaboration in sciences. Social events, such as BBQs, a Swiss mountain hike, and cultural awareness activities, encourage community building and broaden cultural perspectives.

Weekly Talks & Workshops

Weekly workshops bring students together with EPFL faculty, visiting external experts, and EPFL alumni. Topics range from scientific integrity to climate and sustainability challenges, as well as career testimonials from principal investigators and alumni. These workshops inspire a strong sense of community and prepare students for leadership roles in life sciences.

Joint Symposium with UNIL’s SUR Program

A highlight at the end of the summer, the Joint Symposium with the Summer Undergraduate Program (SUR) of the University of Lausanne provides a platform for students to present their research findings, network with peers, and gain valuable presentation experience.

List of participants

	Name	Country	Lab	Sponsor
IBI	**Pavel Feskin**	Russia	Maerkl	Fondation ISREC
	Paria Khalafi	Iran	Dal Peraro	Fondation Valifonds
	Marlene Maager	Germany	Barth	Fondation ISREC
	Fateme Ramezan Zade	Iran	Rahi	Fondation ISREC
	Anna-Lee Thompson	USA	Manley	ThinkSwiss/Ernst Göhner Stiftung
	Elenis Milenys Vergara Martinez	Panama	Sakar	McCall MacBain Foundation
	Wenhui Wang	China	Tang	UCB Community Health Fund
ISREC	**Minjun An**	USA	Thomä	ThinkSwiss/Ernst Göhner Stiftung
	Rebekah Hormigos	Philippines	Brisken	McCall MacBain Foundation
	Alica Kapáková	Slovakia	Karthaus	Ernst Göhner Stiftung
	Alejandro Efraín Marin Peralta	Mexico	Waszak	Fondation Jacqueline Cornaz
	Zhansaya Matkenova	Kazakhstan/Qatar	Gönczy	Fondation ISREC
GHI	**Arpine Grigoryan**	Armenia	Persat	McCall MacBain Foundation
	Arpine Grigoryan	Armenia	Van der Goot	Ernst Göhner Stiftung
	Ketura Yaje Gwei	Cameroon	Antanasijevic	Ernst Göhner Stiftung
	Aditi Arun	India	Schrimpf	McCall MacBain Foundation
Neuro-X	**Oscar Cruz**	Canada	Van de Ville	McCall MacBain Foundation
	Levi Goldberg	USA	Blanke	ThinkSwiss/Ernst Göhner Stiftung
BMI	**Alexa Di Pede**	Canada	McCabe	McCall MacBain Foundation
	Emily Nurden	England	Herzog	Anonymous donor
	Heliya Shakeri	Iran	Mathis A.	Protechno Foundation

IBI: Insitute of Bioengineering

ISREC: Swiss Institute for Experimental Cancer Research

GHI: Global Health Institute

Neuro-X: Institute of Neurosciences, Neurotechnology and Neurocomputation for medicine

BMI: Brain Mind Institute

Participating professors

IBI

Patrick
Barth

Matteo
Dal Peraro

Suliana
Manley

Sebastian
Maerkl

Sahand
Rahi

Selman
Sakar

Li
Tang

ISREC

Kathrin
Brisken

Pierre
Gönczy

Wouter
Karthaus

Nicolas
Thomä

Sebastian
Waszak

GHI

Aleksandar
Antanasijevic

Alexandre
Persat

Gisou
van der Goot

Neuro-X

Olaf
Blanke

Martin
Schrimpf

Dimitri
Van de Ville

BMI

Michael
Herzog

Alexander
Mathis

Brian
McCabe

Participating students

IBI

Pavel
Feskin

Paria
Khalafi

Marlene
Maager

Fateme
Ramezan Zade

Anna-Lee
Thompson

Elenis Milenys
Vergara Martinez

Wenhui
Wang

ISREC

Minjun
An

Rebekah
Hormigos

Alica
Kapáková

Alejandro Efraín
Marin Peralta

Zhansaya
Matkenova

GHI

Arpine
Grigoryan

Arpine
Grigoryan

Ketura Yaje
Gwei

Neuro-X

Aditi
Arun

Oscar
Cruz

Levi
Goldberg

BMI

Alexa
Di Pede

Emily
Nurden

Heliya
Shakeri

Pavel FESKIN

MSU - Lomonosov Moscow State University

Maerkl Laboratory of Biological Network Characterization (LBNC)

Supervisor : Pao-Wan Lee

Pavel is supported by Fondation ISREC

Abstract :

In synthetic biology, we design gene circuits and networks that function like the wiring in electronic devices. These engineered circuits allow cells to process information and make decisions, addressing the challenge of precisely controlling cellular functions. Oscillator and noise filter circuits have been already built in living system based gene circuits design. However, the circuit size is still limited by the availability of components in biological system.

In our study, we constructed artificial repression components. Specifically, we developed a programmable way to repress T7 promoter and designed molecular NAND logic gate. This work reveals new way for designing programmable repressors of gene circuits.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Paria KHALAFI

Sharif University of Technology

Dal Peraro Lab for Biomolecular Modeling

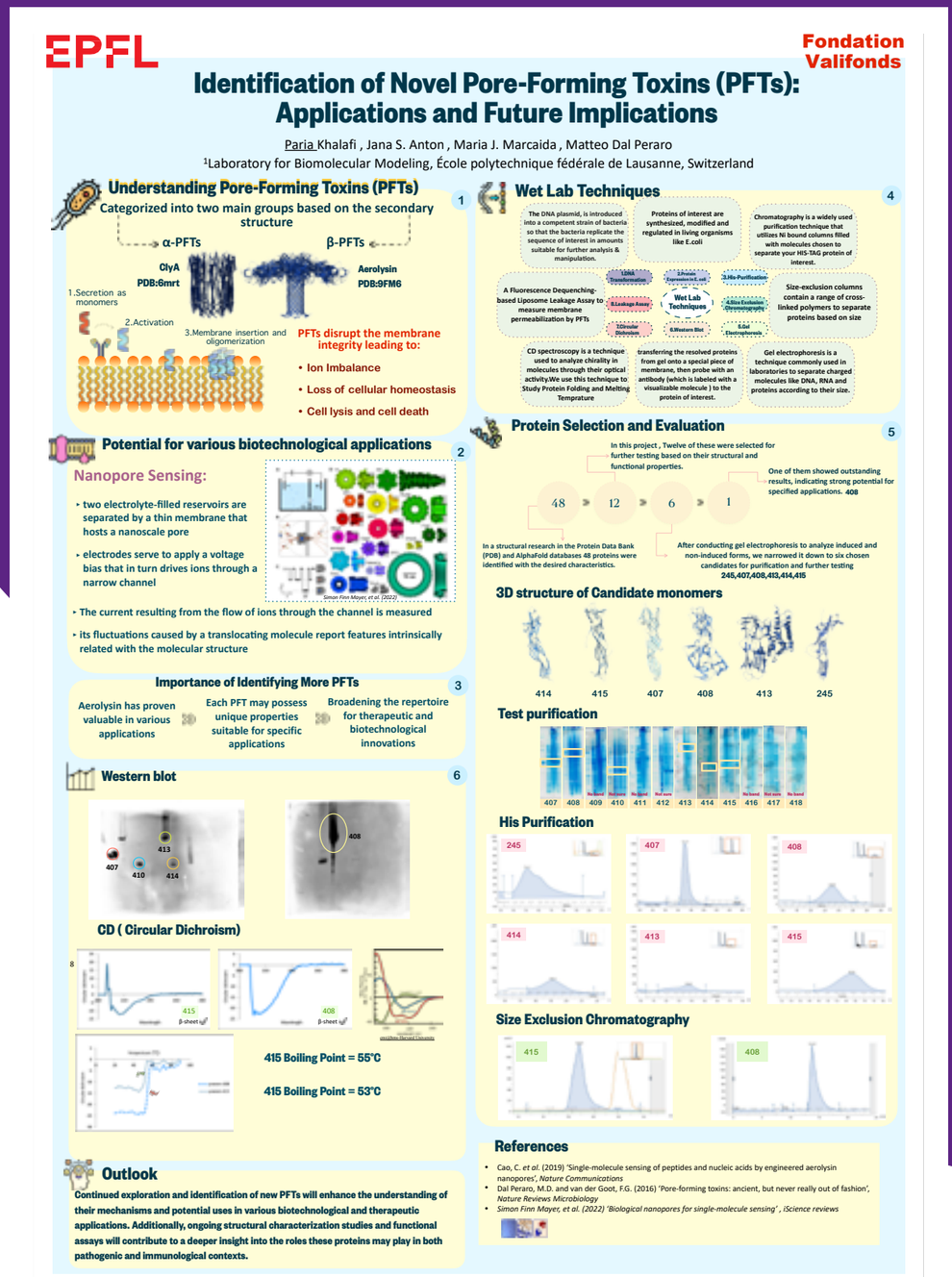
Supervisor : Jana Susanne Anton

Paria is supported by Fondation Valifonds

Abstract :

This project aims to investigate new pore-forming toxins (PFTs), focusing on their structural variations and potential applications in molecular sensing. The objective of the lab is to explore the structure- function relationships of these toxins, particularly aerolysin. Previous findings highlight the role of electrostatics and pore diameter in determining ion selectivity and sensing capabilities, inspiring our aim to identify and characterize other PFTs to expand their application in biotechnological fields.

To achieve this, we will employ advanced computational methods like Alphafold and Foldseek to identify unknown proteins similar to PFTs, followed by structural characterization methods. By integrating these approaches, we aspire to uncover novel insights into the functional roles of PFTs and leverage their tunable properties for various applications, thus advancing our understanding and utilization of these remarkable biological molecules.



Marlene MAAGER

Ruprecht-Karls-Universität Heidelberg

Barth Lab of Protein and Cell Engineering

Supervisors : Shuhao Zhang, Aurélien Oggier

Marlene is supported by Fondation ISREC

Abstract :

G protein-coupled receptors (GPCRs) represent important gateways in transmitting a wide variety of signals into cells, thereupon triggering diverse responses. Building GPCRs from scratch would allow for novel and tunable properties not found in nature, which might pave the way for synthetic biology and therapeutic applications.

To address the challenging task of creating such dynamic and complex molecular machines, this project combines computational and experimental techniques. After conducting biochemical tests on receptor candidates generated using AI tools, we approach the refinement of our design strategy and the optimization of its output.

Towards computational *de novo* GPCR design

Marlene Maager, Shuhao Zhang, Aurélien Oggier, Patrick Barth*

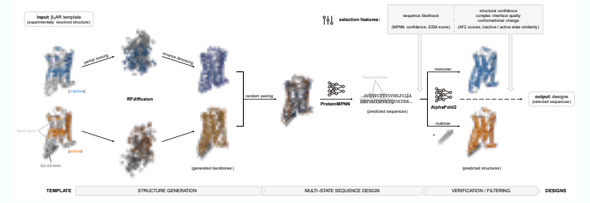
Laboratory of Protein and Cell Engineering, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland

Motivation

- **G protein-coupled receptors (GPCRs) …**
  - … constitute a major family of membrane receptors, with more than 800 members in humans
  - … couple a wide variety of extracellular signals to diverse signaling pathways in order to control cellular function
  - … are involved in a large number of diseases and therefore represent important therapeutic targets
- ***De novo* design of GPCRs …**
  - … overcomes the limited sequence / structural space of natural receptors
  - … allows for novel and tunable functions
- Challenge: design of **dynamic membrane** proteins with **complex intramolecular interactions**

Computational design pipeline:

- structural template: β_2-adrenergic receptor = prototypic class A GPCR
- essential sites for structure / function can be kept fixed (e.g. ligand- / G protein-binding residues, conserved GPCR motifs)



- The **aim of this project** is to contribute to the *de novo* design of GPCRs and to help understand whether signaling can be achieved through novel folds …
  - … by experimentally validating selected receptor designs and
  - … by optimizing the computational sequence generation

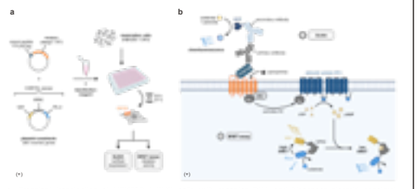
computational design / refinement

Wet lab: characterize nine previously generated receptor designs *in vitro* based on expression / activity measurements

Dry lab: generate new receptor designs + attempt a systematic *in silico* optimization of selected candidates towards high foldability / stability

experimental validation / testing

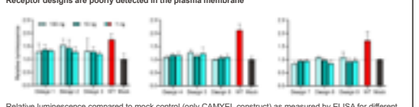
TOOLBOX



a. Transient transfection of HEK293 / CHO cells with receptor DNA and biosensor plasmid construct. CAMYEL = cAMP sensor using YFP-EPAC-RLuc; YFP = yellow fluorescent protein; RLuc = *Renilla* luciferase. **b.** ELISA for measuring surface expression (1); BRET-based activity assay (2). HRP = horseradish peroxidase.

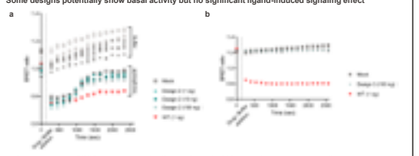
RESULTS

Receptor designs are poorly detected in the plasma membrane



Relative luminescence compared to mock control (only CAMYEL construct) as measured by ELISA for different amounts of transfected receptor plasmid DNA (*n* = 3).

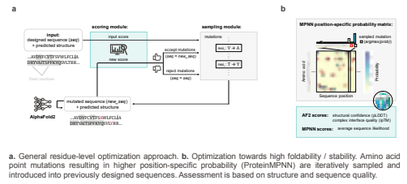
Some designs potentially show basal activity but no significant ligand-induced signaling effect



a. Time-dependent BRET signal curves for Design 2 in HEK293 cells after treatment with RLuc substrate and ligand (100 µM epinephrine) (*n* = 3). **b.** BRET signal for Design 3 in CHO cells (*n* = 2). Buffer controls in gray.

- Surface expression and functionality of the tested designs can neither be conclusively verified nor rejected
- Possible causes for insufficient plasma membrane presentation have to be identified and addressed (e.g. alter transfection / expression conditions, optimize plasmid construct for protein translocation, redesign receptor sequences)

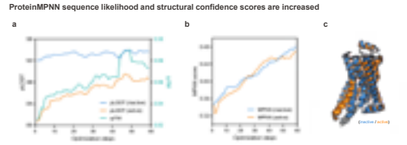
TOOLBOX



a. General residue-level optimization approach. **b.** Optimization towards high foldability / stability. Amino acid point mutations resulting in higher position-specific probability (ProteinMPNN) are iteratively sampled and introduced into previously designed sequences. Assessment is based on structure and sequence quality.

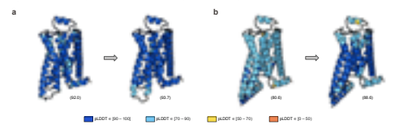
RESULTS

ProteinMPNN sequence likelihood and structural confidence scores are increased



Example run: **a.** AlphaFold2 predicted structural confidence scores (pLDDT) and receptor : G protein interface quality (ipTM) for accepted mutations. **b.** ProteinMPNN average probability of sequence given the structure. **c.** Overlay of final predicted inactive and active structure.

AlphaFold2 becomes more confident in the local fold of transmembrane helices



Example run: Predicted structures after first / last optimization step for **a.** inactive and **b.** active state, colored by AlphaFold2 local confidence band. Respective global scores are given in brackets.

- The proposed strategy proves promising for potentially enhancing foldability / stability of designs
- Further development of this *in silico* tool could increase the success rate for experimental validation *in vitro* and also allow for optimization of other properties or towards specific features in the context of engineering

References: J. L. Watson *et al. Nature* **620**, 1089-1100 (2023) ● J. Dauparas *et al. Science* **378**, 49-56 (2022) ● M. Mirdita *et al. Nat Methods* **19**, 679-682 (2022) ● L. I. Jiang *et al. J Biol Chem* **282**, 10576-10584 (2007)

(*) Figures created with **BioRender.com**

Fateme RAMEZAN ZADE

Sharif University of Technology

Rahi Lab of the Physics of Biological Systems

Supervisor: Alice Gross

Fateme is supported by Fondation ISREC

Abstract :

C. elegans, a tiny roundworm known for its simple brain structure and behaviors, presents a unique opportunity to understand neural computation principles. The internal brain state is believed to determine the worm's locomotive response to chemical stimuli. As a proof, the brain state is manipulated by histamine silencing pairs of the second-layer interneurons in chemosensory network and the change in the rate of exhibiting a specific behavior is examined. Also, a control experiment is performed to confirm that the of recovery of the network is immediate.

EPFL ISREC

Unraveling Internal Brain States by Interneuron Manipulation in *C. elegans*

Fateme Ramezanzade, Alice Gross, Sahand Rahi

Laboratory of the Physics of Biological Systems, École Polytechnique Fédérale de Lausanne (EPFL)

Introduction

C. elegans, a tiny roundworm known for its simple brain structure and behaviors, presents a unique opportunity to understand neural computation principles.

The internal brain state is believed to determine the worm's locomotive response to chemical stimuli. [1] As a proof, the brain state is manipulated by histamine silencing pairs of the second-layer interneurons in chemosensory network and the change in the rate of exhibiting a specific behavior is examined. Also, a control experiment is performed to confirm that the of recovery of the network is immediate.

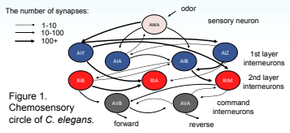


Figure 1. Chemosensory circle of *C. elegans*.

Methods

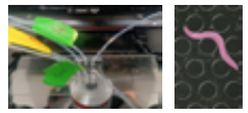


Fig. 2. Microfluidic chip used for experiments (left) and segmented image of the worm inside the chip (right).

Histamine Silencing: Transgenic worms engineered to express inhibitory histamine-gated chloride (HisCl) channels [2] in specific interneurons enable the controlled and reversible silencing of these neurons using histamine.

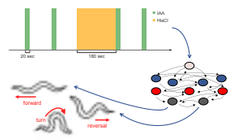
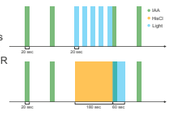


Fig. 3. Experimental procedure. Moving in a microfluidic arena, the worm receives histamine as well as pulses of IAA which acts as an attractive odor.The change in its locomotor behavior is examined.

Optogenetic Activation: Blue light activates interneurons expressing channelrhodopsine (ChR), a light-gated ion channel, facilitating precise control of neural activity. [3]

Fig. 4. Control experiment procedures with RIB::ChR mutant (up) and RIB::HisCl::ChR mutant (down).



Results

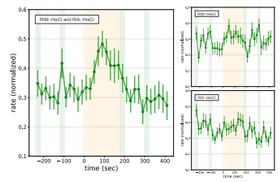


Fig. 5. Forward locomotion rate (normalized) of mutants expressing both RIM::HisCl and RIA::HisCl (left), and each of them (right). The activity is dominated by RIM in the crossed mutant.

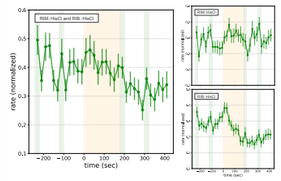


Fig. 6: Forward locomotion rate (normalized) of mutants expressing both RIM::HisCl and RIB::HisCl (left), and each of them (right). The behavior of the crossed mutant is in between.

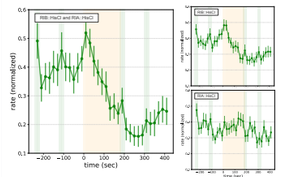


Fig. 7: Forward locomotion rate (normalized) of mutants expressing both RIB::HisCl and RIA::HisCl (left), and each of them (right). The activity is decreased in the crossed mutant due to dominancy of RIB.

Control Experiment

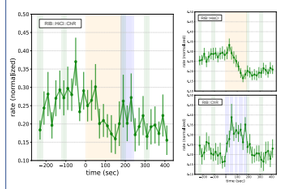


Fig. 8. Forward locomotion speed (normalized) of mutants expressing RIB::HisCl::ChR (left), and each of them (right) The normal activity is retrieved during the light pulse.

Conclusion

- Silencing both RIM and RIA mimics the effect of silencing RIM alone, indicating RIM's dominance.
- When both RIB and RIA are silenced, behavior is intermediate between the effects of silencing each individually.
- Silencing both RIM and RIB closely matches the effect of silencing RIB alone, as predicted by the network.
- Silencing RIB alone does not restore normal activity, suggesting the delay is due to an altered brain state.
- A control experiment rescuing RIB function confirms behavioral changes were due to neural inhibition, as normal behavior was restored with light exposure.
- This project, as a part of a larger plan, helps to link the structural connectome to behavior.

References

[1] Flavell, S. W., et al. (2022). The emergence and influence of internal states. Neuron, 110(16), 2545–2570.

[2] Pokala, N., et al. (2014). Inducible and titratable silencing of Caenorhabditis elegans neurons in vivo with histamine-gated chloride channels. Proc Natl Acad Sci , 111(7), 2770–2775.

[3] Larsch, J., et al. (2015). A Circuit for Gradient Climbing in C. elegans Chemotaxis. Cell Reports, 12(11), 1748–1760.

Anna-Lee THOMPSON

Smith College

Manley Lab of Experimental Biophysics

Supervisors : Giorgio Tortarolo, Suliana Manley

Anna-Lee is supported by ThinkSwiss Scholarships/Ernst Göhner Stiftung

Abstract :

Mitochondrial membrane potential (MMP) is a biophysical property of mitochondria that plays a central role in cellular metabolism and is a key indicator of cell viability.

Here we successfully compared the MMP visualization capabilities of two dyes; TMRE which is traditionally used and an alternative SPIRIT RhoVR which allows for a more precise localization and measurement of MMP.

Our results demonstrate that both TMRE and SPIRIT RhoVR localize in mitochondria. By improving the accuracy of MMP quantification and visualization, we aim to deepen our understanding of mitochondrial function and the biophysical mechanisms underlying cellular metabolism and health.

Improving Mitochondrial Membrane Potential Measurement: Analysis of TMRE and SPIRIT RhoVR Dyes using Fluorescence Microscopy

Anna-Lee Thompson[1], Giorgio Tortarolo[1], Suliana Manley[1]

[1] Institute of Bioengineering, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Introduction

- The inner mitochondrial membrane is essential for cell metabolism
  - Proton pumps regulate membrane potential (MMP).[1]

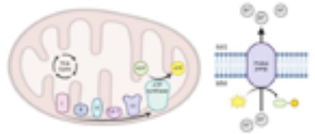


Figure 1. *MMP is regulated by proton pumps within the ETC. Protons are pumped from the mitochondrial matrix (MM) to the intermembrane space (IMS).*

- MMP is most commonly visualized using cationic, lipophilic, rhodamine ester dyes.[2]
  - Limitations: accumulation based, sensitivity, self-quenching

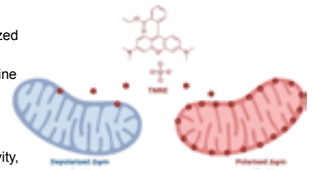


Figure 2. *TMRE structure and labeling mechanism. Figure by Woodley (2023).*[3]

Goals:

1. Examine the localization of TMRE in mitochondria
2. Implement new SPIRIT RhoVR dye
3. Use an optogenetic voltage depolarizer to control membrane potential and compare dye measurements.

Methods

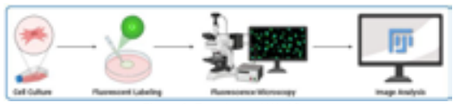


Figure 3. *Experimental Workflow*

Live-Cell Imaging Techniques:

1. Widefield Microscopy - fluorescence intensity measurements in COS7 cells
2. Fluorescence Lifetime Microscopy (FLIM) - TMRE lifetime measurements in U2OS cells

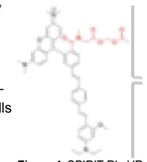


Figure 4. *SPIRIT RhoVR structure.*

Fluorescent Dyes:

- MitoTracker Green (MTG) - mitochondria
- TMRE - MMP, accumulation based
- SPIRIT RhoVR - MMP, activation based
  - "On/off" mechanism via photo-induced electron transfer (PeT).[4]

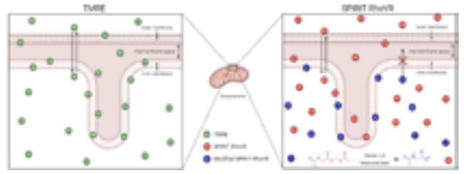


Figure 5. *TMRE vs. SPIRIT RhoVR mechanism of action.*

Results

FLIM to Investigate TMRE Mitochondrial Striping

- Fluorescence lifetime can change with the environment and can be an indicator of pH, molecule binding, or other factors.[5]

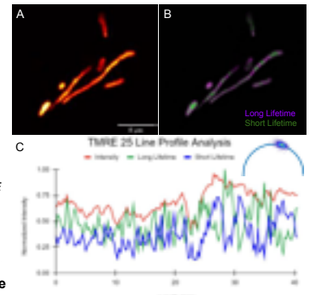


Figure 6. *Fluorescent lifetime striping on TMRE labeled U2OS cells. (A) fluorescence intensity image, (B) lifetime image, (C) line profile plot and phasor diagram.*

Optogenetic Voltage Depolarizer

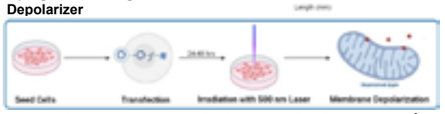


Figure 7. *Procedure for implementing the optogenetic voltage depolarizer.*[6]

- Altered cell and mitochondria morphology
  - Needs further optimization

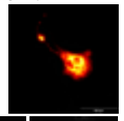


Figure 8. *Image of a COS7 cell transfected with voltage reporter revealed by the fusion YF protein.*

TMRE vs. SPIRIT Images

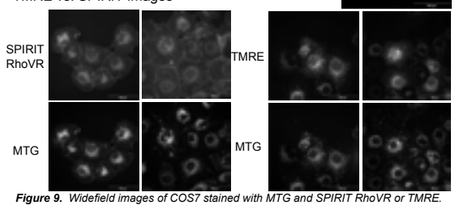


Figure 9. *Widefield images of COS7 stained with MTG and SPIRIT RhoVR or TMRE.*

Conclusion

- Both TMRE and SPIRIT RhoVR localize in mitochondria
- One fluorescence lifetime image of TMRE revealed unprecedented mitochondrial striping
  - Possibly linked to mitochondrial pearling (segmentation).
- Successful preliminary comparison of SPIRIT RhoVR with TMRE
- **Future Directions:**
  - Vary concentration of SPIRIT to minimize cytoplasm staining
  - Optimize optogenetic voltage depolarizer
  - Try out different voltage depolarizers/hyperpolarizers to examine the speed/sensitivity of both dyes

Acknowledgements

I am thankful to Dr. Suliana Manley and Dr. Giorgio Tortarolo for their guidance throughout this project, as well as all members of the Laboratory of Experimental Biophysics. I also grateful for the training provided by Nicolas Chiaruttini at the EPFL BioImaging and Optics Platform. I would also like to thank Alice Emery-Goodman, Dr. Aleksandar Antanasijevic, Dr. Gioele La Manno, and everyone involved in running the EPFL School of Life Sciences Summer Research Program. All figures were made using BioRender and ChemDraw.

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5. Kuschel, L., & DeRose, J. (2022). *What is FLIM - Fluorescence Lifetime Imaging Microscopy?*

Elenis Milenys VERGARA MARTINEZ

Florida International University

Sakar Lab of Microbiorobotic Systems

Supervisor : Lorenzo Francesco John Noseda

Elenis is supported by McCall MacBain Foundation

Abstract :

3D Navigation of a Ribbon - Shaped Microrobot for Brain Interventions

Minimally invasive neurosurgical techniques can significantly enhance the treatment of neurological diseases and brain tumors. As the need for greater precision and control arises, microrobotic surgery becomes crucial, providing the capability to navigate the brain's intricate environment with improved accuracy while minimizing tissue damage.

This study advances an existing ribbon-shaped microrobot, initially designed for planar movement, by incorporating a third degree of freedom for 3D navigation and characterizing its twisting capabilities.

Through these enhancements and the use of novel fabrication techniques, the microrobot gains superior adaptability, control, and accuracy, which are essential for exploring delicate brain structures and performing effective interventions.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Wenhui WANG

Southern University of Science and Technology

Tang Lab of Biomaterials for Immunoengineering

Supervisor : Weilin Li

Wenhui is supported by UCB Farchim

Abstract :

Over the past decade, Chimeric Antigen Receptor T-cell (CAR-T) therapy has transformed cancer treatment by successfully targeting previously untreatable blood cancers. However, scientists have struggled to extend this success to solid tumors, which make up over 90% of cancers.
Our research focuses on genetically modifying CAR-T cells to enhance their ability to kill solid tumors. We have discovered that adding mechano-enhancement intracellular domains improves CAR-T cell function, making them more effective at attacking stiffened tumor cells. This work could help make CAR-T therapy a viable option for solid tumor treatment in the future.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Minjun AN

University of Michigan, Ann Arbor

Thomä Lab – Paternot Chair in Cancer Research

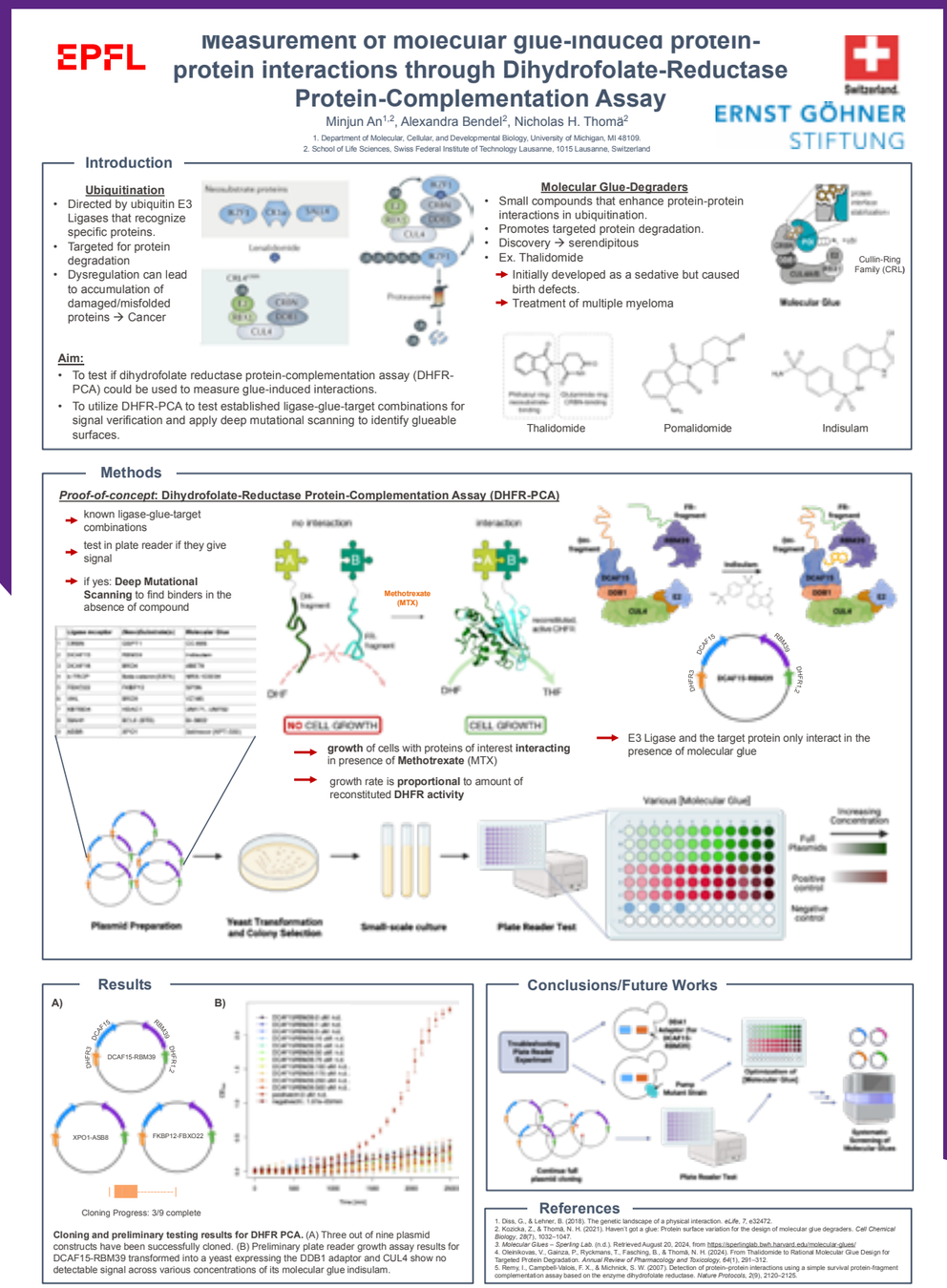
Supervisor: Alexandra Bendel

Minjun is supported by ThinkSwiss Scholarships/Ernst Göhner Stiftung

Abstract :

Molecular glues are small molecules that can induce novel interactions between E3 ubiquitin ligases and proteins causing protein degradation. This holds great potential in drug development. Up to now, there is no systematic screening method to measure the effectiveness of these glue-induced interactions. To address this, we tested the performance of Dihydrofolate-Reductase Protein-Complementation Assay (DHFR-PCA) with a well known glue-induced protein-protein interactions as a proof-of-concept testing its applicability for systematic screening of molecular glues.

These results will guide further development of an experimental pipeline to systematically identify molecular glue degraders for any target protein of interest.



Rebekah HORMIGOS

University of the Philippines - Diliman

Brisken Lab - Hormones: Keys to Breast Cancer Prevention and Therapy

Supervisors : Pranay Dey, Cathrin Brisken

Rebekah is supported by McCall MacBain Foundation

Abstract :

Recent research has shown that testosterone levels slightly increase during certain points in the menstrual cycle in women. This, along with other hormones like estrogen and progesterone, may play a previously uncharacterized role in how breast tissue changes throughout the menstrual cycle. Further, patient-to-patient variation has long been ignored due to technical challenges. The aim of this project is to investigate the complex ways by which estrogen, progesterone, and testosterone-regulated signaling might interact to drive the changes in human breast tissue throughout the menstrual cycle.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Alica KAPÁKOVÁ

Charles University

Karthaus Lab of Endocrine Therapy Resistance and Molecular Genetics

Supervisor : Ester Simkova

Alica is supported by Ernst Göhner Stiftung

Abstract :

Prostate cancer is diagnosed in 1 of 8 men worldwide and displays a wide genetic variability. To better understand the disease, we use organoids—3D structures that replicate the key complexities of human organs.

My project involves designing guides for CRISPR technology to knock out genes commonly deleted in prostate cancer. By introducing these guides into human prostate organoids, we create models that enable the study of cancer progression and the real-time effects of specific gene alterations.

EPFL ERNST GÖHNER STIFTUNG

MODELING PROSTATE CANCER *IN VITRO*: ORGANOIDS AS A WINDOW INTO TUMOR DIVERSITY

Alica Kapáková [2,1], Ester Simkova[1], Wouter R. Karthaus[1]

[1] Laboratory of Endocrine Therapy Resistance and Molecular Genetics, EPFL-ISREC, [2] Charles University in Prague

Introduction

- **1 in 8 men** are diagnosed with prostate cancer in their life
- Heterogenous disease due to its diverse mutational profile
- Understanding relations between specific **gene alterations** and **resulting cancer phenotype** is crucial in determining targets for personalized treatment, stratifying patients and studying disease progression

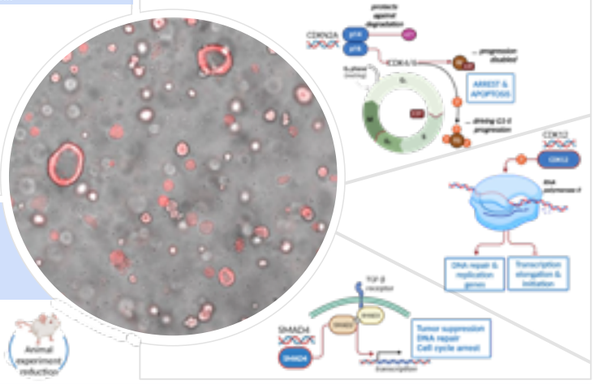
Figure 1: Diverse mutational profiles in prostate cancer

- **Organoids** are self-organized 3D structures mimicking the key complexity of an organ
- Patient-specific organoids can be derived from clinical biopsies

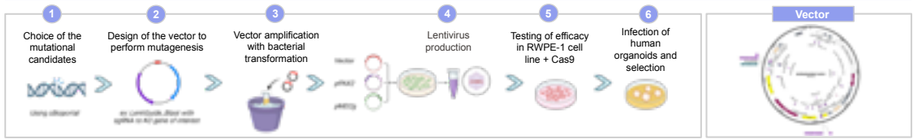
Objectives

- Create guides for CRISPR-mediated knockout (KO) of genes commonly deleted in prostate cancer – **CDK12, CDKN2A, SMAD4**
- Observe effects of KO in organoids on cancer phenotype, proliferation rate and metastatic potential

Figure 2: Signaling pathways of the genes of interest:



Methods



Results

Figure 3: Western blot showing gene knockout efficiency and resulting protein expression in RWPE-1 with Cas 9 cell line

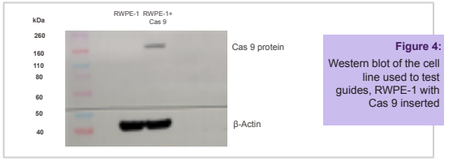


Figure 4: Western blot of the cell line used to test guides, RWPE-1 with Cas 9 inserted

Conclusion

- Results have shown that **guide 2 is a good candidate for CDK12 KO**.
- **SMAD4** KO guide 2 seems to **reduce protein expression** compared to the non-targeting control
- **The presence of p16 was not detected**, potentially due to a overly long blocking time
- The next step would be to test successful guides in prostate organoids to model genetic KO observed in patients
- The models will allow us to study prostate cancer progression ***in vitro*** and track the effects of genetic mutations **in real time**

References

Jillian R Love et al.; Next-Generation Modeling of Cancer Using Organoids, Cold Spring Harb Perspect Med. (2024) 1.
Shujing Liang et al.; CDK12: A Potent Target and Biomarker for Human Cancer Therapy, Cells. (2020) 2.
The Cancer Genome Atlas Research Network; The molecular taxonomy of primary prostate cancer, Cell (2015) 3.

Alejandro Efraín MARIN PERALTA

National Autonomous University of Mexico

Waszak Lab of Computational Neuro-Oncology

Supervisor : Schuyler Stoller

Alejandro is supported by Fondation Jacqueline Cornaz

Abstract :

Liquid biopsy is advancing oncology by offering a minimally-invasive method to detect and monitor solid tumors. Dying cancer cells secrete fragmented genomic DNA into circulation (eg, blood) and sequencing of cell-free DNA can pick up tumor-specific molecular changes. In brain tumor patients, cell-free DNA can be also found in body fluids such as cerebrospinal fluid (CSF), which surrounds the brain and spinal cord.
Taking liquid biopsies via spinal taps emerges as a new approach to monitor brain tumors over time.
In this project, we tracked evolutionary trajectories of aggressive childhood brain tumors during therapy using cell-free genomics.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Zhansaya MATKENOVA

Carnegie Mellon University in Qatar

Gönczy Lab of Cell and Developmental Biology

Supervisor : Gabriela Garcia Rodriguez

Zhansaya is supported by Fondation ISREC

Abstract :

This research project focuses on the dynamics of de novo centriole formation in human cells. Typically, centrioles duplicate from existing ones, much like copying a blueprint. However, under certain experimental conditions, cells can form new centrioles from scratch, without a template. This study addresses the critical question of how these de novo centrioles arise and function in the absence of pre-existing ones.

The dynamics of de novo centriole formation were investigated via live imaging. De novo centrioles emerge sequentially rather than simultaneously in small increments. The Cep135 protein appears to be one of the earliest centriolar markers to emerge, followed by the addition of Cep63 and the formation of microtubule doublets and triplets. The Cep135 protein appears to be one of the earlier centriolar markers to emerge, followed by Cep63 and addition of microtubule doublets and triplets detected by CenSpark650.

Dynamics of *de novo* centriole formation in human cells

Zhansaya Matkenova[1, 2], Gabriela Garcia Rodriguez[2], Pierre Gönczy[2]

[1]Carnegie Mellon University in Qatar

[2]Laboratory of Cell and Developmental Biology, École Polytechnique Fédérale de Lausanne (EPFL)

Introduction

Centrioles are cylindrical organelles with a striking ninefold radial symmetry (Fig. 1). They play a crucial role in cell signalling and motility, as they template the axoneme of cilia and flagella; and in cell division, as part of the centrosome, which is the major Microtubule Organizing Center (MTOC) of most animal cells. The canonical pathway of centriole formation entails that daughter centrioles are formed from pre-existing ones via duplication (Fig. 2A). However, in human cycling cells (*p53-/-*) centrioles can be depleted by inhibiting duplication with Centrinone, which is a small molecule inhibitor of PLK4, a kinase essential for centriole formation. As these cells divide in absence of centrioles via Pericentrin and Cep192-dependent spindle MTOCs, centrioles dilute in the population. Upon release from Centrinone, and recovery of PLK4 activity, cells begin to assemble centrioles *de novo*, that is in absence of pre-existing ones. *De novo* formation in human cells results in a random number of centrioles that are structurally and functionally indistinguishable from intact canonical ones (Fig. 2B). In this research project, the dynamics of *de novo* centriole formation were investigated via live imaging of endogenously fluorophore-tagged cell lines. We found that *de novo* centrioles appear sequentially in RPE-1::*p53-/-* cells upon Centrinone release.

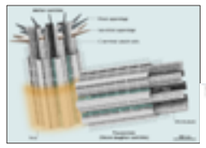


Figure 1. Canonical centriole duplication (Gönczy & Hatzopoulos, 2019).

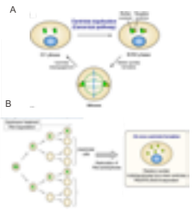
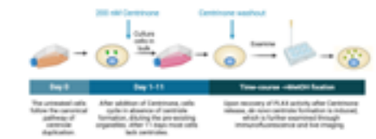


Figure 2. (A) Canonical centriole duplication cycle. (B) Experimental induction of *de novo* centriole formation. (Takumi & Kitagawa, 2022).

Methods



i. Experimental induction of *de novo* centriole formation

Cycling RPE-1::*p53-/-* cells, human retinal pigment epithelial cells with p53 knockout, were used to prevent cell cycle arrest caused by centriole depletion from Centrinone treatment. Post-Centrinone washout (Cent WO), cells were methanol fixed at increasing timepoints.

ii. Long-term Live Imaging

Live microscopy was used to assess the dynamics of *de novo* centriole emergence using the endogenously tagged cell line RPE-1::*p53-/-*; mScarlet-Cep63; GFP-Cep135, incubated with CenSpark650 to determine the timing of microtubule doublet addition.

Conclusions and Perspectives

- *De novo* centrioles emerge sequentially rather than simultaneously in small increments (1-2 centrioles) and during S and G2 phases of the cell cycle.
- Cep135 foci become detectable early during *de novo* centriole formation after Centrinone release, while Cep63 foci are occasionally detected early, followed by their disappearance and subsequent recruitment later in mitosis or early G1 of the next cell cycle. CS650 starts co-localizing with Cep135 foci after approximately 17-18 hours post-Centrinone release.

References

Gönczy, P., & Hatzopoulos, G. N. (2019). Centriole Assembly at a glance. *Journal of Cell Science, 132*(4).

Takumi, K., & Kitagawa, D. (2022, March 14). *Experimental and natural induction of de Novo Centriole Formation.* Frontiers.

Results

1. Sequential appearance of *de novo* centrioles revealed by long-term live microscopy.

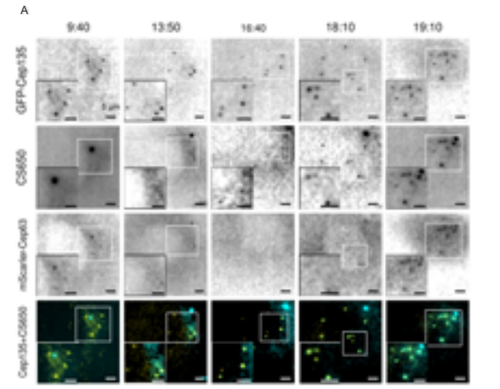


Figure 3. (A) Representative frames from a movie of RPE-1::*p53-/-*; mScarlet-Cep63; GFP-Cep135 incubated with CS650 for 1h. Recording started 9 hours after Centrinone release. Insets show magnified ROIs in each image. (B) Schematic representation of a centriole highlighting the localization of Cep63, Cep135 and doublet and triplet MTs. (C) Counts of GFP-Cep135, mScarlet-Cep63 and CS650 foci per timepoint of the movie (10 mins frames) for a single cell. (D) GFP-Cep135 number of foci per timepoint for 11 cells. (E) The maximum number of Cep135 foci and the time of emergence relative to mitosis for the 11 cells shown in D.

Arpine GRIGORYAN

Yerevan State University

Persat Lab of Microbial Mechanics

Supervisors : Tania Distler, Lucas Meirelles, Alexandre Persat

Arpine is supported by McCall MacBain Foundation

Abstract :

Chronic lung infections represent a significant global health challenge due to their recalcitrance to antibiotic treatment and debilitating effects on patients' lives. In these patients, bacterial pathogens, such as Pseudomonas aeruginosa, persist and interact with host cells for years. These pathogens thrive in the airway environment, causing inflammation, tissue damage, and a severe decrease in respiratory function.

We use single-cell transcriptomics to study the impact of small molecules secreted by P. aeruginosa on tissue regeneration. Our work shed light on how the pathogen may be able to steer tissue differentiation and modulate disease progression.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Arpine GRIGORYAN

Technical University or Munich (TUM)

Van der Goot Lab of Cell and Membrane Biology

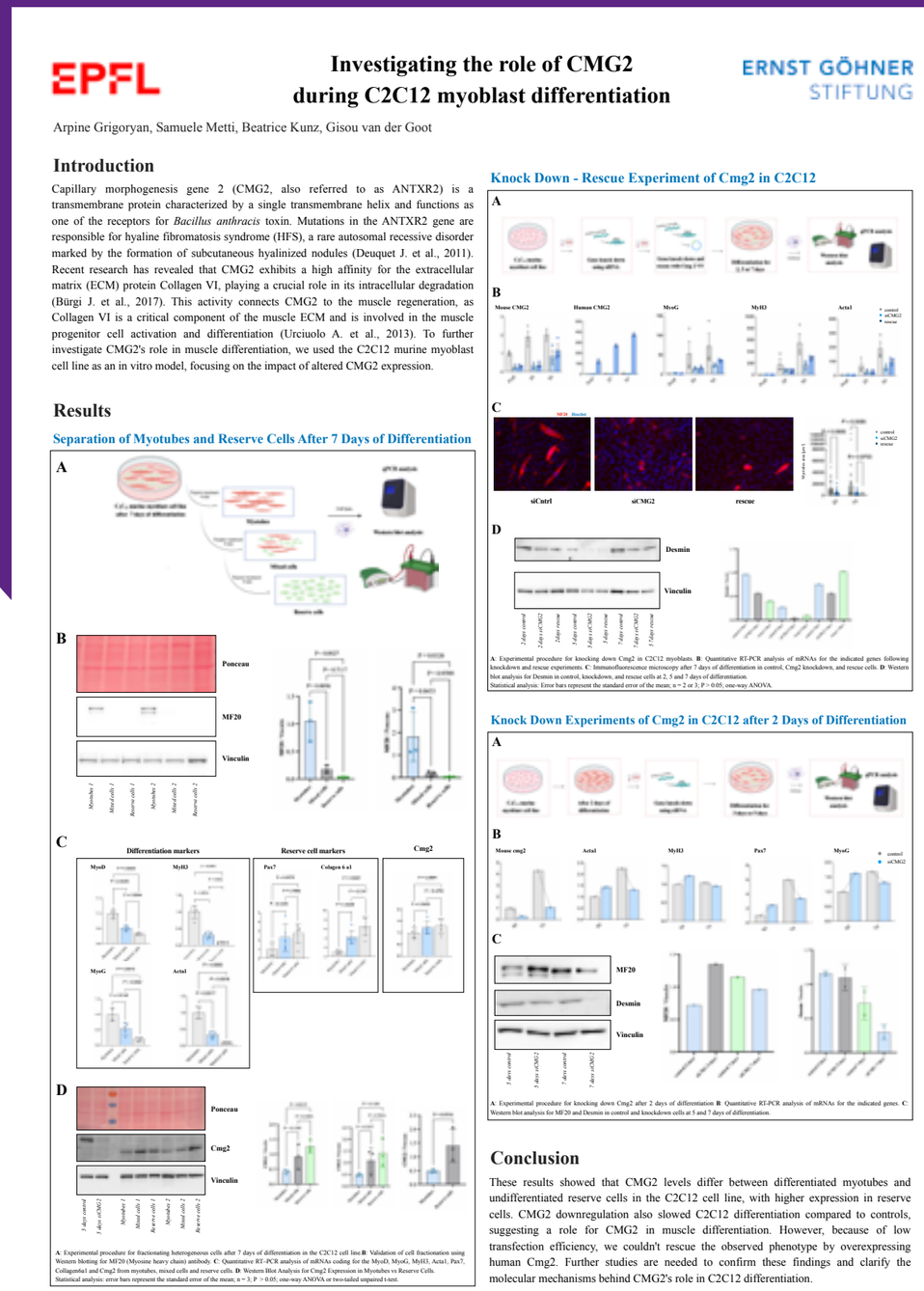
Supervisor : Samuele Metti

Arpine is supported by Ernst Göhner Stiftung

Abstract :

Capillary morphogenesis gene 2 (CMG2), a receptor for Bacillus anthracis toxin, has been linked to muscle regeneration through its interaction with the extracellular matrix protein Collagen VI. Using the C2C12 murine myoblast cell line, I explored CMG2's role in muscle differentiation.

The findings indicate that CMG2 expression is higher in undifferentiated reserve cells compared to differentiated myotubes, and its downregulation slows the differentiation process.



EPFL

Investigating the role of CMG2 during C2C12 myoblast differentiation

ERNST GÖHNER STIFTUNG

Arpine Grigoryan, Samuele Metti, Beatrice Kunz, Gisou van der Goot

Introduction

Capillary morphogenesis gene 2 (CMG2, also referred to as ANTXR2) is a transmembrane protein characterized by a single transmembrane helix and functions as one of the receptors for *Bacillus anthracis* toxin. Mutations in the ANTXR2 gene are responsible for hyaline fibromatosis syndrome (HFS), a rare autosomal recessive disorder marked by the formation of subcutaneous hyalinized nodules (Deuquet J. et al., 2011). Recent research has revealed that CMG2 exhibits a high affinity for the extracellular matrix (ECM) protein Collagen VI, playing a crucial role in its intracellular degradation (Bürgi J. et al., 2017). This activity connects CMG2 to the muscle regeneration, as Collagen VI is a critical component of the muscle ECM and is involved in the muscle progenitor cell activation and differentiation (Urciuolo A. et al., 2013). To further investigate CMG2's role in muscle differentiation, we used the C2C12 murine myoblast cell line as an in vitro model, focusing on the impact of altered CMG2 expression.

Results

Separation of Myotubes and Reserve Cells After 7 Days of Differentiation

A: Experimental procedure for fractionating heterogeneous cells after 7 days of differentiation in the C2C12 cell line.**B**: Validation of cell fractionation using Western blotting for MF20 (Myosine heavy chain) antibody. **C**: Quantitative RT–PCR analysis of mRNAs coding for the MyoD, MyoG, MyH3, Acta1, Pax7, Collagentrôa1 and Cmg2 from myotubes, mixed cells and reserve cells. **D**: Western Blot Analysis for Cmg2 Expression in Myotubes vs Reserve Cells.
Statistical analysis: error bars represent the standard error of the mean; n = 3; P > 0.05; one-way ANOVA or two-tailed unpaired t-test.

Knock Down - Rescue Experiment of Cmg2 in C2C12

A: Experimental procedure for knocking down Cmg2 in C2C12 myoblasts. **B**: Quantitative RT-PCR analysis of mRNAs for the indicated genes following knockdown and rescue experiments. **C**: Immunofluorescence microscopy after 7 days of differentiation in control, Cmg2 knockdown, and rescue cells. **D**: Western blot analysis for Desmin in control, knockdown, and rescue cells at 2, 5 and 7 days of differentiation.
Statistical analysis: Error bars represent the standard error of the mean; n = 2 or 3; P > 0.05; one-way ANOVA.

Knock Down Experiments of Cmg2 in C2C12 after 2 Days of Differentiation

A: Experimental procedure for knocking down Cmg2 after 2 days of differentiation **B**: Quantitative RT-PCR analysis of mRNAs for the indicated genes. **C**: Western blot analysis for MF20 and Desmin in control and knockdown cells at 5 and 7 days of differentiation.

Conclusion

These results showed that CMG2 levels differ between differentiated myotubes and undifferentiated reserve cells in the C2C12 cell line, with higher expression in reserve cells. CMG2 downregulation also slowed C2C12 differentiation compared to controls, suggesting a role for CMG2 in muscle differentiation. However, because of low transfection efficiency, we couldn't rescue the observed phenotype by overexpressing human Cmg2. Further studies are needed to confirm these findings and clarify the molecular mechanisms behind CMG2's role in C2C12 differentiation.

Ketura Yaje GWEI

University of Buea

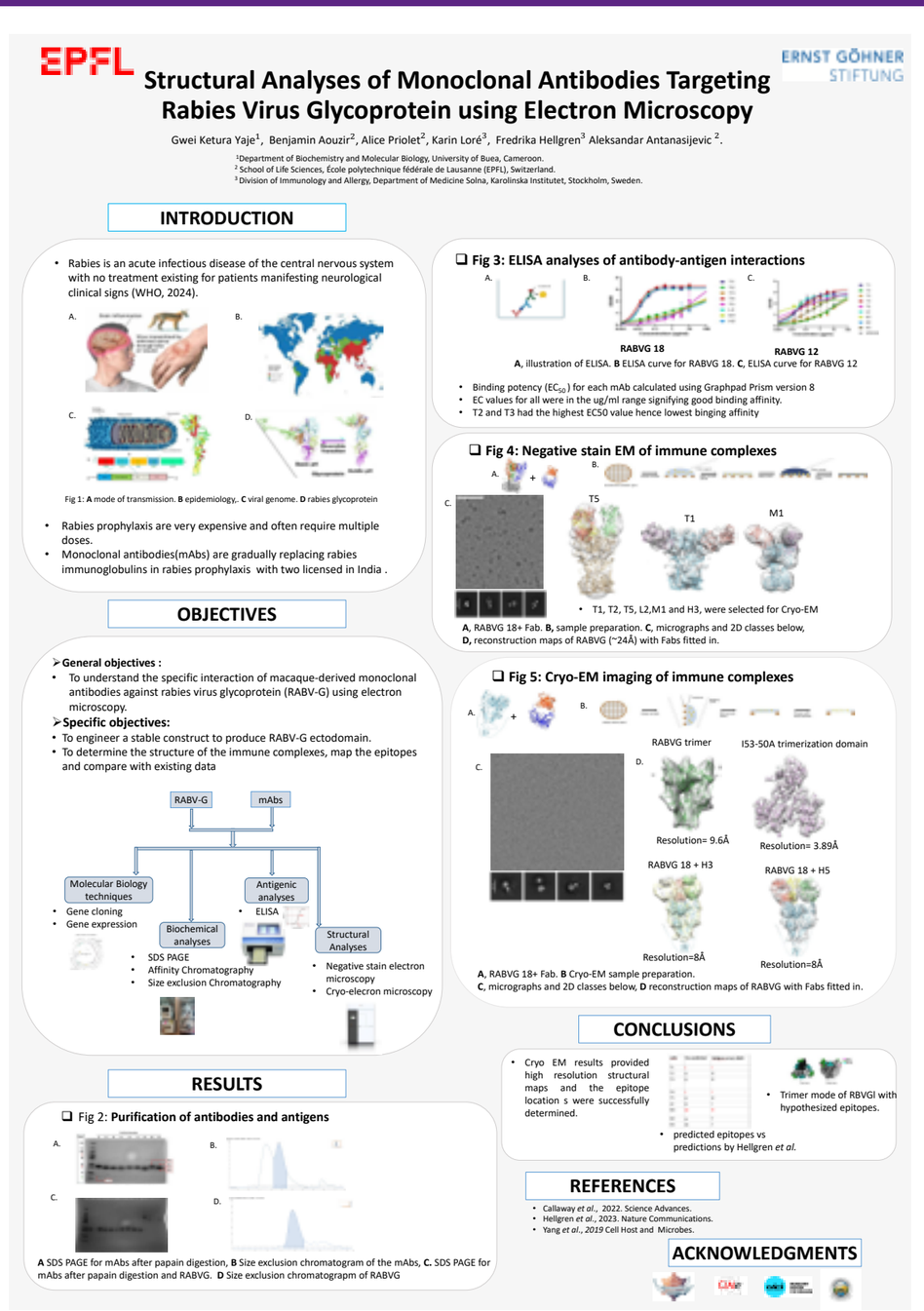
Antanasijevic Lab of Virology and Structural Immunology

Supervisor: Aleksandar Antanasijevic

Ketura is supported by Ernst Göhner Stiftung

Abstract :

Rabies is a serious disease of the central nervous system with no cure for patients showing neurological signs. About 5,000 people die of rabies every year. To prevent and treat rabies, vaccines, and immunoglobulins are used, but they are quite costly and require multiple doses. Monoclonal antibodies (mAbs) are becoming a more cost-effective and safe alternative to rabies immunoglobulins. This project seeks to understand the interaction between mAbs from macaques that were given an mRNA vaccine with the rabies virus glycoprotein (RABVG). The interactions between two different RABVG structures and nine mAbs were analyzed using advanced microscopy techniques. The epitopes were mapped successfully allowing us to learn more about how these antibodies work.
The results reveal important structural information that could help in developing new treatments for rabies.



EPFL

ERNST GÖHNER STIFTUNG

Structural Analyses of Monoclonal Antibodies Targeting Rabies Virus Glycoprotein using Electron Microscopy

Gwei Ketura Yaje[1], Benjamin Aouzir[2], Alice Priolet[2], Karin Loré[3], Fredrika Hellgren[3] Aleksandar Antanasijevic [2].

[1]Department of Biochemistry and Molecular Biology, University of Buea, Cameroon.
[2] School of Life Sciences, École polytechnique fédérale de Lausanne (EPFL), Switzerland.
[3] Division of Immunology and Allergy, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden.

INTRODUCTION

- Rabies is an acute infectious disease of the central nervous system with no treatment existing for patients manifesting neurological clinical signs (WHO, 2024).

A. B. C. D.

Fig 1: **A** mode of transmission. **B** epidemiology,. **C** viral genome. **D** rabies glycoprotein

- Rabies prophylaxis are very expensive and often require multiple doses.
- Monoclonal antibodies(mAbs) are gradually replacing rabies immunoglobulins in rabies prophylaxis with two licensed in India .

OBJECTIVES

➢ **General objectives :**
- To understand the specific interaction of macaque-derived monoclonal antibodies against rabies virus glycoprotein (RABV-G) using electron microscopy.

➢ **Specific objectives:**
- To engineer a stable construct to produce RABV-G ectodomain.
- To determine the structure of the immune complexes, map the epitopes and compare with existing data

RESULTS

❑ Fig 2: **Purification of antibodies and antigens**

A. B. C. D.

A SDS PAGE for mAbs after papain digestion, **B** Size exclusion chromatogram of the mAbs, **C.** SDS PAGE for mAbs after papain digestion and RABVG. **D** Size exclusion chromatogrpm of RABVG

❑ **Fig 3: ELISA analyses of antibody-antigen interactions**

A. B. C.

RABVG 18 RABVG 12

A, illustration of ELISA. **B** ELISA curve for RABVG 18. **C**, ELISA curve for RABVG 12

- Binding potency (EC_{50}) for each mAb calculated using Graphpad Prism version 8
- EC values for all were in the ug/ml range signifying good binding affinity.
- T2 and T3 had the highest EC50 value hence lowest binging affinity

❑ **Fig 4: Negative stain EM of immune complexes**

A. B. C.

T5 T1 M1

- T1, T2, T5, L2,M1 and H3, were selected for Cryo-EM

A, RABVG 18+ Fab. **B,** sample preparation. **C**, micrographs and 2D classes below, **D,** reconstruction maps of RABVG (~24Å) with Fabs fitted in.

❑ **Fig 5: Cryo-EM imaging of immune complexes**

A. B. C. D.

RABVG trimer I53-50A trimerization domain

Resolution= 9.6Å Resolution= 3.89Å

RABVG 18 + H3 RABVG 18 + H5

Resolution=8Å Resolution=8Å

A, RABVG 18+ Fab. **B** Cryo-EM sample preparation.
C, micrographs and 2D classes below, **D** reconstruction maps of RABVG with Fabs fitted in.

CONCLUSIONS

- Cryo EM results provided high resolution structural maps and the epitope location s were successfully determined.
- Trimer mode of RBVGl with hypothesized epitopes.
- predicted epitopes vs predictions by Hellgren *et al.*

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ACKNOWLEDGMENTS

Aditi ARUN

Indian Institute of Science

Schrimpf Lab for NeuroAI

Supervisors : Johannes Mehrer, Martin Schrimpf

Aditi is supported by McCall MacBain Foundation

Abstract :

Human subjects have been found to exhibit several deficits in visual perception after a stroke. In this study, we aim to understand the causal relation between brain lesions in and visual deficits through ANN models. Using topographic neural-networks as models of the visual cortex, we simulate post-stroke lesions to predict visual behavior. Our models replicate behaviors observed in stroke patients, such as visual neglect and perception tasks, using data from key studies.

This approach offers insights into the visual system's mechanisms and provides a framework to evaluate clinical interventions, advancing our understanding of brain-lesion effects and their impact on perception.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Oscar CRUZ

McGill University

Van de Ville Lab of Medical Image Processing

Supervisors : Alex Cionca, Michael Chun Hei

Oscar is supported by McCall MacBain Foundation

Abstract :

This research explores how communication network modeling techniques can be applied to the brain's connectome. By understanding and optimizing how these connections function, we aim to gain new insights into brain activity, potentially leading to better understanding and treatment of neurological disorders. Using fractional programming through convex optimization, two algorithms were tested: one for power control, favoring less connected brain regions, and another for energy efficiency, focusing on more connected areas. The distinct power distribution patterns observed suggest that different brain activities may require unique optimization strategies.

Oscar Cruz, Chun Hei Michael Chen, Alexandre Cionca,
Professor Dimitri Van De Ville
Medical Image Processing Lab
School of Life Sciences, EPFL, Geneva, Switzerland

Power Distribution of Communication Networks Applied to the Brain Connectome

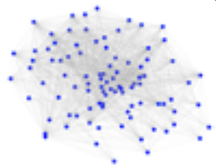
Goal

- Translate communication network modeling system techniques to the brain.
- Use of fractional programming through convex optimization.
- Exploratory research on the possible use case of the models on the brain connectome and their effectiveness.

Results

- The power control algorithm allocates more power to the lesser connected regions. The plot of power and degree shows some decay.
- The energy efficiency algorithm allocates more power to the more connected regions. The plot of power and degree is linear.
- The efficiency function for both algorithms converge.

A. Brain connectome **B. Optimization problem formulation**



$$\underset{x}{\text{maximize}} \sum_{m=1}^{M} \frac{A_m(x)}{B_m(x)}$$

$$\underset{x,y}{\text{maximize}} \sum_{m=1}^{M} \left(2y_m\sqrt{A_m(x)} - y_m^2 B_m(x)\right)$$

$$y_m^\star = \frac{\sqrt{A_m(x)}}{B_m(x)}, \forall m = 1, \ldots, M$$

Figure 1: (**Fig A**) Lausanne 2018 brain connectome (**Fig B**) The upper formula is the multiple ratio fractional programming followed by the quadratic transform, y is an auxiliary variable.

Data and Methodology

- The brain connectome used as input is from 2018 generated by the MIP laboratory, from diffusion weighted imaging and tractography.
- Testing the algorithm for the power control problem for a downlink SISO (single in single out) cellular network with a set of single antenna base stations each serving a single antenna base user.
- Testing the algorithm for the energy maximization problem for a multiple-link case.
- Use of a quadratic transform to go from fractional programming to convex optimization.
- Testing algorithmic stability by changing starting conditions throughout iterations.

Power control algorithm

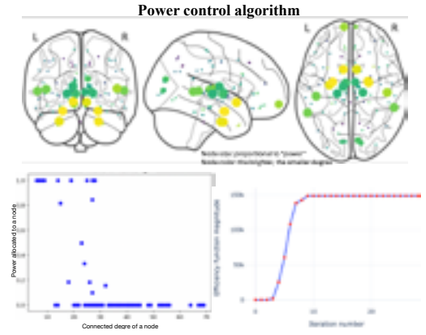


Figure 3: On top is the allocation of power in the brain. Bottom left is the plot of power and the degree of connections. Bottom right is the efficiency function.

A. Efficiency functions

$$A^{(n)}(\mathbf{v}, \mathbf{y}) = \sum_{m=1}^{M} 2y_m\sqrt{v_m^{(n)}} - \sum_{m=1}^{M} y_m^2 \left(\sum_{k=1}^{K} |h_{km}^H \mathbf{v}_k|^2 + \sigma^2\right)$$

$$f_{\text{EE}}(\mathbf{v}^{(n)}, \mathbf{y}^{(n)}) = 2y\left(\sum_{m=1}^{M} \log\left(1 + 2\mathbf{v}^{(n)}\mathbf{G}_m\mathbf{v}^{(n)}\right) - M\left(\mathbf{v}^{(n)}\mathbf{v} + \sum_{m=1}^{M} \mathbf{v}_m\mathbf{v}_m^{(n)}\mathbf{G}_m^{(n)}\mathbf{v}_m\right)\right)^2 - \mathbf{v}^{(n)}\sum_{m=1}^{M} \|\mathbf{v}_m\|_2^2 + P_{\text{max}}$$

B. Power control history **C. Energy efficiency history**

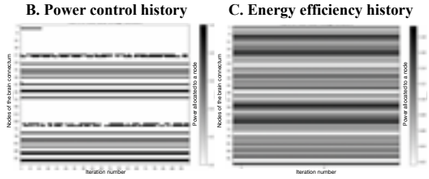


Figure 2: (**Fig A**) On top is the power control algorithm efficiency function. Below is the energy efficiency maximization efficiency function. (**Fig B**) The matrix shows some variability in the same regions (**Fig C**) The matrix shows no variability.

Energy efficiency maximization algorithm

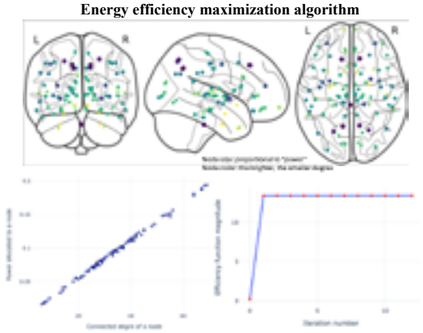


Figure 4: On top is the allocation of power in the brain. Bottom left is the plot of power and the degree of connections. Bottom right is the efficiency function.

Conclusion

- The presence of a decay in the plot of power and degree in the power control algorithm may indicate that there can be different decays for different brain activities, unlike the linearity of the other algorithm.
- The algorithms have opposite behaviour as the power control algorithm depends on the numerator and denominator while the energy efficency algorithm only depends on the denumerator.
- Further exploration including the use of binary inputs, weighting and imaginary signals may yield more conclusive results.

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Levi is supported by ThinkSwiss Scholarships/Ernst Göhner Stiftung

Abstract :

Our research explores how our sense of control, known as the «sense of agency,» affects the cognitive effort we put into tasks and how we weigh cost against rewards. By way of example, imagine trying to steer a car with loose steering; it requires more focus even though you're using the same physical effort.
We use a computerized task to modulate sense of agency and find correlations with apathy, a common symptom in several neurodegenerative diseases. Our study indicates this computerized paradigm could be a valuable tool for researchers to understand the mechanisms behind sense of agency and the effort-reward decision- making process.

To respect the confidentiality of unpublished results, we have included a concise abstract instead of the full poster for this project

Alexa DI PEDE

McMaster University

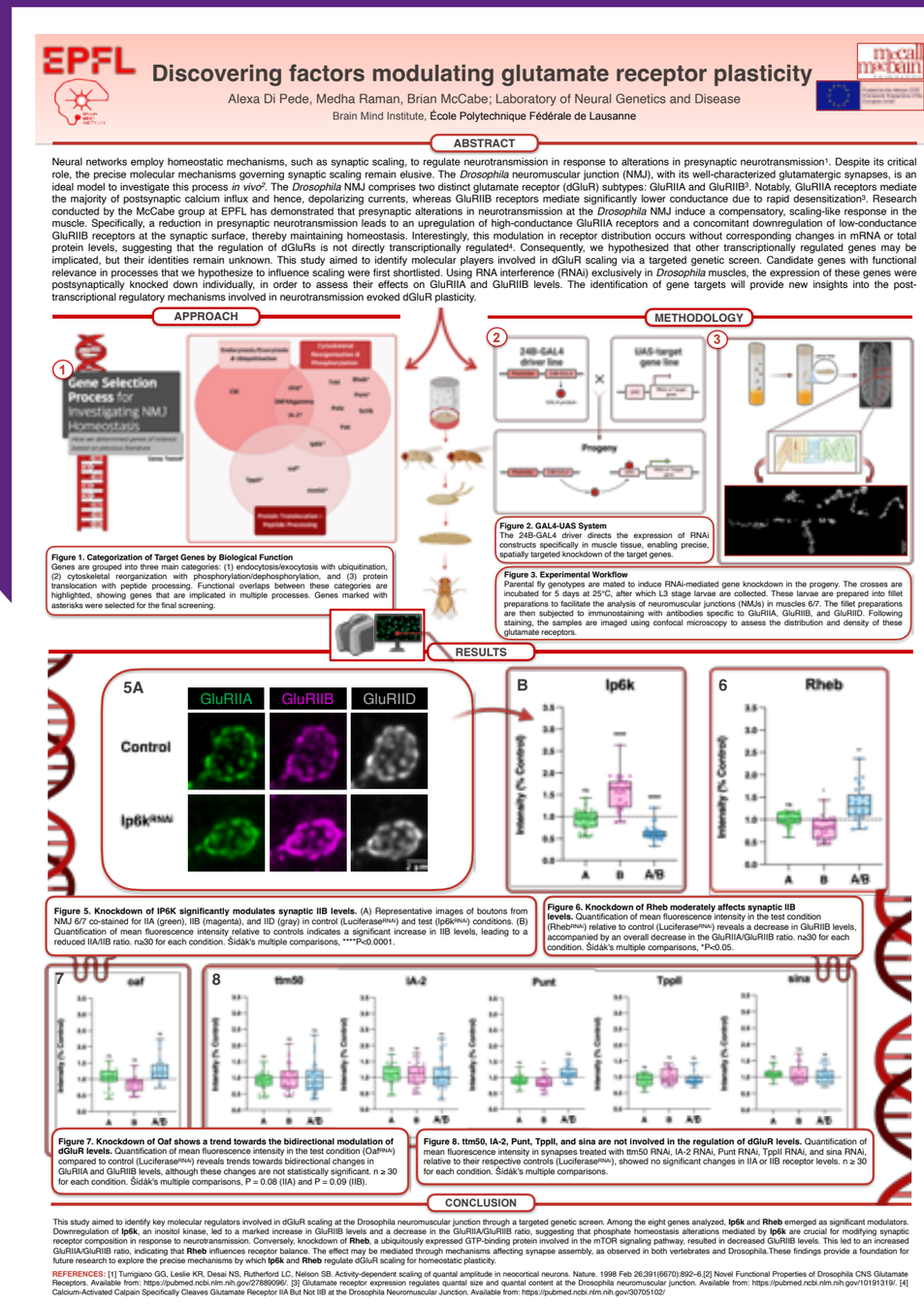
McCabe Lab of Neural Genetics and Disease

Supervisors : Medha Raman, Brian McCabe

Alexa is supported by McCall MacBain Foundation

Abstract :

Aberrations in neurotransmission alter postsynaptic receptor levels at the Drosophila neuromuscular junction. However, previous studies show that this occurs without corresponding changes in mRNA or total protein levels of the receptors. This suggests the involvement of other transcriptionally regulated genes. Our aim was to identify these genes through RNA interference. Among the genes analyzed, Ip6k, an inositol-kinase, and Rheb, a GTP-binding protein, emerged as significant modulators. This provides a foundation for future research exploring mechanisms underlying postsynaptic homeostatic plasticity.



EPFL

Discovering factors modulating glutamate receptor plasticity

Alexa Di Pede, Medha Raman, Brian McCabe; Laboratory of Neural Genetics and Disease

Brain Mind Institute, École Polytechnique Fédérale de Lausanne

ABSTRACT

Neural networks employ homeostatic mechanisms, such as synaptic scaling, to regulate neurotransmission in response to alterations in presynaptic neurotransmission[1]. Despite its critical role, the precise molecular mechanisms governing synaptic scaling remain elusive. The *Drosophila* neuromuscular junction (NMJ), with its well-characterized glutamatergic synapses, is an ideal model to investigate this process *in vivo*[2]. The *Drosophila* NMJ comprises two distinct glutamate receptor (dGluR) subtypes: GluRIIA and GluRIIB[3]. Notably, GluRIIA receptors mediate the majority of postsynaptic calcium influx and hence, depolarizing currents, whereas GluRIIB receptors mediate significantly lower conductance due to rapid desensitization[3]. Research conducted by the McCabe group at EPFL has demonstrated that presynaptic alterations in neurotransmission at the *Drosophila* NMJ induce a compensatory, scaling-like response in the muscle. Specifically, a reduction in presynaptic neurotransmission leads to an upregulation of high-conductance GluRIIA receptors and a concomitant downregulation of low-conductance GluRIIB receptors at the synaptic surface, thereby maintaining homeostasis. Interestingly, this modulation in receptor distribution occurs without corresponding changes in mRNA or total protein levels, suggesting that the regulation of dGluRs is not directly transcriptionally regulated[4]. Consequently, we hypothesized that other transcriptionally regulated genes may be implicated, but their identities remain unknown. This study aimed to identify molecular players involved in dGluR scaling via a targeted genetic screen. Candidate genes with functional relevance in processes that we hypothesize to influence scaling were first shortlisted. Using RNA interference (RNAi) exclusively in *Drosophila* muscles, the expression of these genes were postsynaptically knocked down individually, in order to assess their effects on GluRIIA and GluRIIB levels. The identification of gene targets will provide new insights into the post-transcriptional regulatory mechanisms involved in neurotransmission evoked dGluR plasticity.

APPROACH

Figure 1. Categorization of Target Genes by Biological Function
Genes are grouped into three main categories: (1) endocytosis/exocytosis with ubiquitination, (2) cytoskeletal reorganization with phosphorylation/dephosphorylation, and (3) protein translocation with peptide processing. Functional overlaps between these categories are highlighted, showing genes that are implicated in multiple processes. Genes marked with asterisks were selected for the final screening.

METHODOLOGY

Figure 2. GAL4-UAS System
The 24B-GAL4 driver directs the expression of RNAi constructs specifically in muscle tissue, enabling precise, spatially targeted knockdown of the target genes.

Figure 3. Experimental Workflow
Parental fly genotypes are mated to induce RNAi-mediated gene knockdown in the progeny. The crosses are incubated for 5 days at 25°C, after which L3 stage larvae are collected. These larvae are prepared into fillet preparations to facilitate the analysis of neuromuscular junctions (NMJs) in muscles 6/7. The fillet preparations are then subjected to immunostaining with antibodies specific to GluRIIA, GluRIIB, and GluRIID. Following staining, the samples are imaged using confocal microscopy to assess the distribution and density of these glutamate receptors.

RESULTS

Figure 5. Knockdown of IP6K significantly modulates synaptic IIB levels. (A) Representative images of boutons from NMJ 6/7 co-stained for IIA (green), IIB (magenta), and IID (gray) in control (Luciferase^{RNAi}) and test (Ip6k^{RNAi}) conditions. (B) Quantification of mean fluorescence intensity relative to controls indicates a significant increase in IIB levels, leading to a reduced IIA/IIB ratio. n≥30 for each condition. Šídák's multiple comparisons, ****P<0.0001.

Figure 6. Knockdown of Rheb moderately affects synaptic IIB levels. Quantification of mean fluorescence intensity in the test condition (Rheb^{RNAi}) relative to control (Luciferase^{RNAi}) reveals a decrease in GluRIIB levels, accompanied by an overall decrease in the GluRIIA/GluRIIB ratio. n≥30 for each condition. Šídák's multiple comparisons, *P<0.05.

Figure 7. Knockdown of Oaf shows a trend towards the bidirectional modulation of dGluR levels. Quantification of mean fluorescence intensity in the test condition (Oaf^{RNAi}) compared to control (Luciferase^{RNAi}) reveals trends towards bidirectional changes in GluRIIA and GluRIIB levels, although these changes are not statistically significant. n ≥ 30 for each condition. Šídák's multiple comparisons, P = 0.08 (IIA) and P = 0.09 (IIB).

Figure 8. ttm50, IA-2, Punt, Tppll, and sina are not involved in the regulation of dGluR levels. Quantification of mean fluorescence intensity in synapses treated with ttm50 RNAi, IA-2 RNAi, Punt RNAi, Tppll RNAi, and sina RNAi, relative to their respective controls (Luciferase^{RNAi}), showed no significant changes in IIA or IIB receptor levels. n ≥ 30 for each condition. Šídák's multiple comparisons.

CONCLUSION

This study aimed to identify key molecular regulators involved in dGluR scaling at the Drosophila neuromuscular junction through a targeted genetic screen. Among the eight genes analyzed, **Ip6k** and **Rheb** emerged as significant modulators. Downregulation of **Ip6k**, an inositol kinase, led to a marked increase in GluRIIB levels and a decrease in the GluRIIA/GluRIIB ratio, suggesting that phosphate homeostasis alterations mediated by **Ip6k** are crucial for modifying synaptic receptor composition in response to neurotransmission. Conversely, knockdown of **Rheb**, a ubiquitously expressed GTP-binding protein involved in the mTOR signaling pathway, resulted in decreased GluRIIB levels. This led to an increased GluRIIA/GluRIIB ratio, indicating that **Rheb** influences receptor balance. The effect may be mediated through mechanisms affecting synapse assembly, as observed in both vertebrates and Drosophila.These findings provide a foundation for future research to explore the precise mechanisms by which **Ip6k** and **Rheb** regulate dGluR scaling for homeostatic plasticity.

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Emily NURDEN

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Supervisors : Ben Lonnqvist, Michael H. Herzog

Emily is supported by an anonymous donor

Abstract :

Understanding how neural networks see the world is becoming increasingly important as these computational models are integrated into our lives. Although visual models often produce outputs similar to those of humans, e.g. in object recognition, the processes they use to achieve these responses can differ significantly. Identifying these discrepancies is crucial before we can fully trust models in real-world applications.

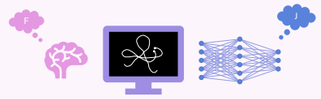
This project compares human and deep neural network performance in a visual pathfinding task, evaluating the similarity of models to humans at the gestalt principle of continuity grouping.

Current DNNs Fail at Human-like Continuity Grouping Even With Practice

Emily Nurden, Ben Lonnqvist, Michael H. Herzog

INTRODUCTION

- Performance of visual DNNs align well with primate neural data [1][2].
- But measurements that lead to these conclusions rarely target specific mechanisms [3].
- Identifying discrepancies in these mechanisms is crucial for building DNNs, well-aligned to human processing, for applications.



RESEARCH QUESTION

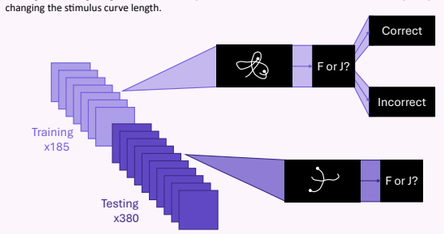
- How well do models and humans align on continuity grouping?

APPROACH

- Humans and models perform the same overlapping pathfinder task.
- At this task, do models match human performance?

METHOD

Fig. 1. Training and testing image flow. Stimuli are presented for 200ms with no instructions. Complexity varied by changing the stimulus curve length.



- During training, feedback was provided to humans after each response.
- After, they were presented with testing stimuli (no feedback).
- Humans were split into 3 groups based on experimental conditions (In-lab, Online, Instructions—provided with instructions instead of a training arm).
- DNNs' response obtained for 11 models available on Brain-Score [2].
- A linear regression was fit on the penultimate layer of the DNN's network activations during training.
- This regression was used to classify images during testing.

RESULTS

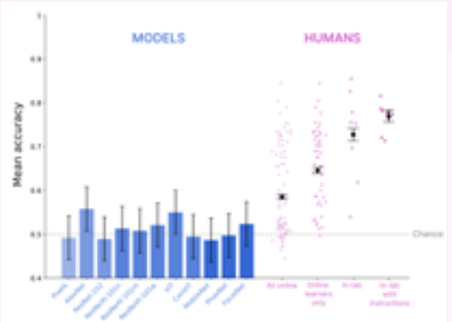
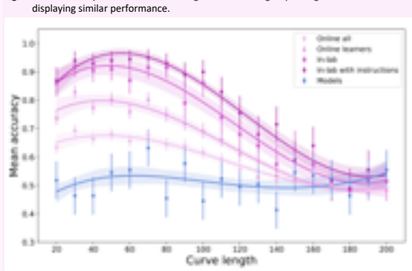


Fig.2. Overall mean accuracy across all curve length conditions with 95% confidence interval.
*learners are those that on average performed statistically above chance. Only online are separated as this was the only group with participants that did not learn.
*the different ResNeXt variants (101n, 101m, 101w) refer to narrow, medium, wide.

Fig.3. Mean accuracy across each curve length. Models are grouped together due to displaying similar performance.



Humans display distinct differences between groups.

Online participants performed at significantly lower accuracy across the trials than those uninstructed in-lab (p=0.00075, d=1.32) (Fig.2, 3).

When considering only the online participants that learnt, this group still performed worse than in-lab participants (p=0.026, d=0.7) (Fig2, 3). This suggests in-lab participants learnt a rule more closely correlated to the true one.

Human performance converged to chance as complexity increased.

At higher curve lengths it became more difficult to distinguish which category the stimuli belonged to (Fig.3).

The accuracy of DNNs remained consistently at chance across all curve lengths (Fig.3) indicating that DNNs cannot reason about relations in abstract images.

Humans outperformed models on average.

All DNNs performed at chance level or below (Fig.2), compared to 39% of humans that performed at chance (considering only those with no instructions).

No models learnt what to do demonstrating a failure with continuity grouping in these stimuli where most humans succeeded.

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Heliya is supported by Fondation ProTechno

Abstract :

Estimating and tracking the 3D pose of individual fish within densely populated fish schools is crucial for understanding collective behavior and social dynamics in aquatic ecosystems. However, the highly dynamic behavior of the fish results in overlapping bodies, rapid movements, which together with similar appearances among individuals, makes the state-of-the-art multi-object tracking algorithms (i.e., ByteTrack, DeepLabCut [1]) fail to track consistent identity and thus failing in 3D pose lifting. To address this, we enhance the ByteTrack with a more powerful detector in DeepLabCut v3.0 [1]. To tune the hyper-parameters of ByteTrack in a iterative way, we created a ground truth dataset for all views in a semi-automatic way. We can now leverage the multi-view 2D poses from DeepLabCut3 and the camera parameters to obtain accurate 3D poses for all the fish.

3D POSE ESTIMATION OF FISH SCHOOLS

Heliya Shakeri, Niels Poulsen, Haozhe Qi, Valentine Gabeff, Andy Bonnetto, Adriana Rotondo and Alexander Mathis

ABSTRACT

Estimating and tracking the 3D pose of individual fish within densely populated fish schools is crucial for understanding collective behavior and social dynamics in aquatic ecosystems. However, the highly dynamic behavior of the fish results in overlapping bodies, rapid movements, which together with similar appearances among individuals, makes the state-of-the-art multi-object tracking algorithms (i.e., ByteTrack, DeepLabCut [1]) fail to track consistent identity and thus failing in 3D pose lifting. To address this, we enhance the ByteTrack with a more powerful detector in DeepLabCut v3.0 [1]. To tune the hyper-parameters of ByteTrack in a iterative way, we created a ground truth dataset for all views in a semi-automatic way. We can now leverage the multi-view 2D poses from DeepLabCut3 and the camera parameters to obtain accurate 3D poses for all the fish.

DETECTION AND TRACKING

- A DeepLabCut 3.0 model was utilized to predict the bounding boxes for each fish across all frames in the videos.
- The ByteTrack algorithm was modified to incorporate DLC's predicted bounding boxes, replacing its native detection system with these more accurate outputs [2, 3].

GROUND TRUTH ANNOTATION

- Tracking results were refined using CVAT, an open-source annotation tool designed for labeling images and videos in computer vision tasks, with manual adjustments to bounding boxes for accurate semi-automatic ground truth generation [5].
- Annotations were corrected for three videos from different viewpoints, with 500 annotated frames per video. As up to 16 fish are visible, this was a substantial amount of work.

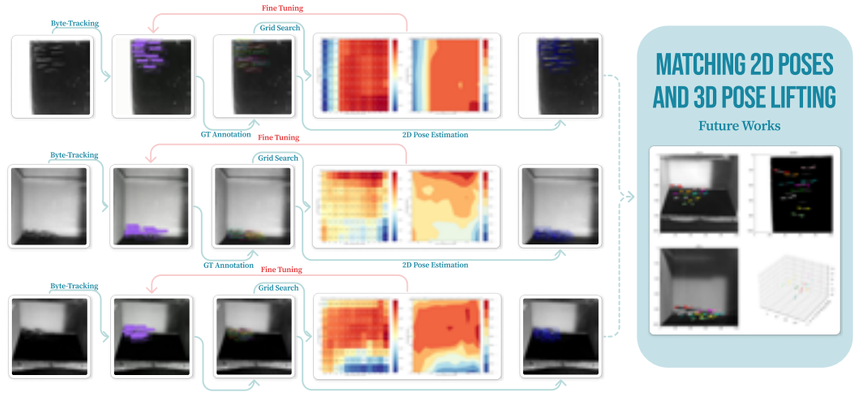
EVALUATION AND FINE-TUNING

- The modified ByteTrack algorithm's performance was compared to the semi-automatic generated ground truth across different views.
- A grid search was performed to optimize hyperparameters of byteTrack for each viewpoint, improving tracking accuracy [4].

METRIC \ VIEW	DORSAL VIEW	LATERAL VIEW	ANGLE VIEW
MOTA	88.85%	72.98%	62.21%
HOTA	90.04%	78.86%	74.95%

METRIC \ VIEW	DORSAL VIEW	LATERAL VIEW	ANGLE VIEW
MOTA	92.80%	78.87%	70.89%
HOTA	97.03%	80.07%	77.84%

RESULTS



2D POSE ESTIMATION AND 3D POSE LIFTING

- Advanced methods in DLC3 enhance 2D pose estimation, which results in enabling more accurate identification and matching of poses across different views using camera parameters and 2D pose confidence scores.
- With these matched 2D poses on selected frames, 3D lifting will be performed by computing singular value decomposition (SVD), utilizing data from all cameras and incorporating pose confidence scores to generate precise 3D estimates.
- The lifted 3D poses can be manually selected and then re-projected back to 2D to augment the training data for 2D pose estimation [1].

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3. Y. Zhang, et al. ByteTrackV2: 2D and 3D Multi-Object Tracking by Associating Every Detection Box.
4. J. Luiten, et al. HOTA: A Higher Order Metric for Evaluating Multi-object Tracking
5. https://www.cvat.ai

Donors

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EPFL School of Life Sciences
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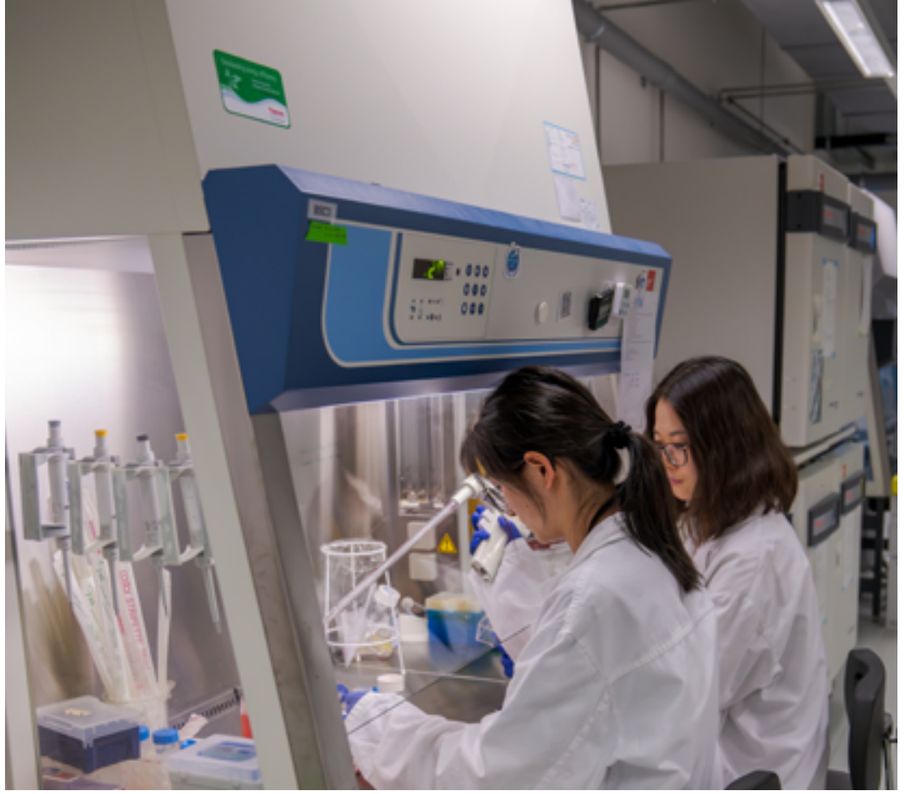
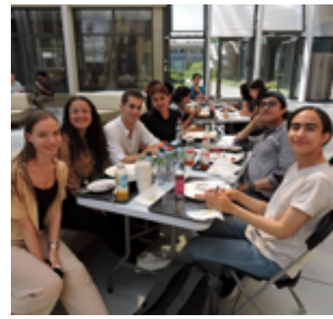
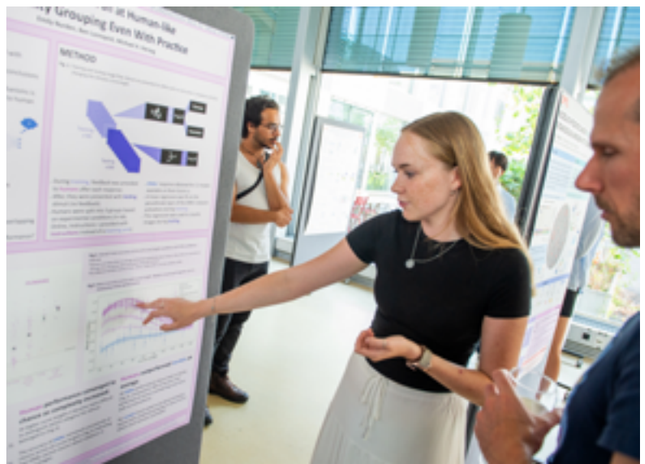
ThinkSwiss Scholarships
UCB Farchim
Fondation Valifonds

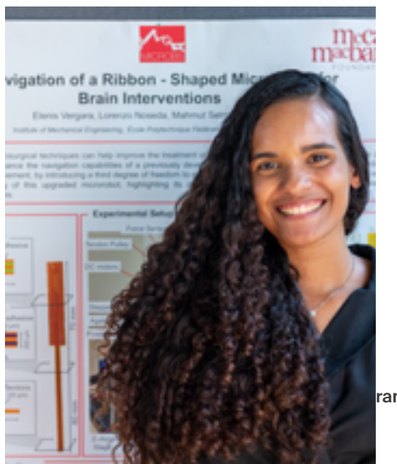

EPFL
Materials & Methods
Background
Results

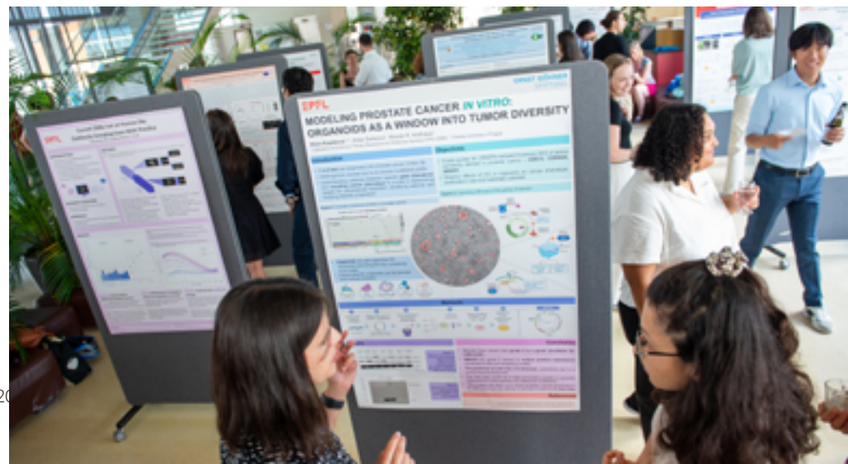




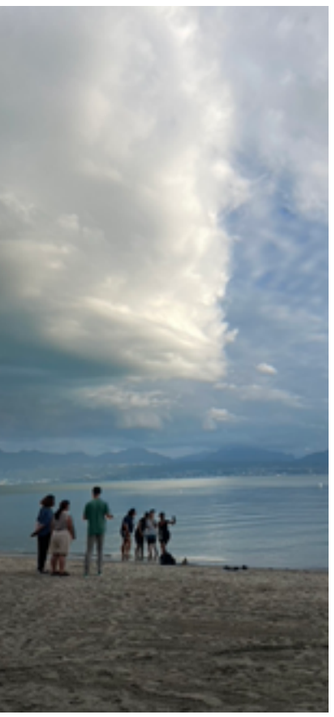

EPFL
3D Navigation of a Ribbon - Shaped
Brain Interventions


Grouping Even With Practice
METHOD

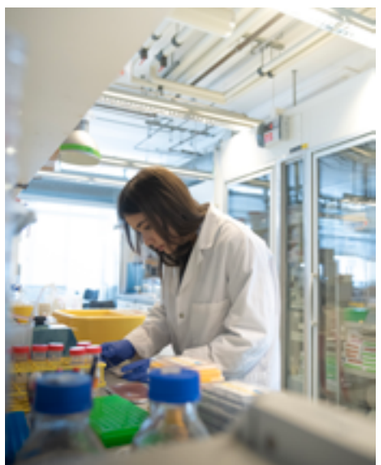

Brain Interventions


EPFL
MODELING PROSTATE CANCER IN VITRO:
ORGANOIDS AS A WINDOW INTO TUMOR DIVERSITY


EPFL
AGP
Power Distribution of Communication Networks Applied to the Brain Connectome
Results




INTRODUCTION
OBJECTIVES



Thank you

From the students

Being part of SRP was truly life-changing. I met people from all over the world, which taught me so much about different cultures and perspectives. It really opened my mind, and I feel more motivated and empowered for my future.

The confidence the program showed in me by letting me plan and carry out my own experiments—and even implement my own ideas—motivated me so much. This has been such an encouraging experience that I will carry forward in my career.

The SRP felt like being part of a big family. From picnics with directors to BBQs with friends, these moments created such a positive and welcoming community. I could see myself coming back here in the future to continue my studies.

Talking with PhD students and professors helped me reflect on what I really love. I learned that choosing a path isn't just about 'what I should do' but about 'what I want to do.' SRP gave me a clearer view of how to become a researcher and where I truly fit in.

From the supervisors

One of my SRP students achieved reliable, impactful results that contributed directly to our lab's project. Her enthusiasm made me even more enthusiastic—it's exactly this energy that makes the SRP special.

Working with students who are both curious and driven has been refreshing! The SRP brings some of the brightest students into the EPFL ecosystem, and I'd happily supervise another SRP student next year.

The best part of SRP is its impact on students' scientific journeys. It's rewarding to watch them grow and gain confidence in their skills, knowing this experience may guide them toward future research careers.

The diversity of student backgrounds and nationalities in SRP is incredibly enriching. This exchange of perspectives benefits everyone involved and creates a truly unique environment.

Where are they now?

SRP redirected my path, keeping me at EPFL for a PhD in computational biology—crucial steps that shaped my career in genomics.

Samira Asgari
Assistant Professor of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, NY
SRP 2014

SRP was a milestone for me, building my confidence and scientific thinking skills that now guide my research on molecular mechanisms in neuroimmunology and single-cell genomics. It also connected me with peers worldwide—friends I still keep in touch.

Arek Kendril
Associate Investigator, Munich Cluster for Systems Neurology (SyNergy), Germany
SRP 2014

SRP sparked my path in critical inquiry, essential for problem-solving at both the bedside and community level. My experience laid a foundation for a PhD in Public Health and my continued work in Ghana today. EPFL also gave me life-long friends, also medical doctors now.

Shadrack Frimpong
Medical Student at Yale School of Medicine, Public Health Advocate, Forbes 30 Under 30 Social Entrepreneur
SRP 2013

My experience at EPFL had everything to do with my career path—it solidified my passion for bench research, ultimately guiding me toward a PhD and work on neurodegenerative diseases.

Veselina Petrova
Neuroscience Research Fellow, Harvard Medical School and Boston Children's Hospital
SRP 2014

Alice Alias «SRP Mom»

Alice Emery-Goodman
Summer Research Program Coordinator
since 2009

When I came to EPFL in 2009 and was handed the reins of the Summer Research Program (SRP) for the School of Life Sciences, I had no idea that it would become such a large part of my life. At the time, we were receiving only about 350 paper applications which more than doubled when we went on-line a few years later, and now stands at over 1'100 every January. We have never had to advertise the program; the success of the SRP spread on its own by the alumni themselves when they returned home after their 2 months in Lausanne.

More often than not, the SRP is a transformative experience both scientifically and personally for the student. It helps students discern their goals and dreams and it gives them the tools and experience to open those doors.

Over the 15 years, both I and SRP have grown and developed our sense of "mission". The original raison d'être is to showcase the outstanding research done here at SV to the world and make connections between universities while giving talented students a chance to experience research first-hand. With SRP, we hope to attract excellent students back for our PhD programs. As good as these goals are, after a few years, I realized that SRP could be even more.

In a world where polarization, conflicts and mistrust of people who are different from ourselves is increasing, programs like SRP can help to build bridges of understanding between stereotypically opposing groups. By working together, living together, and playing together, SRP students develop long-lasting friendships which will serve them and others long after their summer is over. Moreover, we here in Switzerland have a responsibility to extend a helping hand to talented students world-wide, especially to those who do not have opportunity in their home country. We keep these principals in the back of our minds as we go through the selection process and plan the weekly workshops.

It is exciting to see that the SRP will celebrate its 20th anniversary next year and I am honored to have been given the chance to be such a big part of it. It has been a gift to be trusted to coordinate SRP over the years and I sincerely hope that SRP will continue its multifaceted mission for many years to come, making its small contribution towards a world that is more understanding, curious and kind. Receiving the EPFL Outstanding Commitment Award in 2024 has been a deeply meaningful recognition of this journey and a welcome acknowledgment of the importance of SRP at EPFL.

Alice Emery-Goodmann

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