Tural Aksel

Nautilus Biotechnology
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RESEARCH INTERESTS

- Development of DNA nanotechnology tools for structural biology, proteomics, immunotherapy and bioenergy production.
- Scientific software development for biomolecular design, image processing and data analysis.
- Protein engineering and design for hybrid DNA Origami-protein complexes.

EDUCATION

Ph.D. Biophysics — 2012
Johns Hopkins University, Baltimore, MD
Thesis Advisor: Doug Barrick

B.S. Biological Sciences and Bioengineering — 2006
Sabanci University, Istanbul, Turkey
Thesis Advisor: Ugur Sezerman

PROFESSIONAL & ACADEMIC EXPERIENCE

2019– Nautilus Biotechnology, San Carlos
Senior Scientist, DNA Nanotechnology

- I lead a team to develop DNA Origami devices for proteomics research. I direct day-to-day and long term research activities of my team members.
- I have developed the key DNA Origami technologies for Nautilus platform.
- My research achievements have led to three patent applications as the lead inventor.

2018–20 University of California, San Francisco
Applications Programmer III
PI: Shawn Douglas

- I developed a DNA nanotechnology platform and image processing pipeline on AWS cloud for high-resolution cryo-EM studies of small proteins. The technology enables structural studies of small DNA binding proteins that wouldn't be otherwise studied using conventional cryo-EM. The method is published in Nature Biotechnology.

  Publication: Aksel T et al.(2021) *Nature Biotechnology*.

  Cryoorigami software package: github.com/douglaslab/cryoorigami.

- I developed new methods and software for 1) Thermodynamically optimized DNA Origami designs, and 2) DNA Origami structure prediction. The tools will be made publicly available in a webserver (in progress).

2015–18 University of California, San Francisco
Postdoctoral Fellow, Department of Cellular and Molecular Pharmacology
PI: Shawn Douglas

- I worked on the development of a DNA nanotechology platform for high-resolution cryo-EM studies of small proteins.
- I developed a scalable technology for the production of custom DNA Origami scaffolds.
- I designed a DNA Origami structure for tunable activation of Car-T cells. The DNA Origami design and the results for the publication are published in PNAS.

  Publication: Dong R, Aksel T et al.(2021) *PNAS*
- I designed a chimeric adapter protein for the display of non-DNA binding proteins on our DNA Origami platform (in progress).

2013–15 Stanford University
Postdoctoral Fellow, Biochemistry Department
PI: James Spudich

- I developed a loaded actin gliding assay to quantify the power output generated by cardiac myosins.
- I developed an image processing software for automated filament tracking. The assay and the filament tracking software helped us quantify the power output generated by cardiac myosin mutants.

  Publication: Aksel T et al.(2015) *Cell Reports*.

  FASTrack filament tracking software: github.com/turalaksel/FASTrack.

2006–12 Johns Hopkins University
Ph.D. student, Department of Biophysics
PI: Doug Barrick

- I studied the origins of cooperativity and pathway diversity in protein folding using consensus Ankyrin repeat proteins (CARPs). I generated CARPs from identical consensus Ankyrin repeat units by a modular cloning method.

  Publication: Aksel T et al.(2011) *Structure*
- I developed a nearest-neighbor statistical physical model called Ising model to dissect folding energetics into individual repeat stability and repeat-repeat interface terms for repeat proteins from experimental data. I developed a python package to fit the Ising model to a series of equilibrium and kinetic folding data to determine the folding energy for single repeat folding and repeat-repeat interface formation.

  Publication: Aksel T et al.(2009) *Methods in Enzymology*

  Isingbul data fitting software: github.com/turalaksel/IsingBul1.0.
- I developed an efficient software, written in C++, to calculate the 3D Ising Model partition function for biological systems. I used this tool to predict the pKa values of titratable residues from protein structure.

2006 Sabanci University, Istanbul, Turkey
Instructor Computer Science Department
Course: Data Structures

- I taught the summer school Data structures course in computer science department.

• I developed an homology model algorithm for structure prediction of protein sequences. The algorithm recursively finds the best matching patterns between two protein sequences using dynamic algorithm.

PROGRAMMING SKILLS

- Computing Environments: Matlab, IPython, Scilab, R, AWS clound computing.
- Languages: Python, C, C++, Perl, Shell scripting.
- Operating Systems: Unix/Linux, Windows, Mac OS.
- Biomolecular Modeling: Pymol, PyRosetta, Cadnano.

LABORATORY SKILLS

- Bioconjugation.
- DNA Nanotechnology, DNA Origami design, production and scale-up.
- Cryogenic electron microscopy (cryo-EM), negative-stain TEM.
- Recombinant DNA technologies, bacterial and mammalian protein expression, protein chromatography.
- CD and fluorescence spectroscopy, biomolecular NMR, SAXS/WAXS, analytical ultracentrifugation, stopped-flow kinetics.
- Single molecule force spectroscopy, fluorescence microscopy.

SELECTED PUBLICATIONS

Journal Articles

For Complete list of publications, please see Google scholar

2021 Dong R, **Aksel T**, Chan W, Germain RN, Vale RD, Douglas SM "DNA origami patterning of synthetic T cell receptors reveals spatial control of the sensitivity and kinetics of signal activation." *Proc. Natl. Acad. Sci. U. S. A.* 118 (40) e2109057118 doi:10.1073/pnas.2109057118

In this paper, DNA Origami is utilized to control the density of the ligands presented to Car-T cells. The findings demonstrate that there is a minimum density of ligands required for Car-T cell activation. This study could be regarded as a proof-of-principle work for the DNA Origami assisted immunotherapy applications.

2021 **Aksel T**, Yu Z, Cheng Y , Douglas SM "Molecular goniometers for single-particle cryo-EM of DNA-binding proteins." *Nature Biotechnology* 39 (3):378–386. doi:10.1038/s41587-020-0716-8

This paper presents a DNA Origami platform for the positional control of DNA binding proteins in cryo-EM studies. For single-particle cryo-EM, samples are deposited randomly on a grid. For small proteins, knowing the orientation of particles could be critical to reach higher resolutions. Here, we demonstrated that knowing the orientation of particles is necessary to detemine the structure of an 80 kDa DNA binding protein. Without the positional information provided by DNA Origami, the reconstruction algorithms fail to determine the correct orientation of the particles. This work is the stepping-stone for programmable and multiplexed cryo-EM using DNA Origami.

2021 Marold JD, Sforza K, Geiger-Schuller K, **Aksel T**, Klein S, Petersen M, Poliakova-Georgantas E, Barrick D. "A collection of programs for one-dimensional Ising analysis of linear repeat proteins with point substitutions." *Protein Science* 30 (1):168–186 doi:10.1002/pro.3977

This paper presents a collection of python scripts for the Ising-model analysis of repeat protein equilibrium folding data. These tools are developed onto the Ising-model formalism I developed during my Ph.D studies.

2020 Wang F, Yu Z, Betegon M, Campbell MG, **Aksel T**, Zhap J, Li S, Douglas SM, Cheng Y, Agard DA. "Amino and PEG-amino graphene oxide grids enrich and protect samples for high-resolution single particle cryo-electron microscopy." *Journal of Structural Biology* 209 (2):107437 doi:10.1016/j.jsb.2019.107437

This paper presents the production of amine coated graphene-oxide grids for cryo-EM sample preparation. These grids have low background and they keep DNA Origami structures intact for cryo-EM studies.

2018 Nafisi P, **Aksel T**, Douglas SM. "Construction of a novel phagemid to produce custom DNA origami scaffolds." *Synthetic Biology*,3 (1):ysy015 doi:10.1093/synbio/ysy015

Here, we present a scalable method to create DNA Origami scaffolds with custom sequence. This method enables the production of very small and large DNA Origami structures. This method provides a path for the development of DNA Origami assemblies in a single pot reaction with high yields. This method also allows the development of DNA Origami structures with unique functional sequences presented in the scaffold. This method has allowed us the development of DNA Origami Goniometers with the target protein binding sequence.

2016 Spudich JA, **Aksel T**, Bartholomew SR, Nag S, Kawana M, Yu EC, Sarkar SS, Sung J, Sommese RF, Sutton S, Cho C, Adhikari AS, Sutton S, Taylor R, Liu C, Trivedi D, Ruppel KM. "Effects of hypertrophic and dilated cardiomyopathy mutations on power output by human β-cardiac myosin." *Journal of Experimental Biology* doi:10.1242/jeb.125930

This paper reviews the studies performed in Spudich lab to understand how cardiomyopathy mutations impact the power output of human cardiac myosin. The review points that all dilated cardiomyopathy mutations lead to power output. On the other hand, hypertrophic cardiomyopathy (HCM) mutations lead to higher or lower power output suggesting that there could be different mechanisms by which HCM mutations lead to disease phenotype.

2015 **Aksel T**, Yu EC, Sutton S, Ruppel KM, Spudich JA. "Ensemble Force Changes that Result from Human Cardiac Myosin Mutations and a Small-Molecule Effector." *Cell Reports* 11 (6):910–920. doi:10.1016/j.celrep.2015.04.006

This paper presents a new microscopy assay for the quantification of cardiac myosin power output and a new image processing software for the analysis of assay movies. The paper also presents a physical model to convert the quantities measured using the assay to a "power parameter" that is required to compare different mutants. We demonstrated the utility of the assay and the analysis tool using alpha and beta cardiac myosin isoforms, two cardiomyopathy mutants and a drug that leads to higher cardiac output. This assay and the analysis tool have been used by members of Spudich Lab and other research groups to study cardiac and other myosin variants.

2015 Preimesberger MR, Majumdar A, **Aksel T**, Sforza K, Lectka T, Barrick D, Lecomte JT, Barrick, D. "Direct NMR Detection of Bifurcated Hydrogen Bonding in the α-Helix N-Caps of Ankyrin Repeat Proteins." *J Am Chem Soc.* 137 (3):1008–11 doi:10.1021/ja510784g

This paper talks about the observation of bifurcated hydrogen bonding with a burried histidine in Ankyrin repeats using NMR. It is shown that the bifurcated hydrogen bonding is important for the stability of Ankyrin repeats.

2014 **Aksel T**, Barrick D. "Direct observation of parallel folding pathways revealed using a symmetrical repeat protein system." *Biophysical J.* 107 (1):220–232 doi:10.1016/j.bpj.2014.04.058

In this paper, we show that there are degenarate folding pathways for consensus ankyrin repeat proteins. We demonstrate the existence of parallel pathways by showing that the folding rate linearly depends on the number of repeats. These findings suggest that multiple folding pathways can be observed for proteins with symmetrical folding landscapes.

2011 Rouget JB, **Aksel T**, Roche J, Saldana JL, Garcia AE, Barrick D, Royer CA. "Size and sequence and the volume change of protein folding." *J Am Chem Soc.* 133 (15):6020–6027 doi:10.1021/ja200228w

This paper shows that there is a correlation between the volume change in protein folding and the volume of internal cavities estimated from the structure.

2011 **Aksel T**, Majumdar A, Barrick D. "The contribution of entropy, enthalpy, and hydrophobic desolvation to cooperativity in repeat-protein folding." *Structure* 19 (3):349–360 doi:10.1016/j.str.2010.12.018

In this paper, we show that hydrophobic desolvation is a major contributor to folding cooperativity. We used a symmetrical repeat protein system to dissect folding energetics into repeat stability and coperativity terms using Ising model.

2009 **Aksel T**, Barrick D. "Analysis of repeat-protein folding using nearest-neighbor statistical mechanical models." *Methods in Enzymology* 455:95–125. doi:10.1016/S0076-6879(08)04204-3

This is a methods paper presenting Ising model formalism to study repeat protein folding. The paper presents a framework to extract repeat stability and repeat-repeat coupling terms from repeat protein equilibrium folding data.

Manuscripts in preparation

2021 **Aksel T***, Damasceno P, Douglas SM*. "Rapid coarse-grained 3D structure prediction of multidomain DNA origami."

2021 **Aksel T***, Navarro E, Douglas SM*. "Thermodynamic optimization of DNA origami staple routing via k-shortest-paths."

2021 **Aksel T***†, Fong N†, Douglas SM*. "NanoToolkit: a web-based framework for DNA origami design, simulation, and gel analysis."

PATENTS

2021 Coinventor of US Patent Application assigned to Nautilus Biotechnology, Filed 2021, Confidential.

2021 Coinventor of US Patent Application assigned to Nautilus Biotechnology, Filed 2021, Confidential.

2020 Coinventor of US Patent Application assigned to Nautilus Biotechnology, Filed 2020, Confidential.

GRANTS AND AWARDS

Awards and Honors

2008 Brian Key PhD Student Travel Award.

2001–06 High Honor Scholarship, Sabanci University. Istanbul, Turkey. Full tuition and accommodation coverage.

2001 Ranked 62nd in Turkish university entrance exam among 1.4 million participants.

1998 Ranked 56th in Turkish high school entrance exam among 0.5 million participants.

Grants and Fellowships

2016–17 F32 Ruth L. Kirschstein Postdoctoral Individual National Research Service Award (NIGMS:F32GM119322).

ACADEMIC REFERENCES

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