BIOGRAPHICAL SKETCH

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NAME: Shaye, Hamidreza

eRA COMMONS USER NAME (credential, e.g., agency login): HAMIDREZA

POSITION TITLE: Graduate Student Research Assistant

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Sharif University of Technology, Tehran, Tehran	BS	07/2016	Chemistry
University of Southern California, Los Angeles, California	PHD	01/2022	Chemistry

A. Personal Statement

I have always been interested in medicinal chemistry and decided to investigate the ways in which drugs affect our lives. My research interests involve in unrevealing how drugs can alter protein structures and function which will lead to rational drug design based on their structure. As an undergraduate, I had the opportunity to conduct research with Dr. Hadi Parastar on developing statistical methods to determine pharmaceuticals in environmental samples. In this work, I've used numerous statistical techniques that are not straight forward to be used by chemists who are not expert in programming or in advanced statistic. Therefore, I've implemented them into a cross-platform application that can be launched using smartphones with no complexity that almost everyone can use. My undergraduate research resulted in two journal papers and I got the chance to present my work in national and international conferences. As a graduate student, I've moved to the field of structural biology so I can investigate the effect of pharmaceuticals in the molecular level. I joined Dr. Vadim Cherezov research group, taking advantage of the experienced predoctoral and postdoctoral fellows. My research was involved in determining the structure of G-protein coupled receptors (GPCRs) in complex with potential/existing drugs. Initially, I got trained how to heterologously express, purify and crystallize GPCRs to be used for in meso X-ray crystallography. As a result, we have successfully determined the structure of Angiotensine II type 2 receptor in complex with a small molecule using X-ray crystallography (manuscript in preparation). We moved further and attempted to solve the structure of metabotropic GABAB receptor. GABAB receptor is an obligatory heterodimer that belongs to class C GPCRs and is the main inhibitory neurotransmitter in the central nervous system. Due to the size and the dynamic nature of GABAB receptor we have utilized single particle cryo-EM as a powerful technique for protein structural determination. We therefore made a collaboration with the Stanford-SLAC cryo-EM facility. In less than a year, we were able to solve the structure of GABAB receptor in four different conformations. This is the first cryo-EM structure solved by our research group and the manuscript is accepted to be published in the journal Nature. As a follow up, I'm interested to solve the structure of the sweet and umami receptors. They also belong to the class C GPCRs and from a heterodimer. However, unlike GABAB, they respond to a wide range of chemicals and make the perception of "taste" in our mind. Elucidating the structure of the taste receptors will greatly advance our understanding of their function and activation mechanism. I'm looking forward to collecting my cryo-EM data, so I can have my own independent research group in the future.

1. H. Parastar*, **H. Shaye**, "Comparative study of partial least squares and multivariate curve resolution for simultaneous spectrophotometric determination of pharmaceuticals in environmental samples", RSC Advances 2015, 5 (86), 70017-70024.
2. **H. Shaye**, A. Ishchenko, J.H. Lam, G.W. Han, L. Xue, P. Rondard, J. Pin, V. Katritch, C. Gati*, V. Cherezov*, "Structural basis of metabotropic GABA receptor activation", Nature 2020 (accepted).

B. Positions and Honors

Positions and Employment

2017 - 2018 Graduate Student Teaching Assistant, University of Southern California, Los Angeles, CA
2019 - Graduate Student Research Assistant, University of Southern California, Los Angeles, CA

C. Contribution to Science

Undergraduate Research: My undergraduate research was focused on developing new tools in the field of chemometrics. We've evaluated different multivariate calibration methods to determine different pharmaceuticals in environmental sample. In parallel, we have developed a cross-platform application that allows us to carry out various multivariate calibration methods using a smartphone. It was the first smartphone application introduced in the field and we further optimized it for cloud processing. My undergraduate research resulted in two journal and three national/international conference papers with my contribution as the main author.

1- H. Parastar*, **H. Shaye**, "Comparative study of partial least squares and multivariate curve resolution for simultaneous spectrophotometric determination of pharmaceuticals in environmental samples", RSC Advances 2015, 5 (86), 70017-70024.

2- H. Parastar*, **H. Shaye**, "MVC app: A smartphone application for performing chemometric methods", Cheometr. Intel. Lab. Syst. 2015, 147, 105-110.

3- **H. Shaye**, H. Parastar*, "Comparative study of rPLS and MCR-ALS for simultaneous spectrophotometric analysis of pharmaceuticals in environmental samples", 21th Iranian Analytical Chemistry Conference, Ahvaz, Iran, 14-16 March, 2015.

4- **H. Shaye**, H. Parastar*, "Chemometrics in Your Hands: Development of a Smartphone Application for Performing Chemometrics Methods", Chemometrics in Analytical Chemistry, Changsha, China, 22-26 June, 2015.

5- **H. Shaye**, H. Parastar*, "Development of New Interfaces for Performing Chemometric Methods in Portable Instruments and Smartphones",5th Iranian Biennial Chemometrics Seminar, Tehran, Iran, 25-26 Nov, 2015.

Graduate Research: My ongoing predoctoral research is focused on determining the structure of cell surface receptors. Our focus is to determine the structure of G-protein coupled receptors, which are an important drug target and approximately 34% of FDA approved drugs target this family of receptors. We started to work on Angiotensin II type 2 receptor (AT2R), and successfully characterized the structure of AT2R in complex with a small molecule. We used in meso X-ray crystallography to capture the structure of AT2R in its semi-native lipid environment. With the help of our collaborators, we were able to show the inhibition of AT2R can be used as a novel therapeutic strategy to combat Glioblastoma multiforme (GBM) one of the malicious forms of brain tumor. The manuscript is currently under preparation with my contribution as the co-first author. Concurrently, we have also attempted to characterize the structure of metabotropic GABAB receptor. GABAB belongs to class C GPCRs and forms a heterodimer. It is involved in the modulation of synaptic function in the central nervous system (CNS) and is a major therapeutic target for a variety of neurological diseases, pain regulation, and addiction. With the help of our collaborator at the Stanford-SLAC cryo-EM facility, we were able to solve the structure of GABAB receptor in active, inactive and two intermediate states. We further investigated the binding modes of GABAB and established a new ligand binding site at the interface of the heterodimer subunits by collaborating with a research group at the University of Montpellier. This work represents a breakthrough in the field and enables the design of new therapeutic drugs.

1- **H. Shaye**, A. Ishchenko, J.H. Lam, G.W. Han, L. Xue, P. Rondard, J. Pin, V. Katritch, C. Gati*, V. Cherezov*, "Structural basis of metabotropic GABA receptor activation", Nature 2020 (accepted)