# A Writer's Journey to an Unexpected Career in Science

Dennis Gessmann

September 7<sup>th</sup>, 2023

#### Disclaimer:

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"We are free to choose our paths...



"We are free to choose our paths...but we can't choose the consequences that come with them."

Sean Covey, The 7 Habits of Highly Effective Teens



"We are free to choose our paths...but we can't choose the consequences that come with them."

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I always wanted to be a writer of fiction

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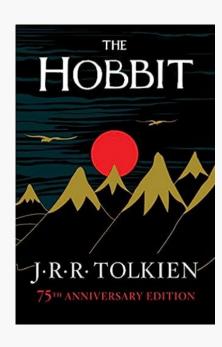
Sean Covey, The 7 Habits of Highly Effective Teens

1983: Born in the suburbs of Stuttgart, Germany

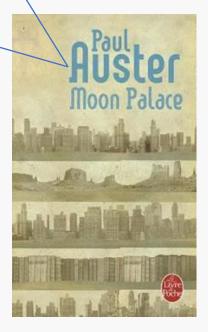
2003: Graduated high school in Germany, focus in Physics, English and Ethics

2009: Masters in <u>comparative literature</u> with a <u>minor in philosophy</u>

2010: Writer of fiction



"All we have to decide is what to do with the time that is given us." TLOTR



NYT: Mr. Auster employs the form of the picaresque adventure to create a sad-funny tale of coming of age.

Myself: Pulp Western vs Urban Philosophy

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THE END



Plan B

or marine biologist
THE END Part 2



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### Desired Journey

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Explain biology through physics & mathematics and apply engineering to create biotechnologies





or marine biologist

END Part 2

The technical biology Bachelor's study program presents an interdisciplinary profile combining biology and technology that is unique in Germany. The studies concentrate on current, globally relevant challenges in research and industry. Modern biosciences, physics and chemistry (especially biochemistry and technical biochemistry) work closely with engineering-, materials-, and systems sciences and bioprocess engineering.

Numerous research-related laboratory exercises as well as sojourns in industry and abroad ensure a high degree of practical relevance. The study program is in great demand and well reputed in research and business.

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or marine biologist

THE END Part 2

The boulder 'making me' chase a career in science.

"We are free to choose our paths, but we can't choose the consequences that come with them."

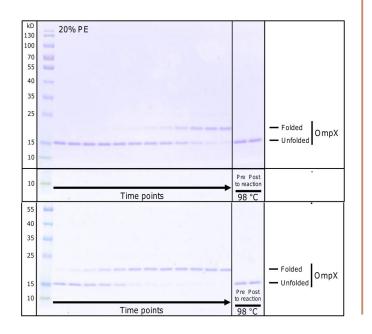
Sean Covey, The 7 Habits of Highly Effective Teens

•	1983:	Born in the suburbs of Stuttgart, Germany
	2003:	Graduated high school in Germany, focus in Physics, English and Ethics
,	2009:	Diplom Biologist (t.o.) from the University of Stuttgart
		Focus on Bioenergetics, Microbiology and Technical Biochemistry
		Diplom Thesis: Structural biology of eukaryotic $\beta$ -barrel membrane proteins
	2012:	Dr. rer. Nat. from the University of Stuttgart
		Bioengineering of eukaryotic $\beta$ -barrel membrane proteins
	2012	
	- 2014:	Postdoctoral Research Fellow at Johns Hopkins University in Baltimore, MD, USA
		Biophysics of prokaryotic $\beta$ -barrel membrane protein folding
	2014	
	- 2014:	Research Associate at Department of Bioengineering at University of Illinois Chicago, USA
		Computational biology of prokaryotic $\beta$ -barrel membrane protein folding
	2014	
	- 2015	Therapeutic Proteins International, LLC, Chicago IL
		95% Biophysics 5% Mass spectrometry of biotherapeutics
	2015	
	- Present	Pfizer Inc.
		Mass spectrometry of biotherapeutics

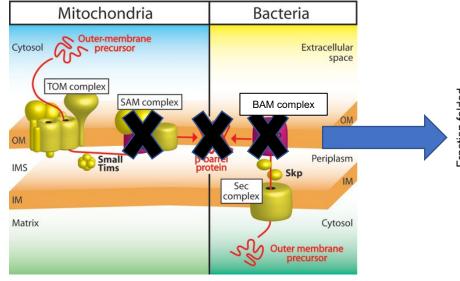
2015-2022 in Lake Forest IL, 2022 – present in Andover, MA

Biophysics of prokaryotic  $\beta$ -barrel membrane protein folding

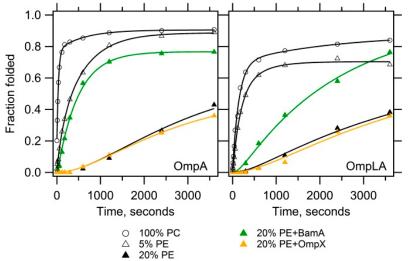
Be bold.



#### Scientific Question or Biological 'Paradox'



The higher the amount of native lipid headgroups, the slower the folding *in vitro* (2012, Johns Hopkins)

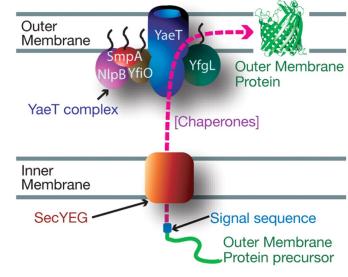


Structure and Function of an Essential Component of the Outer Membrane

**Protein Assembly Machine** 

Seokhee Kim, <sup>1</sup> Juliana C. Malinverni, <sup>2</sup> Piotr Sliz, <sup>3,4</sup> Thomas J. Silhavy, <sup>2</sup> Stephen C. Harrison, <sup>3,4</sup> Daniel Kahne <sup>1,3</sup>\*

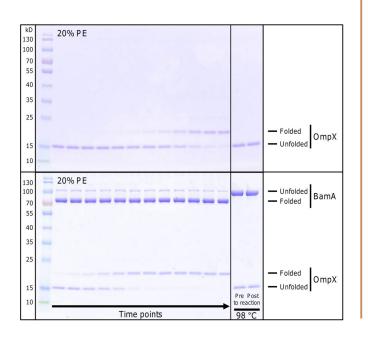
Published 2007 in Science



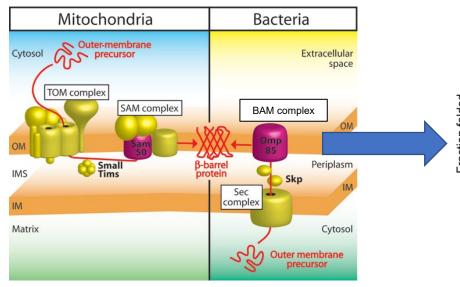
<sup>&</sup>lt;sup>1</sup>Department of Chemistry and Chemical Biology, <u>Harvard</u> University, Cambridge, MA 02138, USA. <sup>2</sup>Department of Molecular Biology, <u>Princeton</u> University, Princeton, NJ 08544, USA. <sup>3</sup>Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115, USA. <sup>4</sup>Howard Hughes Medical Institute and Children's Hospital Laboratory of Molecular Medicine, Boston, MA 02115, USA.

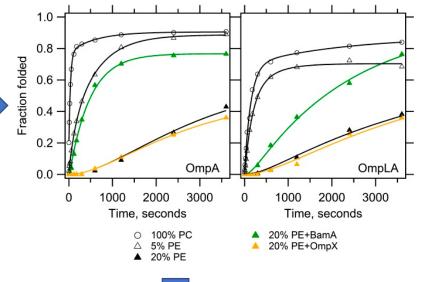
Biophysics of prokaryotic  $\beta$ -barrel membrane protein folding

Be bold.

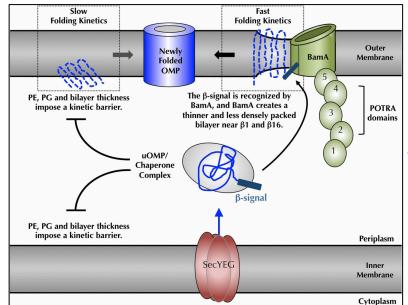


### Scientific Question or Biological 'Paradox'





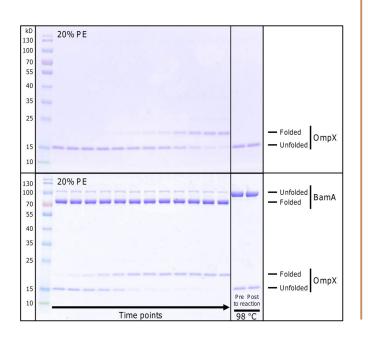
#### Published 2014



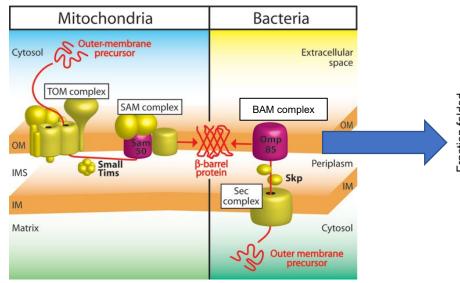
Outer membrane β-barrel protein folding is physically controlled by periplasmic lipid head groups and BamA

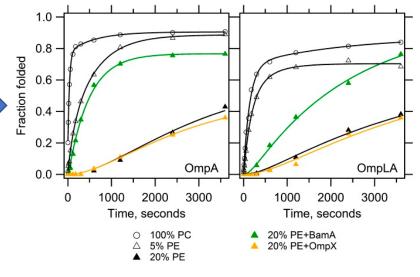
Biophysics of prokaryotic  $\beta$ -barrel membrane protein folding

Be bold.

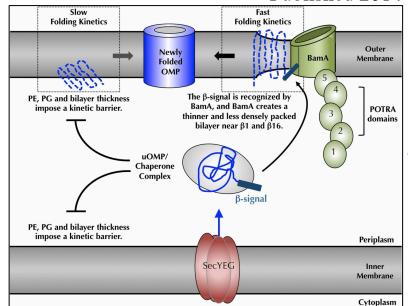


### Scientific Question or Biological 'Paradox'





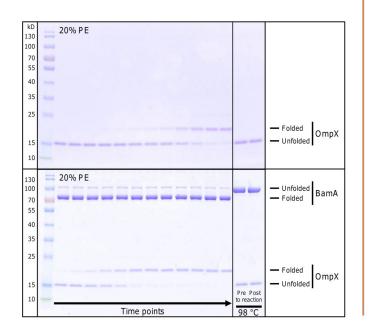
#### Published 2014



New pathway(s) to common ground so that one may begin to merge in vivo and in vitro observations on the biogenesis of beta barrel OMPs

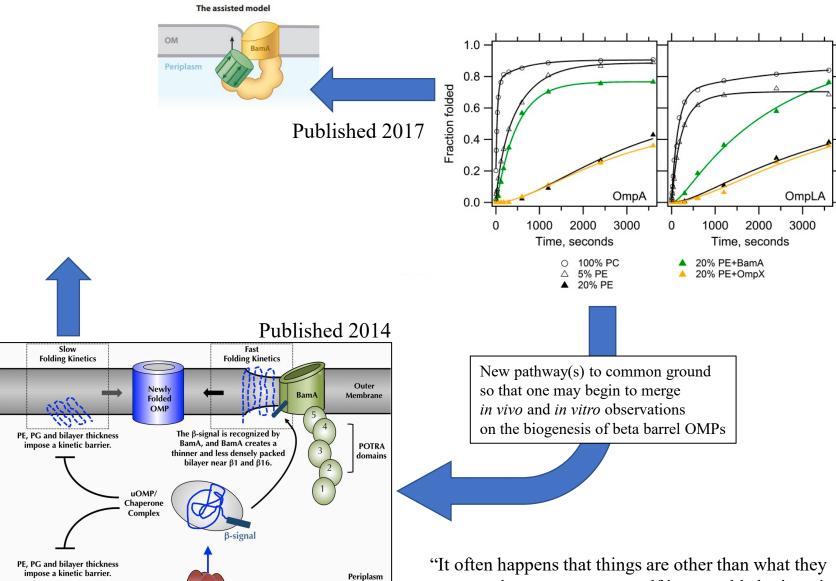
Biophysics of prokaryotic  $\beta$ -barrel membrane protein folding

Be bold, be humble.



#### **Biogenesis of Outer Membrane Proteins**

SecYEG



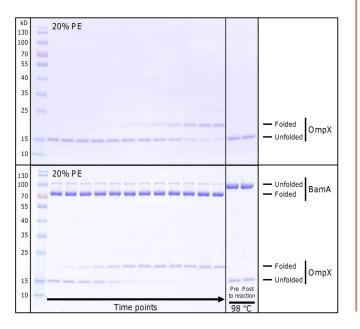
Membrane

Cytoplasm

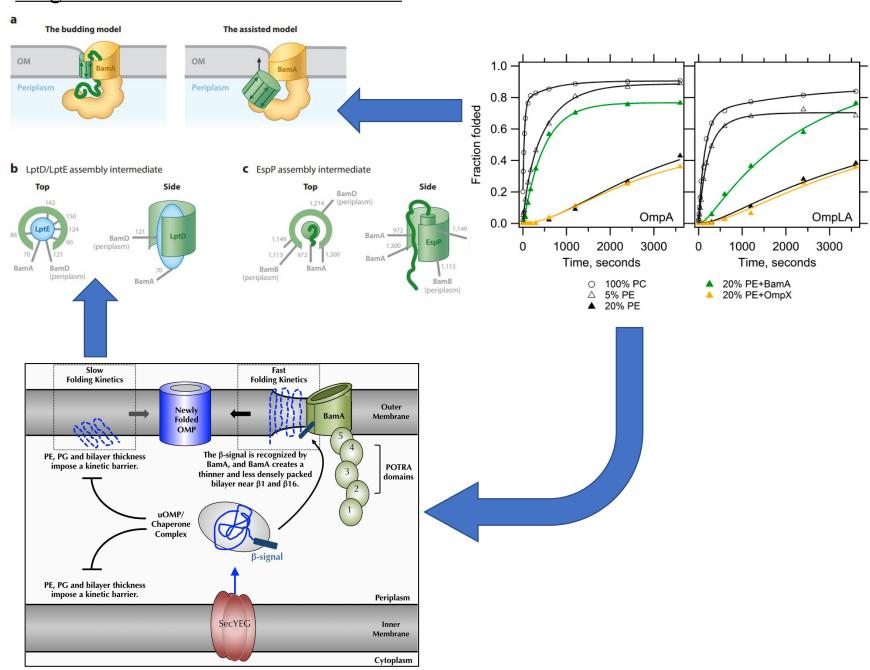
"It often happens that things are other than what they seem, and you can get yourself into trouble by jumping to conclusions" Paul Auster, Moon Palace

Biophysics of prokaryotic  $\beta$ -barrel membrane protein folding

Use the tools at your disposal that allow you to answer the question you are asking.



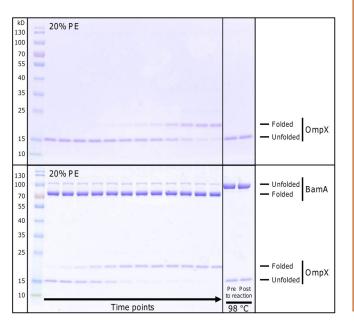
#### **Biogenesis of Outer Membrane Proteins**



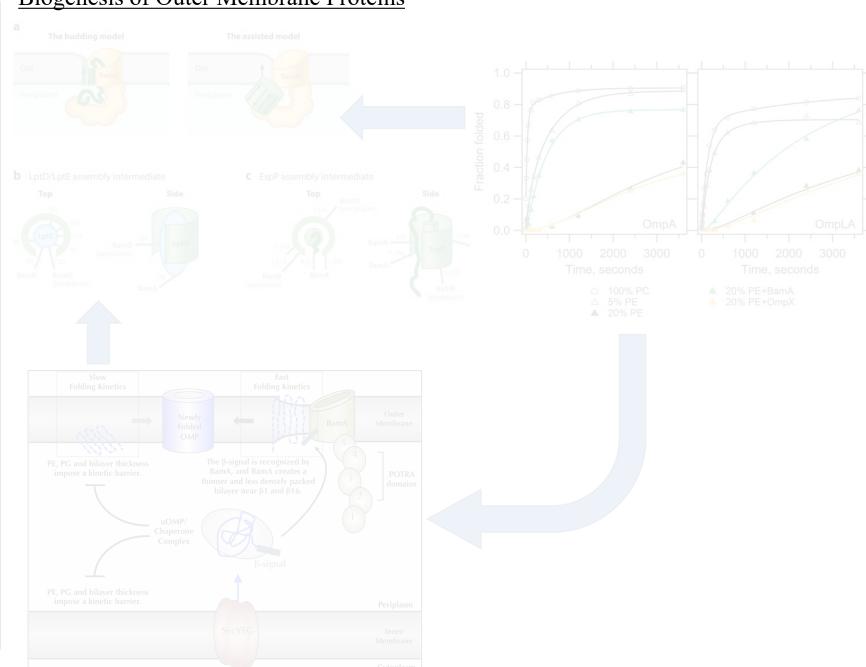
Biophysics of prokaryotic  $\beta$ -barrel membrane protein folding

Use the tools at your disposal that allow you to answer the question you are asking.

You might not get a bigger boat...



#### **Biogenesis of Outer Membrane Proteins**



What if we do need a bigger boat?



### Doctorate 2009-2012

### University of Stuttgart

Bioengineering of eukaryotic  $\beta$ -barrel membrane proteins

What if we do need a bigger boat?

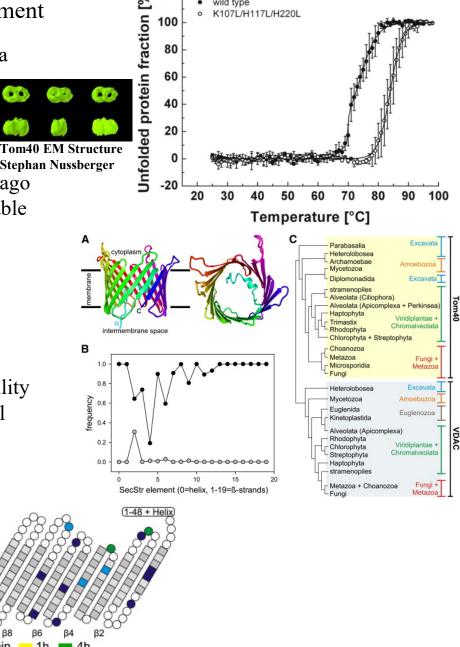
Built the toolbox that you require through collaboration.

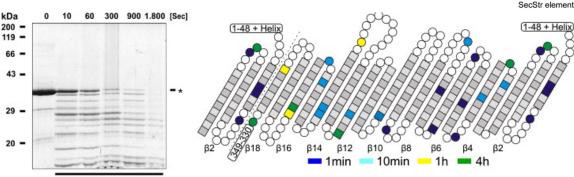
#### Collaboration is key to thrive in any environment

Goal: Bioengineer a β-barrel membrane protein to a functional nanopore capable of DNA sequencing

- → there was no high-resolution atomic structure
- Collaboration with the University of Illinois Chicago → computational model to determine thermal instable (barrel) elements
- Collaboration with the University of Frankfurt
- → 'mine' all known sequences to build a structural homology model
- Collaboration with Life Science Center Core Facility
- → Mass Spectrometry to confirm homology model

Lys-C digestion





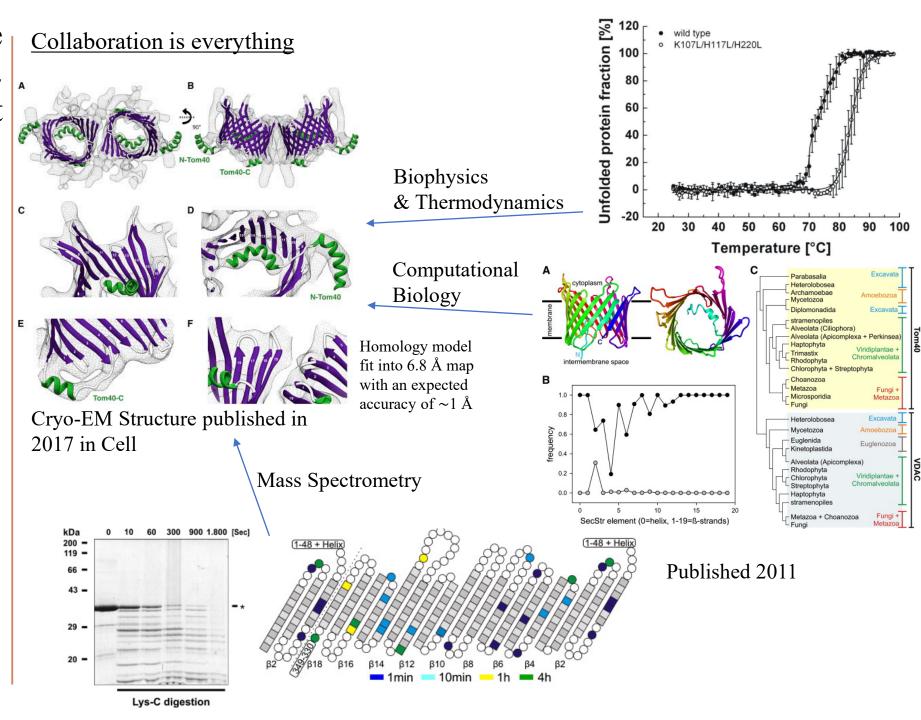
Stephan Nussberger

# Doctorate 2009-2012 University of Stuttgart

Bioengineering of eukaryotic  $\beta$ -barrel membrane proteins

What if we do need a bigger boat?

Built the toolbox that you require through collaboration.



# Doctorate 2009-2012 University of Stuttgart

Bioengineering of eukaryotic  $\beta$ -barrel membrane proteins

What if we do need a bigger boat?

Built the toolbox that you require through collaboration.

#### Collaboration: thrive to be constructive

Credit where credit's due

written

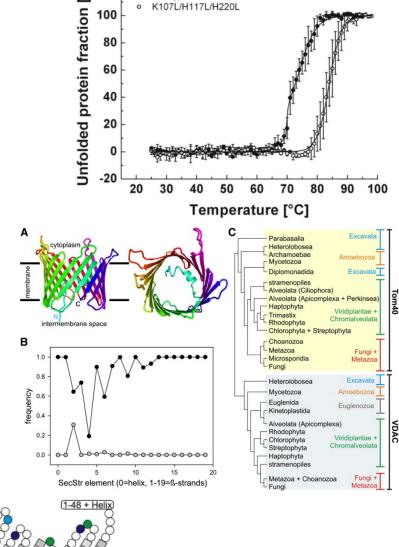
papers reports

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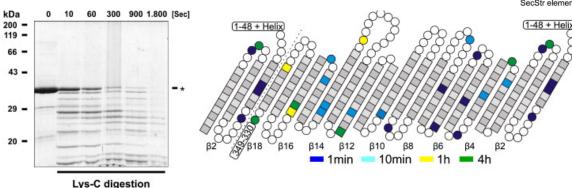
verbally

in meetings in conversations

. .



wild type



What if we do need a bigger boat?



What if we do need a bigger boat?

Constructive collaboration is everything and will allow you to thrive in any environment.



"Change is constant."

Heraclitus

## 1<sup>st</sup> Postdoc at JHU 2012-2014

Biophysics of prokaryotic  $\beta$ -barrel membrane protein folding

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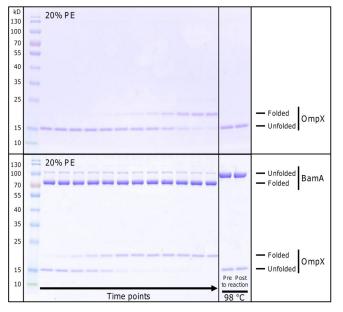
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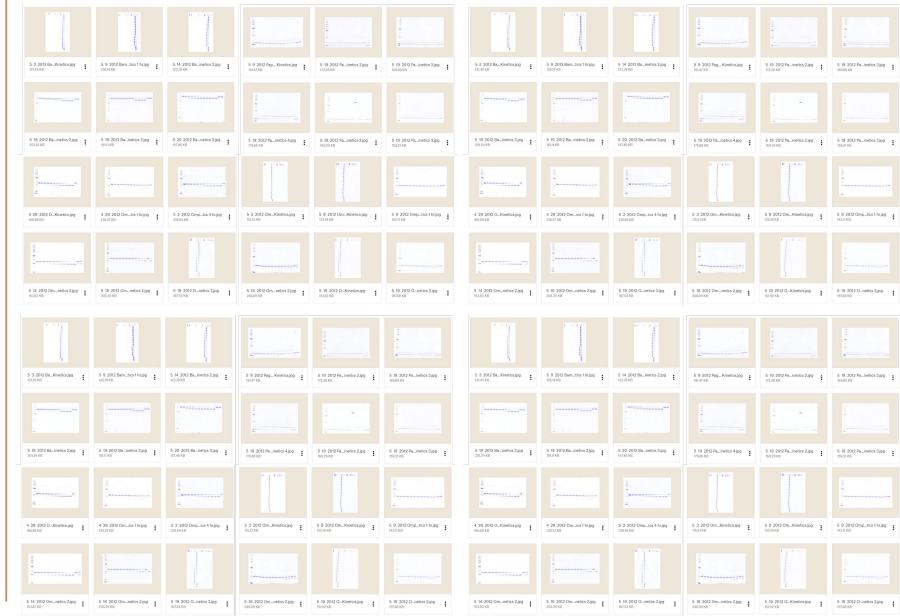
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### <u>Diversify your skill set</u> recognize when it is time to move on!

1096 gels...



### 2<sup>nd</sup> Postdoc at UIC 2014-2014

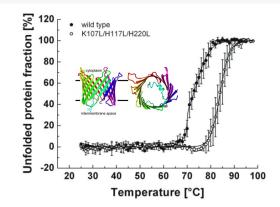
Computational biology of prokaryotic β-barrel membrane protein folding

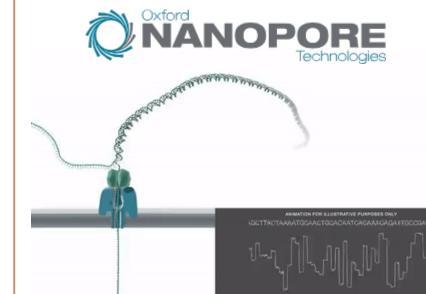
"Change is constant."

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#### Recognize what is realistic, when not to be bold, and trust your 'gut'

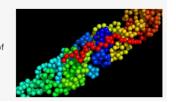






### Computational Design of Bionanopores and Decellularized Biomaterial. *𝑉*

We also have unique and significant strengths in designing novel devices for data measurement. Bionanopores has the promise to sequence and quantify virtually all biologically relevant macromolecules. It is successful development will enable detection of modified state of proteins, as well as the presence of bacterial/virus.



#### Make the most of it!



Article

pubs.acs.org/JACS

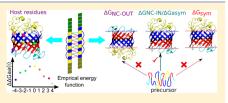
### Outer Membrane Protein Folding and Topology from a Computational Transfer Free Energy Scale

Meishan Lin, Dennis Gessmann, Hammad Naveed, and Jie Liang\*

Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois 60607, United States

Supporting Information

ABSTRACT: Knowledge of the transfer free energy of amino acids from aqueous solution to a lipid bilayer is essential for understanding membrane protein folding and for predicting membrane protein structure. Here we report a computational approach that can calculate the folding free energy of the transmembrane region of outer membrane β-barrel proteins (OMPs) by combining an empirical energy function with a reduced discrete state space model. We quantitatively analyzed the transfer free energies of 20 amino acid residues at the center of the lipid bilayer of OmpLA. Our results are in



excellent agreement with the experimentally derived hydrophobicity scales. We further exhaustively calculated the transfer free energies of 20 amino acids at all positions in the TM region of OmpLA. We found that the asymmetry of the Gram-negative bacterial outer membrane as well as the TM residues of an OMP determine its functional fold in vivo. Our results suggest that the folding process of an OMP is driven by the lipid-facing residues in its hydrophobic core, and its NC-IN topology is determined by the differential stabilities of OMPs in the asymmetrical outer membrane. The folding free energy is further reduced by lipid A and assisted by general depth-dependent cooperativities that exist between polar and ionizable residues. Moreover, context-dependency of transfer free energies at specific positions in OmpLA predict regions important for protein function as well as structural anomalies. Our computational approach is fast, efficient and applicable to any OMP.

## the journey so far... 2009-2012

"Change is constant."

Heraclitus





Explain biology through physics & mathematics and apply engineering to create biotechnologies

### Pharma Startup 2014-2015

95% Biophysics 5% Mass spectrometry of biotherapeutics

"In the end we retain from our studies only that which we practically apply."

Johann Wolfgang von Goethe

#### How I diversified my skill set in the biopharmaceutical industry



Therapeutic Proteins International, LLC 95% Biophysics 5% Mass Spectrometry of Biotherapeutics

Pharma startup was a 1-year 'boot camp' of 40-70 something hours of weekly work

- 1. (c)GMP and GDP training
- 2. Physical lab notebooks was key for me to develop GDP skills
- 3. Draft, write, publish and execute analytical methods in (c)GMP environment
- 4. FDA audit experience
- 5. Part time in QA (Quality Assurance)

→ This year set the foundation for me to be able to join the biopharmaceutical industry

### Pfizer 2015-2022

Mass spectrometry of biotherapeutics

"In the end we retain from our studies only that which we practically apply."

Johann Wolfgang von Goethe

#### How I diversified my skill set in the biopharmaceutical industry

A time to be mentored...

95% Biophysics 5% Mass Spectrometry of Biotherapeutics

How would you feel about making this 50:50?

- $\rightarrow$  jump at an offer likes this
- → do not be afraid to learn something new

I became a mass spectrometrist and realized I had a passion for something I would have never expected.

Listen to the advice you do not want to hear:

- 1. The feedback that 'bugs you'
- 2. The comments you were 'dreading'
- 3. The experiment you do not want to do/repeat

Digest them

Write them down

Then work on it and make it a platform to stand on

### Pfizer 2015-2022

Mass spectrometry of biotherapeutics

"In the end we retain from our studies only that which we practically apply."

Johann Wolfgang von Goethe

How I diversified my skill set in the biopharmaceutical industry and succeeded

A time to be mentored...

95% Biophysics 5% Mass Spectrometry of Biotherapeutics

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### Pfizer 2015-2022

Mass spectrometry of biotherapeutics

"When the trust account is high, communication is easy, instant, and effective."

Stephen R. Covey, The 7 Habits of Highly Effective People: Powerful Lessons in Personal Change

### Crucial lessons learned...some thoughts on trust

I personally never appreciated the following:

"...trust is built over time and lost quickly..."

Do trust your peers and your peers will trust you.

or, in other words

Respect your peers and your peers will respect you.

Trust creates room for independence and creativity.

(c)GMP is the 'opposite of trust': check, review & verify.

→ yet again, trust is needed.

## Pfizer 2022-present

Mass spectrometry of biotherapeutics

"Change is constant."

Heraclitus

### Be bold in hindsight



## **Evolution is Essential in the Dynamic Pharmaceutical Industry**

March 19, 2020 PAP-Q1-20-CL-033

"The pharmaceutical industry is defined by constant change and evolution."

Adapt and evolve with change

or

Make yourself a change

Decision to leave IL after seven years and transfer internally to MA

→ re-orient and align my personal scientific passions with my professional scientific passions

What may we take away from this?

Be bold, be humble.

Use the tools at your disposal that allow you to answer the question you are asking. *or* 

Built the toolbox that you require through collaboration.

Constructive collaboration is everything and will allow you to thrive in any environment.

Specialize and diversify through hands on experience. They are not mutually exclusive!

Listen to the advice you do not want to hear.

Do trust your peers and your peers will trust you.

Change is constant: adapt and evolve with it, or, make a change yourself.

What may we take away from this?

"All we have to decide is what to do with the time that is given us."

J.R.R. Tolkien, The Hobbit







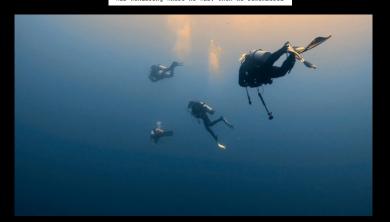
#### Two Hunters

Written by Dennis Gessmann

A bird was screeching. It was sitting at the top of the tree. Its screams reached high into the sky, out of the jungle, traveled over the trees and were finally answered by the sound of the crashing waves out in the bay. Behind the bay lay the reef. The reef itself was a sunken jungle. If someone were to walk through it, breathing like a fish, one could see a perfect reflection of the jungle that was sitting on the island itself. It was filled with beautiful plants and fascinating creatures of all the colors of the spectrum. Spikes of dead beings grew on underwater trees, which created shadows on the bottom of the sea, often mistaken for the predators hunting in this jungle. The smaller beings sought refuge in one of the many underwater caves. The smaller things hunted even smaller things and the small things were eaten by bigger things. Around them, the world was growing in a never ending circle, forced on them, by nothing more than the laws of the universe itself. Every tiny aspect of this world embraced all facets of its world in a perfect symbiosis. It seemed indestructible. Lasius woke up and looked around. At first, he was wondering where he was. Then he remembered









### Acknowledgements

### Jason Rouse Lisa Marzilli

### Carolyn Slade

### scientific colleagues

All former and current

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