14TH ANNUAL · 2023

GoldLab SYMPOSIUM

HUMAN RELATIONSHIPS TO MOLECULAR INTERACTIONS:

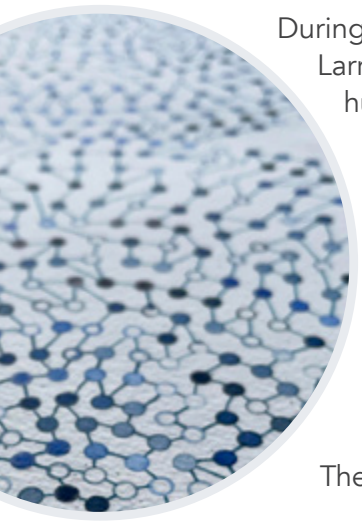
It's Networks All the Way Down

MAY 18 & 19, 2023

ABOUT THE COVER ART

‘HEMISPHERES’

Watercolor on Paper, 2023



A Message from the Artist

During this year’s conversation about the GoldLab Symposium, both Larry Gold and Larry Hunter expressed that this event is a further exploration (and celebration) of our human desire to understand ourselves and our own minds, most notably through computational biology.

The piece this year is simply an abstraction of that desire and of the mirroring effect we create with our systems of understanding. Biological complexity is reflected back at us through a lens of our own creation, our data, our technology.

These dots were plotted and connected by hand according to a set of limitations, perhaps considered ‘prompts’ if dictated to a computer.

The pigmented dots form a network that may resemble – and of course is not limited to:

A Spider’s Web
A Map
A(n) (Un)Known Realm
The World
The Skies
The Brain, A Neural Network
A Chain Reaction
A Ripple
A Process
A Labyrinth
A Microscopic Structure
Binary
A Dreamcatcher
Body Parts (Larry Gold, I see you)

Darin Grassman is an artist, designer, and bookbinder. She studied Painting at California College of Art and Textile Design at the Royal College of Art. Her work spans a wide range of media, but is largely inspired by the world of print – including analog, digital, and 3D.

She manages large projects for an art book printing company and operates her own small stationery and notebook business called LA Bookmaker.

Artist Website: dgrassman.com

LA Bookmaker Website: la-bookmaker.com

SYMPOSIUM AGENDA

HUMAN RELATIONSHIPS TO MOLECULAR INTERACTIONS:

It's Networks All the Way Down

DAY 1 : THURSDAY, MAY 18TH

9:00-9:15am **Larry Gold**
Introduction

SESSION 1: NETWORKS, HUMAN & MOLECULAR

Moderator: Simon Lovestone

9:15-10:00am **Bill Martin**
The Map Is Not the Territory: Redefining the Diagnosis and Treatment of Neuropsychiatric Conditions

10:00-10:45am **Yamuna Krishnan**
Next-Generation Targeting Has Organelle-Level Precision

10:45-11:15am **Break**

11:15am-12:00pm **Mike Klymkowsky**
Coping with the Noisy Nature of Life in Teaching and Other Philosophic Ruminations

12:00-12:45pm **Alejandro Sánchez Alvarado**
Dissecting the Biological Complexity of Animal Regeneration

12:45-2:15pm **Lunch**

SESSION 2: NETWORKS, INTERPERSONAL & DEVELOPMENTAL

Moderator: Melissa Haendel

2:15-3:00pm **Nona Willis Aronowitz**
Bad Sex: Reconciling the Personal, Political, and Biological

3:00-3:45pm **Peter McGraw**
Living Single in a World Built for Two

3:45-4:15pm **Break**

4:15-5:00pm **Roland Baron**
From Rare Diseases of the Skeleton to Treatment for All, and Back: Sclerostin and Its Inhibition

5:00-5:45pm **Lauren Rosenberg**
The Story of Sophie's Neighborhood: Moving Mountains for MCTO (Multicentric Carpotarsal Osteolysis)

5:45-6:00pm **Closing Remarks**

DAY 2 : FRIDAY, MAY 19TH

9:00-9:15am **Larry Hunter**
Introduction

SESSION 3: NETWORKS, INFORMATION & KNOWLEDGE

Moderator: Ruth Crowe

9:15-10:00am **Phil Fernbach**
Knowledge Overconfidence

10:00-10:45am **Michelle Holko**
Wearable Sensors and the Future of Health

10:45-11:15am **Break**

11:15am-12:00pm **Jack Gallant**
Decoding Brains: Imaging to Advance Mental Health

12:00-12:45pm **Lex Van der Ploeg**
The Language of Song: AI-Powered RIFFIT Enhances Communication and Learning

12:45-2:15pm **Lunch**

SESSION 4: NETWORKS, COMPUTATIONAL & TRANSCRIPTIONAL

Moderator: Tim Harris

2:15-3:00pm **Larry Hunter**
Five Questions About Generative AI and Health

3:00-3:45pm **Nicholas Tatonetti**
AI-Driven Biomedical Discoveries Using Observational Data

3:45-4:15pm **Break**

4:15-5:00pm **Karolin Luger**
Genomes Packaged to Perfection, in All Domains of Life

5:00-5:45pm **Andreas Beyer & Argyris Papantonis**
Living in the Fast Lane: Accelerated Copying of Genetic Information with Aging

5:45-6:00pm **Closing Remarks**

All times are in Mountain Time | MDT UTC-06:00

WELCOME FROM LARRY GOLD

As I did last year, I've been thinking about the raw pleasure of seeing so many old friends again, this time both virtually and in person. This year, after a three-year COVID-induced interruption, we are back at our old venue and we are also virtual. Probably we will have more attendees than ever, for which we are grateful. As I have aged – it does seem inexorable – I have come to love our event even more. The chance to integrate biology, mathematics, and life-stuff feels like the right thing for me, and I am grateful to all of you for continuing to think these days are a worthy way to spend your time. I should add here that Meredith and I were like an old (and odd) couple, saying the same things to each other year after year, hoping one of us would surprise the other. Last year we invited Larry Hunter (the "other Larry") to join us permanently, and our discussions have improved. Larry Hunter knows things we have never understood, and the integration of thinking about biology with mathematics/computation has been a pleasure. Meredith and I are more thoughtful people after two years of weekly discussions with Larry Hunter – why we did not invite him into our lives earlier is a mystery to us.

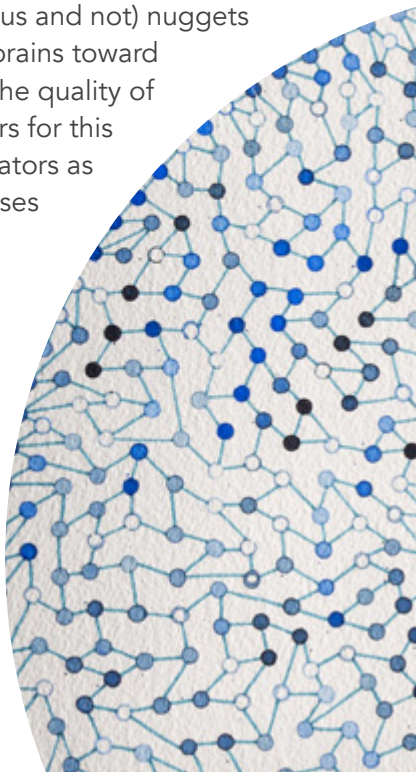
I also want to thank all our sponsors and the many of you who sent us unsolicited gifts. The three of us take those donations as a way of saying "don't stop" and we commit to not stopping. We already have a nearly complete list of speakers for next year. And we do owe a special thank you to Agilent and SomaLogic who have been major sponsors each year since we started these events in 2010. While companies often are accused of caring only about the earnings for the next quarter, Agilent and SomaLogic have understood that an informed citizenry is good for everyone. We believe that an informed citizenry is one of our major goals!

We are focused on biology and big data – they are now our future. I said that "nothing can surprise us more than when our policies fail us."

Last year Tim Snyder gave the most timely and remarkable talk, almost as though we had bumped into him in a bar and he sidled up to us to ask if we wanted to know his thoughts about Ukraine. Then, for almost an hour, we heard a set of truths that we will never forget. We also heard last year about solving the protein folding problem and the year before we heard about Artificial General Intelligence (which has now swept the world through ChatGPT) from an inventor at Open AI. We were ahead of the world because Craig Mundie is our friend! This year, as promised, we continue our exploration of big data, because the world of biology and big data is facing an explosion of insights (some might say incites!) and we are pressed to stay informed, even though our skill sets may not be up to that task. We did understand what was coming but had not understood the "gold rush" quality to the changes. We hope to stay calm and thoughtful…and useful to all of you, this year and in the years to come.

We are now about to embark on another visit into the unknown, the result of having good people wonder about important things, with hopes that at the interfaces (both obvious and not) nuggets and thoughts will drive our brains toward contributions that enhance the quality of life. We thank all the speakers for this year, and the session moderators as well. We expect many surprises over the next two days.

Larry Gold



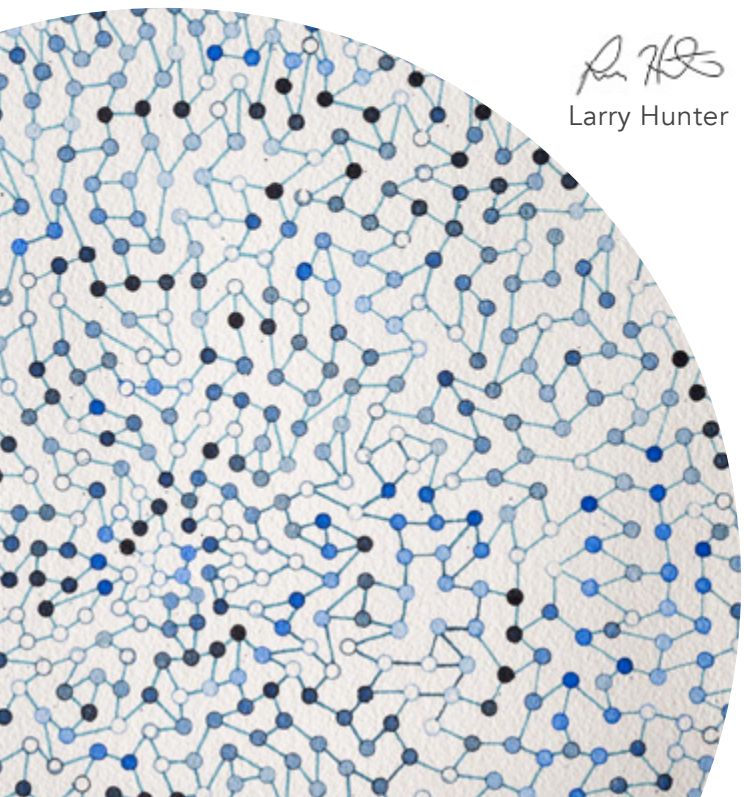
FROM LARRY HUNTER

This marks my first full year as a co-organizer of the GoldLab Symposium. Working closely with Meredith and Larry on putting together this year's symposium has been tremendous fun, and I hope you enjoy this program as much as we have enjoyed putting it together. I am excited we are back in a larger venue where once again we can welcome the general public, as well as build on our COVID-era streaming audience to share these great talks worldwide.

In last year's letter, I wrote about appreciating how algorithms can be partners in understanding life and improving human health, and wondering how our values can be reflected in those algorithms so that together we might shape a healthier, happier, and more just existence for us all. Little did I know that a breakout AI technology would capture the world's imagination, making those fundamental questions even more pressing.

The intense global focus on AI has put many of my favorite thinkers on these topics very much in the spotlight, making it difficult for me to recruit them to this year's symposium. As a consolation, Larry and Meredith enlisted me to demystify the technology and provide some context to think about it, particularly as applied to human health. I promise to bring more diverse voices to discuss these important issues next year.

This year, however, is as exciting as ever. I look forward to our shared learning from a marvelous collection of speakers on topics as broad as the human experience. Being among the community that the symposium nucleated remains one of the highlights of my year. Seeing such wonderful old friends and making fascinating new ones brings me such joy, and I hope you feel the same.



Larry Hunter

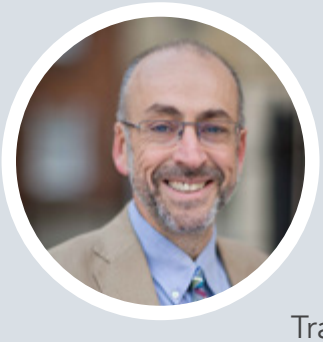
SCHEDULE DAY ONE

SESSION 1: NETWORKS, HUMAN & MOLECULAR

Moderator: Simon Lovestone

9:15-10:00am	**Bill Martin** The Map Is Not the Territory: Redefining the Diagnosis and Treatment of Neuropsychiatric Conditions
10:00-10:45am	**Yamuna Krishnan** Next-Generation Targeting Has Organelle-Level Precision
10:45-11:15am	**Break**
11:15am-12:00pm	**Mike Klymkowsky** Coping with the Noisy Nature of Life in Teaching and Other Philosophic Ruminations
12:00-12:45pm	**Alejandro Sánchez Alvarado** Dissecting the Biological Complexity of Animal Regeneration
12:45-2:15pm	**Lunch**

MODERATOR SESSION ONE



SIMON LOVESTONE, PhD

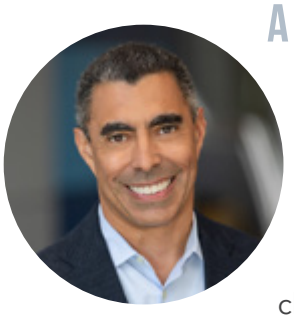
Global Head of Discovery and Translational Research, Neuroscience, Janssen Research & Development

Simon joined Janssen as Neuroscience DAS leader for neurodegenerative disorders in 2018 and is now Global Lead for Neuroscience Discovery and Translation. Prior to moving to industry, he was Professor of Translational Neuroscience at Oxford University where he founded and led the ARUK Dementia Drug Discovery Institute with Chas Bountra, and before that was at King's College London where he led the Biomedical Research Centre for Mental Health. His research interests are in the mechanisms of Alzheimer's Disease and in the search for biomarkers and building on these, in drug discovery and experimental medicine. He studied Microbiology at Sheffield University, Medicine at Southampton University and his PhD was from the University of London for research on role of GSK3 in phosphorylation of tau. He was knighted for services to Neuroscience research in 2017.

BILL MARTIN, PhD

Global Therapeutic Area Head, Neuroscience, Janssen Research & Development

ABSTRACT



The Map Is Not the Territory: Redefining the Diagnosis and Treatment of Neuropsychiatric Conditions

How we conceptualize disease informs how we treat it, as exemplified by approaches to treating diseases of the mind. More than a century ago, Edward Colwes wrote about the importance of steady progress towards a truth, informed by understanding clinical symptoms and the course of disease. The aspiration of using mechanistic insights of disease to guide development of novel therapeutics for neuropsychiatric conditions has been elusive. The neuropharmacological revolution in treating serious mental illnesses occurred in the absence - not because of - scientific advances into the understanding of the brain. Serendipity-based drug discovery helped to transform patient care and left a legacy of important medicines; however, these successes contributed to the codification of categorical diagnoses which were reinforced by the descriptors of drug classes. The field of psychiatry came to view the "map as the territory." That is, the representation of mental illnesses became 'ground truths' to be further refined into ever more precise definitions, without the benefit of biological underpinnings to define this reality. Categorical definitions limited the generation of mechanistic insights and, absent a model for scientific innovation, large pharma exited or significantly scaled back investments in neuroscience therapeutics development. Yet, today, not only are more neuroscience companies forming, but a high proportion of these companies cite 'precision neuroscience' as a core part of their strategy. What does this mean for the field and where will we go from here? This presentation reviews the rationale and need for a new conceptual framework for neuropsychiatric research and drug development. By leveraging recent advances in brain imaging, data science and the tools of precision medicine, the field of neuropsychiatry is positioned to evolve a classification system from categorical CNS conditions to biologically informed diseases which could transform diagnostics and therapeutics development for the next century.

BIOGRAPHY

Bill Martin leads the Neuroscience therapeutic area of Janssen Research & Development, LLC in discovering and developing important new therapies for people living with brain disorders. His role is focused on addressing areas where the greatest unmet needs in neuroscience remain, and where the biggest impacts can be made for patients and society, including serious mental illness (such as treatment-resistant depression and schizophrenia) and neurodegenerative disorders (such as Alzheimer's disease).

Prior to joining Janssen R&D, Martin co-founded Blackthorn Therapeutics, where he first served as the company's Chief Scientific Officer and Head of R&D before becoming President and Chief Executive Officer. Blackthorn integrates computational and clinical neuroscience and applies a precision medicine approach to creating novel therapeutics for central nervous system (CNS) disorders. Before Blackthorn, Martin held leadership positions at Theravance Biopharma. He started his career at Merck, contributing to the company's Neuroscience franchise.

Martin is also a member of the Board of Directors for Brown University's Carney Institute for Brain Science and has held leadership positions in the Society for Neuroscience, the Alliance for Artificial Intelligence in Healthcare, the American Physiological Society and the International Brain Research Organization. He has published extensively on neuroscience and brain disorders, with more than 75 publications in scientific journals.

Martin received a bachelor's in Psychology from Swarthmore College and a doctorate in Experimental Psychology from Brown University. He conducted postdoctoral research at the Keck Center for Integrative Neuroscience at the University of California, San Francisco.

YAMUNA KRISHNAN, PhD

Professor of Chemistry, Department of Chemistry, University of Chicago

ABSTRACT

Next-Generation Targeting Has Organelle-Level Precision

Intracellular organelles are relatively autonomous sub-systems within the cell, whose activity and chemical composition reflect the cell's metabolic state. Metabolism is altered in diseased or aging cells, reflected at the level of specific organelles within them. Often, introducing compensatory changes in organelles can restore cells to normalcy given the intrinsic feedback between cells and their organelles. Nature already targets the delivery of exogenous cargo with organelle-level precision in living organisms as evidenced by invading pathogens as well as endogenous signaling molecules. DNA can be self-assembled into molecularly precise, well-defined, synthetic assemblies on the nanoscale, commonly referred to as designer DNA nanodevices. Over the last decade, Krishnan's lab developed a way to target DNA nanodevices to specific cells in vivo, but with organelle-level precision. The first discovery in 2011 revealed that DNA nanodevices could reach organelles called lysosomes in specific cells of live nematodes, where it functioned as a reporter of pH. Until this innovation, it was not at all obvious whether such DNA nanodevices could function inside a living cell without being interfered with, or interfering with, the cell's own networks of DNA control. Her team spent 10 years studying the environment within lysosomes. This presentation will explain how lysosomes can be used to control cell state, flip the cell "from baddie to goodie," and turn cold tumors hot in mice.

BIOGRAPHY

Yamuna Krishnan, Professor of Chemistry at the University of Chicago, has led her group to pioneer the development of DNA-based molecular devices for the study of cell physiology at the nanoscale. This breakthrough has enabled chemical imaging and eliminated decades-old bottlenecks. Krishnan's achievements have earned her numerous accolades, including the Shanti Swarup Bhatnagar Award for Chemical Sciences, the Infosys Prize for Physical Sciences, and the NIH Director's Pioneer Award. She was also included in Cell's 40 under 40 list of scientists shaping current and future trends in biology. Krishnan has co-founded two companies, Esya Inc and MacroLogic Inc, which use her patented organelle-targeting nanotechnology for diagnostics and therapeutics. She serves as an editor for *Chemical Reviews* and the *Journal of Physiology,* and is a member of the Scientific Advisory Board of the Max Planck Institute of Cell Biology and Genetics, as well as the Brain Research Foundation (USA).

MIKE KLYMKOWSKY, PhD

Professor of Molecular Biology, Department of Molecular, Cellular, and Developmental Biology, University of Colorado Boulder

ABSTRACT

Coping with the Noisy Nature of Life in Teaching and Other Philosophic Ruminations

Klymkowsky's goal for this talk is to illustrate how stochastic (noisy) processes influence all aspects of life and how they can be best introduced to students. Physics is often seen as the model for how science works, with its explanatory power implying that our universe is deterministic. However, many events, such as radioisotope decay, are unpredictable individually. Stochasticity is more prominent and functionally significant in living systems, where complexity is built through evolutionary processes in ever-changing conditions, resulting in a range of emergent behaviors, including consciousness and self-consciousness. The basic living unit, the cell, is particularly susceptible to the effects of stochasticity. Cells typically contain two gene copies and small numbers of regulatory molecules, causing a wide range of unpredictable variations in gene expression, axon firing, and network behaviors that influence the organism's development and behavior. Stochastic variation can explain why identical twins are similar but not identical and how genetic differences influence phenotype, disease susceptibility, and responses to pathogens and drugs. Despite this, our educational system rarely introduces students to stochastic processes' origins and implications, and the myth of genetic determinism influences many scientific discussions. Introducing students to the functionally valuable roles and implications of stochastic processes can place deterministic myths in context. It raises questions about what determinism means if we cannot predict individual behaviors accurately. Developing an appreciation and understanding of the stochastic nature of living things may lead to a more realistic, humane, and hopeful perspective among people.

BIOGRAPHY

Mike Klymkowsky, the son of German and Ukrainian immigrants, is a renowned biologist and professor who has been part of the Molecular, Cellular, and Developmental faculty at CU Boulder since 1983. He holds degrees in biophysics from Penn State and CalTech and has done post-doctoral work at University College London and the Rockefeller University. His research has focused on neurotransmitter receptor structure, cytoskeletal and ciliary organization and function, and developmental signaling systems. He is also passionate about improving science education and has developed the NSF-supported Biology Concepts Instrument and a suite of virtual laboratory activities with his colleagues.

Klymkowsky has collaborated with Professor Melanie Cooper to develop open education resources (OER) course materials in chemistry, organic chemistry, and biology, which incorporate web-based interactive graphical beSocratic activities. These materials aim to help students recognize and apply underlying principles and have been shown to have a positive impact on student engagement and learning outcomes. He has also co-directed CU's science teacher recruitment and certification program and participated in various education research talks and programs.

Klymkowsky's contributions to science education have earned him numerous awards and honors, including being named a Pew Biomedical Scholar and a fellow of the American Association for the Advancement of Science. He was also recognized as the 2013 Outstanding Undergraduate Science Teacher by the Society for College Science Teaching and received teaching excellence awards from the Boulder Faculty Assembly and the UC Boulder campus for his contributions to the use of OER course materials. Klymkowsky shares his insights and research findings regularly on his blog, bioliteracy.blog.

ALEJANDRO SÁNCHEZ ALVARADO, PhD

Executive Director and Chief Scientific Officer, Stowers Institute for Medical Research

ABSTRACT

Dissecting the Biological Complexity of Animal Regeneration

Under normal physiological conditions, the functions of many organs depend on the continuous destruction and renewal of their cells. Equally remarkable is the fact that the adult tissues and organs of many organisms can be fully restored after amputation. In fact, metazoans have evolved a series of renewal and repair mechanisms to respond to both trauma and normal wear and tear. Such mechanisms are under tight regulatory control such that the form and function of tissues, organs, and systems can be maintained throughout life.

As important as repair and restoration are to the survival of multicellular organisms, we know little about how these processes are affected and regulated at the cellular and molecular levels. In this presentation, Sánchez Alvarado will discuss how the planarian Schmidtea mediterranea is beginning to shed light on the way adult animals regulate tissue homeostasis and the replacement of body parts lost to injury.

BIOGRAPHY

Alejandro Sánchez Alvarado is the Priscilla Neaves Chair in Biomedical Sciences at Stowers Institute for Medical Research and serves as its Executive Director and Chief Scientific Officer. His laboratory investigates the genetic and cellular control of regeneration and tissue maintenance, identifying dozens of genes and genetic programs involved in these processes. Additionally, his research has revealed insights into the molecular and genetic drivers of both regenerative and degenerative cellular processes that contribute to disease. Sánchez Alvarado's work has the potential to improve understanding of how higher organisms, including humans, carry out their biological functions.

Sánchez Alvarado is the recipient of numerous honors and awards, and is an elected member of the National Academy of Sciences, the American Academy of Arts and Sciences, and a fellow of the American Association for the Advancement of Science.

SCHEDULE DAY ONE

SESSION 2: NETWORKS, INTERPERSONAL & DEVELOPMENTAL

Moderator: Melissa Haendel

2:15-3:00pm	**Nona Willis Aronowitz** Bad Sex: Reconciling the Personal, Political, and Biological
3:00-3:45pm	**Peter McGraw** Living Single in a World Built for Two
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5:00-5:45pm	**Lauren Rosenberg** The Story of Sophie's Neighborhood: Moving Mountains for MCTO (Multicentric Carpotarsal Osteolysis)
5:45-6:00pm	**Closing Remarks**

MODERATOR SESSION TWO

MELISSA HAENDEL, PhD

Chief Research Informatics Officer, University of Colorado Anschutz Medical School

Melissa Haendel is the Chief Research Informatics Officer at University of Colorado Anschutz Medical School, and Director of the Center for Data to Health (CD2H). Her background is molecular genetics, developmental biology, and toxicology as well as translational informatics, with a focus over the past decade on open science and semantic engineering. Her vision is to weave together healthcare systems, basic science research, and patient generated data through development of data integration technologies and innovative data capture strategies. Haendel's research has focused on integration of genotype-phenotype data to improve rare disease diagnosis and mechanism discovery.

NONA WILLIS ARONOWITZ

Writer, Editor, and Author

ABSTRACT

Bad Sex: Reconciling the Personal, Political, and Biological

History's feminists and sexual revolutionaries have always had to grapple with an infuriating dilemma: Love and lust are major roadblocks to political clarity. It's never easy to live out dearly held values in one's personal life, a task that's especially messy for heterosexual women fighting for gender equality. The social and biological forces of sex, romance, and heartbreak introduce particularly acute chaos into otherwise coherent activism. This talk will explore how the most radical among us—from anarchist rabblerouser Emma Goldman to the Second Wave's political celibates to Nona's own pro-sex feminist mother, Ellen Willis—have attempted to reconcile personal desire with political conviction.

BIOGRAPHY

Nona Willis Aronowitz is a writer, editor, and author. Her book, *Bad Sex*, a memoir-social history blend that examines the enduring barriers to true sexual freedom, was published in August 2022. She have a biweekly sex and love advice column for *Teen Vogue*, and has written for publications like *The New York Times, The Cut, Elle, VICE,* and *Playboy*. She co-authored the road-trip book Girldrive: *Criss-crossing America, Redefining Feminism* with Emma Bee Bernstein. She's also the editor of two award-winning anthologies of her mother Ellen Willis's work: a book of her rock criticism, *Out of the Vinyl Deeps*, and a fatter collection, *The Essential Ellen Willis*. She's been to almost every U.S. state but now splits her time between NYC and Tannersville, NY.

PETER MCGRAW, PhD

Professor of Marketing and Psychology, Leeds School of Business, University of Colorado Boulder

ABSTRACT

Living Single in a World Built for Two

Single living is on the rise. Half of adults in the United States are unmarried and 28% of households in the United States are one person, surpassing the nuclear family as the most common household.

The rise of singles is not slowing, with one in four Millennials in the United States projected to never marry and half of single adults not interested in dating in the first place. This trend is a global phenomenon, with people going solo from Sweden to South Korea.

With the nuclear family waning, policy makers, religious leaders, and your Aunt Sally lament the loss of the good old days of the 1960's, where nearly everyone married and had children. As well-intentioned as their concerns are, they hold myths and stereotypes about singles that don't hold up to scientific scrutiny:

- Singles are sad, lonely, and desperate to find a partner and settle down.
- Singles are unwilling or unable to put in the hard work required to create a family.
- The rise of singles is a symptom of a world in decline.

Drawing from extensive interviews with hundreds of singles, surveys of thousands of singles and non-singles, and the latest research in psychology, anthropology, and demography, McGraw debunks these myths and highlights the diverse experiences and contributions of singles to society.

McGraw will conclude by sharing three valuable lessons that married people can learn from singles in order to live a remarkable life.

BIOGRAPHY

Peter McGraw is a behavioral economist, bachelor, and business school professor at the University of Colorado Boulder. He hosts the podcast *Solo-The Single Person's Guide to a Remarkable Life,* and he writes for *Single Insights – The Science of Solos*, a resource for organizations seeking to better serve their single customers and employees. McGraw is an author of two books: *The Humor Code: A Global Search for What Makes Things Funny* and *Shtick to Business: What the Masters of Comedy can Teach You about Breaking Rules, Being Fearless, and Building a Serious Career.* His third book, *Solo: Breaking the Rules in a World Built for Two*, launches later this year.

ROLAND BARON, PhD, DDS

Professor of Medicine, Harvard Medical School, Endocrine Unit, Massachusetts General Hospital,Professor and Head of the Division of Bone and Mineral Research, Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine

ABSTRACT

From Rare Diseases of the Skeleton to Treatment for All, and Back: Sclerostin and Its Inhibition

Osteoporosis, characterized by bone loss and skeletal fragility, affects hundreds of millions of patients worldwide, resulting in millions of fractures, reduced mobility, and frequent death. For many decades, the only treatments available aimed at reducing the resorption of bone (anti-resorptives: bisphosphonates, denosumab, estrogens). Treatments that increase bone formation (bone anabolics) have emerged later with the intermittent activation of the parathyroid hormone (PTH) receptor (teriparatide, abaloparatide). But the ability to enhance both mechanisms (anti-resorptive and anabolic) remained elusive until the mutations causing several rare human skeletal diseases were identified within the WNT signaling machinery, uncovering the essential role played by this pathway in the homeostasis of the skeleton. One WNT signaling component, sclerostin, is an endogenous canonical WNT signaling inhibitor secreted locally by the cells residing within the bone matrix, the osteocytes. Sclerostin acts locally to regulate both bone formation and bone resorption. Physiologically, sclerostin expression is regulated by mechanical loading, PTH/PTHrP signaling, and sex hormones. Studies of sclerostin-null mice, or inhibition of sclerostin by anti-sclerostin monoclonal antibodies (romosozumab) revealed the molecular and cellular mechanisms by which sclerostin inhibition simultaneously enhances bone formation and decreases resorption, leading to rapid increases in bone mass. Clinical trials have confirmed that, although the anabolic effects are limited in time, sclerostin inhibition increases bone density markedly and rapidly, decreasing fracture risk in patients with severe osteoporosis. Thus, elucidation of the causes of rare diseases led to a treatment for millions of osteoporotic patients. In turn, these findings are now tested in the treatment of other rare diseases with skeletal fragility (Osteogenesis Imperfecta). Recent advances in the treatment of other rare skeletal diseases may also find applications in more common skeletal conditions.

BIOGRAPHY

Roland Baron is a Professor at Harvard Medical School and Head of the Division of Bone and Mineral Research at the Harvard School of Dental Medicine. Prior to joining Harvard, Baron held a Professorship in the departments of Medicine, Orthopedics, and Cell Biology at Yale University School of Medicine.

Baron held the position of Vice President and Head of the Bone Diseases Group at Hoechst Marion Roussel and later at Aventis Pharma. In 2002, he founded ProSkelia, a small pharmaceutical company devoted to the discovery and development of new drugs for bone and hormonal-dependent diseases, which is now part of Galapagos. Baron held the positions of President and Chief Scientific Officer of ProSkelia and then ProStrakan, until April 2006.

He currently serves as the co-Chair of the International Federation of Musculoskeletal Research Societies (IFMRS). Previously, he served as President of the European Calcified Tissue Society, and as President of the American Society for Bone and Mineral Research (ASBMR).

He received his DDS and PhD degrees from the Medical School, University of Paris, France. Additionally, he is the founder and past Editor-in-Chief of BONE, a prominent research journal in the field. Baron has received several awards, including the Doctor Honoris Causa of the Université René Descartes (2002, Paris, France), the MERIT Award from the NIH, NIDCR, the William Neuman Award (2009) and the Avioli Founder Award (2002) from ASBMR, the Harold Copp Award from the International Bone and Mineral Society (2005, IBMS), and the Excellence in Research Award from the European Calcified Tissue Society (2014, ECTS). He has published over 390 scientific papers in the field of bone biology, bone diseases, and their treatment.

LAUREN ROSENBERG

Co-Founder of Sophie's Neighborhood

ABSTRACT

The Story of Sophie's Neighborhood: Moving Mountains for MCTO (Multicentric Carpotarsal Osteolysis)

A journey to find treatments for an ultra rare bone and kidney disease impacting less than 50 patients worldwide, including 5 year old Sophie Rosenberg.

BIOGRAPHY

Sophie's Neighborhood is a nonprofit 501c3 organization founded in response to 5-year-old Sophie Rosenberg's diagnosis of an ultra-rare, genetic disorder: Multicentric Carpotarsal Osteolysis (MCTO). Sophie is from Boulder, Colorado. Daughter of local restaurant owners, Hosea and Lauren Rosenberg of Blackbelly & Santo, she is one of ~50 people worldwide identified with MCTO, a rare, progressively crippling genetic bone and kidney disease. MCTO is linked to a mutation in the MafB gene. Over time the mutation is causing her joint bones to disappear and develop abnormally and threatens end stage kidney failure. There is currently no treatment or cure to stop the disorder from its path of destruction. Sophie's Neighborhood was formed to change that RAPIDLY. By funding scientific research worldwide, guided by an expert team of scientific advisors, the organization is urgently working to understand exactly how a single, heterozygous MafB mutation causes MCTO. All MafB MCTO mutations have been within a short amino acid domain that controls MafB concentration within cells in the very small amino acid range that invariably causes MCTO. Sophie's Neighborhood is working with scientists at academic institutions and biotech companies specializing in the various disciplines related MCTO pathology. Research spans understanding the biology of bone building cells in MCTO, as well as the cells involved in bone resorption - blood cells, hematopoietic stem cells, and kidney cells. Further progress can be attributed to the groundbreaking scientific partnerships with companies in cell engineering, transcriptomics, and proteomics. Studies are underway to uncover viable therapeutics through drug repurposing, as well as novel modalities for the purposes of halting MCTO in its patients. We are here to move mountains for MCTO, and we will not stop fighting to help patients with this rare disease.

Sophie's Neighborhood

SCHEDULE DAY TWO

SESSION 3: NETWORKS, INFORMATION & KNOWLEDGE

Moderator: Ruth Crowe

9:15-10:00am	**Phil Fernbach** Knowledge Overconfidence
10:00-10:45am	**Michelle Holko** Wearable Sensors and the Future of Health
10:45-11:15am	**Break**
11:15am-12:00pm	**Jack Gallant** Decoding Brains: Imaging to Advance Mental Health
12:00-12:45pm	**Lex Van der Ploeg** The Language of Song: AI-Powered RIFFIT Enhances Communication and Learning
12:45-2:15pm	**Lunch**

MODERATOR SESSION THREE

RUTH CROWE, MD, PhD

Associate Dean for Medical Education, New York University Long Island School of Medicine

Ruth Crowe is an internist in New York City. As an Associate Dean for Medical Education at New York University Long Island School of Medicine, she focuses on implementing innovative medical education to foster growth of physicians who will be entrustable to deliver high value care and facilitate health care reform.

PHIL FERNBACH, PhD

Professor of Marketing and Co-Director of the Center for Research on Customer Financial Decision Making,
Leeds School of Business, University of Colorado Boulder

ABSTRACT

Knowledge Overconfidence

Fernbach will describe research examining the interrelationships between opposition to expert consensus on controversial scientific issues, how much people actually know about these issues and science in general, and how much they think they know. Those with the greatest levels of opposition to the consensus have the lowest levels of objective knowledge but the highest levels of subjective knowledge. Studies focus on controversial issues that enjoy a substantial scientific consensus such as climate change, genetically modified foods, vaccination, and homeopathic medicine, as well as attitudes about the COVID-19 pandemic.

Fernbach will discuss implications for science education and public discourse. In addition, he will reflect on the communal nature of knowledge and related issues like conspiracy theories and misinformation.

BIOGRAPHY

Philip (Phil) Fernbach is an Associate Professor of Marketing and Director of the Center for Research on Consumer Financial Decision-Making at the Leeds School of Business at the University of Colorado, Boulder. He teaches data analytics and behavioral science to undergraduates and Master's students, and is published widely in the top journals in cognitive science, consumer research and marketing.

Fernbach is co-author of *The Knowledge Illusion: Why We Never Think Alone,* (Riverhead Books, 2017) which was chosen as a *New York Times* Editors' Pick. He has also written for *The New York Times* and *Harvard Business Review*, and his research has been featured in outlets such as *The Wall Street Journal, The Washington Post, National Public Radio,* and the BBC. The Society for Consumer Psychology awarded Fernbach the Early Career Award for contributions to consumer research. He received his PhD in cognitive science from Brown University, and his undergraduate degree in philosophy from Williams College.

MICHELLE HOLKO, PhD

Innovating at the intersection of biology, technology, and security

ABSTRACT

Wearable Sensors and the Future of Health

Data from wearable sensors and other digital health technologies (DHT), including Apple Watch, Fitbit, and Oura Ring, are increasingly used in health and research. Continuous data streams like these may provide more granular information about biology, physiology, and health versus sporadic, non-continuous measurements. Sensor data are ripe for AI/ML; algorithms to detect anomalies and other bio-related phenomena in wearable sensor data are being integrated into research, moving into clinical practice, and also being used for non-clinical health-adjacent applications (e.g. human performance optimization). While there is obvious progress, there are also challenges including regulatory, reimbursement, security, privacy, and equity. This talk reviews current technologies, clinical and other health adjacent use cases, availability of data and tools, investor landscape, and a discussion about barriers and strategies to overcome and realize a new future of health.

BIOGRAPHY

Michelle Holko is a strategic innovator who works at the intersection of biology, technology, and security. She recently served as a Principal Architect and Scientist at Google, where she worked on healthcare and science solutions with Google Cloud Public Sector. Previously, Holko was a Presidential Innovation Fellow (PIF) and worked with various government agencies, including the Department of Homeland Security's (DHS) Cybersecurity and Infrastructure Security Agency (CISA), the Department of Defense (DoD) Chemical and Biological Defense Program (CBDP), the NIH's All of Us Research Program, HHS Biomedical Advanced Research and Development Authority (BARDA), the White House Office of Science and Technology Policy (OSTP), and the National Security Council (NSC). Holko also worked at the Defense Advanced Research Projects Agency (DARPA) and HHS BARDA's Division of Research, Innovation, and Ventures (DRIVe) before joining the PIF program. In addition, Holko was a fellow in the 2018 cohort of Johns Hopkins University's Center for Health Security's Emerging Leaders in Biosecurity Initiative and served as a Staff Scientist at NIH's NCBI, where she worked to promote re-use and re-analysis of biomedical research data.

Holko's technical expertise lies in genomics and bioinformatics, and she has experience in research and development of capabilities for pandemic prevention and preparedness, infectious diseases, cancer, biosurveillance, biosecurity, data science, emerging technologies, digital health technologies, precision medicine, cybersecurity, and machine learning/artificial intelligence. She currently serves as the Director of U.S. Markets for Airfinity, a leader in disease forecasting and intelligence, and is building strategic alliances for UCSF's Quantitative Biosciences Institute. Additionally, Holko is a PI at the International Computer Science Institute at Berkeley.

JACK GALLANT, PhD

Chancellor's Professor of Psychology, University of California at Berkeley

ABSTRACT

Decoding Brains: Imaging to Advance Mental Health

Functional magnetic resonance imaging (fMRI) provides powerful tools for mapping the human brain. However, because conventional fMRI provides little information about brain function in individuals, it is rarely used for clinical applications. Given that mental disorders and neurodegenerative diseases disrupt normal thought processes, the lack of any principled method for assessing thought patterns directly presents a serious limitation to our ability to diagnose these disorders. Recent breakthroughs in individualized functional brain mapping could provide new opportunities to improve diagnosis, prognosis, and monitoring of brain disorders and neurodegenerative diseases.

BIOGRAPHY

Jack Gallant is Chancellor's Professor and Class of 1940 Chair at the University of California at Berkeley. He holds appointments in the Departments of Psychology, Neuroscience, and Electrical Engineering and Computer Sciences. He is a senior member of the Institute of Electrical and Electronics Engineers (IEEE) and past Chair of the IEEE Brain Community.

Professor Gallant's research focuses on high-resolution functional mapping and quantitative computational modeling of human brain networks. His lab has created detailed functional maps of human brain networks mediating vision, language comprehension, and navigation. They have used these maps to decode and reconstruct perceptual experiences directly from brain activity.

LEX VAN DER PLOEG, PhD

Chairman and CEO, RIFFIT

ABSTRACT

The Language of Song: AI-powered RIFFIT Enhances Communication and Learning

For millennia, humans have used music to convey information. Songs and melodies heighten interest, facilitate comprehension, and promote long-term recall. The timing and variations in pitch and rhythm of a song lead the listener to process the information differently when compared to spoken or silently read information. Extensive research using neuroimaging highlights unique cognitive processing of content in song. Individuals with language processing challenges may benefit from sung information, but teachers and care providers may not have the time or skill to sing information during a lesson. While it is possible to pre-record and play back sung information, pre-recorded lesson plans are inflexible and cannot be rapidly tailored to individual student needs.

RIFFIT is a generative AI startup that uses advanced technology to convert any text into personalized songs in real-time. RIFFIT's products use AI to make this "language of song" available to anyone, anytime, anywhere. With the recent advancements in AI and technology, RIFFIT is at the forefront of a new era in which generating songs in real-time is now possible. This technology has the potential to revolutionize the way we communicate and learn.

The RIFFIT Learning App (https://app.riffitNow.com) supports learning and therapeutic applications (currently focusing on people with neurological conditions including dyslexia, autism and aphasia) while SongR App (https://app.songR.ai/), allows users can create their own songs for entertainment or social communication in just three clicks.

BIOGRAPHY

Lex Van der Ploeg is the Founder, President, Chairman, and CSO of RIFFIT, an edtech company focused on AI-enabled digital applications to advance learning and communication for diverse neurological conditions, as well as general communication and entertainment. He is also an advisor to DeuteRx, Neuromity, Rhythm Pharmaceuticals, and IRIS Kinetics.

Van der Ploeg is an experienced biotech executive, scientist, and entrepreneur, contributing to the development of novel therapeutics and successful M&A transactions. Over the past ten years, he has played a key role in the development of Rhythm Pharmaceuticals' setmelanotide (IPO in 2017), the sale of Motus Therapeutics for relamorelin (acquired by Allergan in 2016), and the sale of DeuteRx's DRX065 (now PXL065 following its 2018 acquisition by Poxel). He also supported the sale of Deuteria Pharmaceuticals to Celgene, the sale of Deuteria assets to Salarius, and the founding of Neuromity.

Prior to RIFFIT, Van der Ploeg was Senior Vice President of Integrative Medicine and Translational Sciences at Abraxis Bioscience, acquired by Celgene in 2010. He spent 17 years at Merck, establishing and growing the Merck Boston research laboratories, discovering the ghrelin receptor, and contributing to the discovery of the target for ivermectin and the development of vorinostat. Van der Ploeg put over 15 programs into clinical development and guided programs at Banyu Res labs in Japan for ten years, and restructured the Merck San Diego laboratory. Before joining industry, he was a tenured faculty member at Columbia University in infectious diseases.

Van der Ploeg has received numerous awards, has over 250 peer-reviewed publications, and is an inventor on over 70 patents.

SCHEDULE DAY TWO

SESSION 4: NETWORKS, COMPUTATIONAL & TRANSCRIPTIONAL

Moderator: Tim Harris

2:15-3:00pm	**Larry Hunter** Five Questions About Generative AI and Health
3:00-3:45pm	**Nicholas Tatonetti** AI-Driven Biomedical Discoveries Using Observational Data
3:45-4:15pm	**Break**
4:15-5:00pm	**Karolin Luger** Genomes Packaged to Perfection, in All Domains of Life
5:00-5:45pm	**Andreas Beyer & Argyris Papantonis** Living in the Fast Lane: Accelerated Copying of Genetic Information with Aging
5:45-6:00pm	**Closing Remarks**

MODERATOR SESSION FOUR

TIM HARRIS, PhD, DSc

Biotechnology Consultant and Science Advisor

Tim Harris is a molecular biologist, biochemist, and geneticist. He started work in the biotech industry almost at its inception. He began his scientific career in 1974, working on animal viruses - cloning picornavirus RNAs. He was one of the first molecular biologists to join the UK biotech company Celltech (now UCB Pharma) in 1981. He spent nearly five years from 1989 to 1993 at Glaxo Group Research (now GSK) as Director of Biotechnology.

Harris moved to the United States in 1993 to be Executive Vice President (EVP) of R&D at Sequana Therapeutics. It was acquired by Arris Pharmaceutical to form Axys Pharmaceuticals in 1998. Harris founded SGX Pharmaceuticals in 1999 (formerly Structural Genomix), where he built the company to more than 130 employees, raised $85M in capital, and generated more than $20 million/annum in revenue during his six years as CEO, before the company was sold to Eli Lilly. He served briefly as President and CEO of Novasite Pharmaceuticals before moving in 2006, to become the Chief Technology Officer and Director of the Advanced Technology Program (ATP) at SAIC-Frederick, Inc. (now Leidos). In 2011, Harris moved to Biogen as Senior Vice President of Translational Medicine, before joining the Hematology spin out Bioverativ, as EVP R&D in March 2017. Bioverative was acquired by Sanofi in June of 2018. From April 2020 until April 2022, Harris was EVP and Chief Science Adviser at Repertoire Immune Medicines, a private Flagship Pioneering company working on T cell engineering and antigen decoding. Harris is presently a consultant to several biotechnology companies focusing mainly on matters of R&D and R&D management. He is also a Venture Partner at SV Health Investors. In this role he founded Caraway Therapeutics, an autophagy company in 2016 and in 2018 Catamaran Bio, a company developing NK cell therapeutics. He is chairman of the Scientific Advisory Board of both companies and an observer on the Board. He is also on the Board of Directors of PhenoTX in Edinburgh, a company focusing on remyelination.

Harris has published over 110 peer reviewed research papers and reviews. He has written several book reviews and is a contributor at the annual GoldLab Symposium. He has written several commentaries for BioCentury and other industry magazines. He has recently finished writing a book on the history of the biotech industry - to be published by Cold Spring Harbor Laboratory Press.

LARRY HUNTER, PhD

Professor of Biomedical Informatics, University of Colorado Anschutz School of Medicine

ABSTRACT

Five Questions About Generative AI and Health

Generative AI systems such as ChatGPT and Dall-E are the first artificial intelligence tools broadly embraced by the public. They have been overwhelmingly popular; ChatGPT reached a million users within five days of its November 2022 release; and by January 2023 50% of Americans say they had seen AI generated text, and 12% had generated some themselves. Credible estimates suggest generative AI will produce >$1B in software and service revenue in 2023 and grow rapidly from there. This clearly disruptive technology engenders wildly divergent predictions about its impact, ranging from visions of wonder (and profit!) from its industrial champions to dire warnings of its existential risk to humanity. In this talk, Hunter will cut through the hype to address five crucial questions about this startling new technology: How does it work? Why does it work? What are its strengths and weaknesses? What is it good for (focusing on health and biomedicine)? What could go wrong? It is Hunter's hope that a deeper understanding will ameliorate many of the most extreme concerns and suggests a path forward that reaps the potential benefits while managing the risks and guarding against harm.

BIOGRAPHY

Larry Hunter is the Director of the University of Colorado's Computational Bioscience Program and a Professor of Biomedical Informatics (School of Medicine) and Computer Science (Boulder).

He is widely recognized as one of the founders of bioinformatics; he served as the first President of the International Society for Computational Biology (ISCB), and created several of the most important conferences in the field, including ISMB, PSB and VizBi. Hunter's research interests span a wide range of areas, from cognitive science to rational drug design. He has published more than 100 scientific papers, holds two patents and has been elected a fellow of both the ISCB and the American College of Medical Informatics. His primary focus recently has been the integration of natural language processing, knowledge representation, machine learning and advanced visualization techniques to address challenges in interpreting data generated by high throughput molecular biology.

He received a PhD in computer science from Yale University in 1989, and then joined the National Institutes of Health as a staff scientist, first at the National Library of Medicine and then at the National Cancer Institute, before coming to Colorado in 2000.

NICHOLAS P. TATONETTI, PhD

Vice Chair of Operations, Department of Computational Biomedicine and Associate Director of the Cancer Center, Cedars-Sinai in Los Angeles

ABSTRACT

AI-Driven Biomedical Discoveries Using Observational Data

Observation is the starting point of discovery. Based on observations, scientists form hypotheses that are then testedand evaluated. In the information-age, trillions of observations are being made and recorded every day – from online social interactions to the emergency room visit. With so much data readily available, generating hypotheses using a single scientist's mind is no longer sufficient. Instead, we must turn to computational algorithms to "mine" for new hypotheses and relationships for us. Data mining is an emerging field dedicated to training algorithms to recognize patterns in enormous sets of data to automatically identify new hypotheses.

In this talk, Tatonetti will discuss how his team uses data mining algorithms to identify unexpected effects of drugs used singly and in combination with other drugs. Drug-drug interactions (DDIs) are an important and understudied public health concern. DDIs are difficult and expensive to study because of the complex combinatorial nature to their investigation. Tatonetti has developed new methods for mining clinical data and then discovered and validated two previously unknown novel drug-drug interactions. His studies are the first to use big patient data to discovery a drug interaction and then use prospective experiments to validate the findings. Using integrative informatics methods, we are able to discover drug-drug interactions that no one considered possible before. In many cases these experiments can be executed in high-throughput and by robotic systems, with the ultimate goal of automating the scientific method.

BIOGRAPHY

Nicholas Tatonetti is the Vice Chair of Operations in the Department of Computational Biomedicine and Associate Director of Computational Oncology in the Cancer Center at Cedars-Sinai Medical Center. He earned his PhD from Stanford University, where he specialized in developing statistical and computational methods for mining observational data. Over the last 14 years, he has applied these methods to drug safety surveillance, identifying previously unknown serious drug-drug interactions, and discovering dangerous adverse drug effects.

At Cedars-Sinai, Tatonetti's lab uses massive-scale real clinical and molecular data to make robust and validated scientific discoveries, with a specific focus on detecting, explaining, and validating drug effects and drug interactions. He has published over 180 peer-reviewed scientific publications in medicine, systems biology, machine learning, and bioinformatics. He is passionate about integrating real-world datA, such as electronic health records, and high-dimensional biological data captured using next-generation sequencing, high-throughput screening, and other "omics" technologies, to reimagine and rescale the scientific method.

KAROLIN LUGER, PhD

Professor and Jennie Smoly Caruthers Endowed Chair of Biochemistry, University of Colorado Boulder

ABSTRACT

Genomes Packaged to Perfection, in All Domains of Life

All eukaryotes organize their DNA into nucleosomes, consisting of an octamer of the four core histone proteins H2A, H2B, H3, and H4, around which 147 base pairs of DNA are wrapped in two tight superhelical turns. Histones were an early acquisition in eukaryogenesis that allowed for massive genome expansion, a prerequisite for the diversity observed in modern-day eukaryotes. They are the targets of epigenetic modifications through the incorporation of histone variants and histone post-translational modifications, and require elaborate assembly and remodeling machinery for gene regulation. Who provided the chromatin starter kit to the early eukaryote? Many archaea organize their genomes with single, non-diversified histones that form slinky-like structures, without the requirement for additional machinery to assemble and disassemble nucleosomal structures. A subclass of giant viruses (ancient double-stranded DNA viruses that infect amoebae) also encode their own histones, and these form meta-stable nucleosome-like structures with distinct features. Unexpectedly, it was recently discovered that histones are sporadically present in the bacterial domain of life. In a stunning reversal of 'histone logic', these small histones encase straight DNA rather than wrapping it around them. As such, histones are no longer a prerogative of eukaryotes but appear to be an ancient DNA packaging principle that has adapted to varying constraints in different domains of life.

BIOGRAPHY

Karolin Luger is the Jennie Smoly Caruthers Endowed Chair of Biochemistry at the University of Colorado, and a Howard Hughes Medical Institute Investigator. She is a structural biologist who is recognized for her work on the nucleosomes and on the factors that maintain chromosome integrity. Her lab studies chromatin organization in domains of life that predate modern eukaryotes, providing insight into what enabled the massive genome expansion that accompanied the emergence of eukaryotic organisms. Her team also investigates the human DNA damage recognition protein PARP1 with the goal of developing novel PARP inhibitors for cancer therapy.

Luger has a strong track record in training the next generation of scientists, both in the classroom and in the lab. She is an active contributor to the scientific community at large, through collaborative research as well as through evaluation of manuscripts, grants and academic programs all over the world. She also paved the way for the acquisition of a state-of-the art cryo electron microscope for the CU Boulder campus, the only such instrument in Colorado and surrounding states, allowing the visualization of macromolecules at exquisite detail and empowering structural biologists in the region at large.

Luger was born in Austria and obtained a degree in Biochemistry from the University of Innsbruck. She earned her PhD in Biophysics from the Biocenter Basel, then moved to a postdoc at the ETH Zuerich in 1990. She started her independent career at Colorado State University in 1999, and in 2015 moved to the University of Colorado Boulder where she is now a Distinguished Professor. She is a fellow of the Biophysical Society, a member of the National Academy of Science, the American Academy of Arts and Science, and EMBO. She loves all outdoor activities, in particular hiking and biking.

ANDREAS BEYER, PhD

Professor for Systems Biology,
University of Cologne

AND

ARGYRIS PAPANTONIS, PhD

Chair of Translational Epigenetics, University Medical Center Goettingen, Germany

ABSTRACT

Living in the Fast Lane: Accelerated Copying of Genetic Information with Aging

Physiological homeostasis becomes compromised during aging, as a result of impairment of cellular processes, including transcription and RNA splicing. However, the molecular mechanisms leading to the loss of transcriptional fidelity are so far elusive, as are ways of preventing it. Beyer and Papantonis' groups profiled and analysed genome-wide, aging-related changes in transcriptional processes across different organisms: nematodes, fruitflies, mice, rats and humans. The average transcriptional elongation speed (RNA polymerase II speed) increased with age in all five species. Along with these changes in elongation speed, they observed changes in splicing, including a reduction of unspliced transcripts and the formation of more circular RNAs. Two lifespan-extending interventions, dietary restriction and lowered insulin–IGF signalling, both reversed most of these aging-related changes. Genetic variants in RNA polymerase II that reduced its speed in worms and flies increased their lifespan. Similarly, reducing the speed of RNA polymerase II by overexpressing histone components, to counter age-associated changes in nucleosome positioning, also extended lifespan in flies and the division potential of human cells. Their findings uncover fundamental molecular mechanisms underlying animal aging and lifespan-extending interventions, and point to possible preventive measures.

BIOGRAPHY

ANDREAS BEYER is Professor for Systems Biology at the Cologne Excellence Cluster on Cellular Stress Responses in Age-Associated Diseases (CECAD). Further, he is affiliated with the Institute of Genetics of the University of Cologne and with the Center for Molecular Medicine Cologne (CMMC). After receiving his PhD from the University of Osnabrück, he worked as a post-doctoral researcher in the teams of Thomas Wilhelm (FLI Jena, Germany) and Trey Ideker (UC San Diego, CA). In 2007, Andreas Beyer became junior group leader at the TU Dresden (Germany), and since 2013, he is a full professor at the University of Cologne.

Beyer's research employs computational biology approaches to investigate transcriptional and post-transcriptional processes, including their changes with age and in diseases. His work has contributed numerous approaches for the computational analysis of high-throughput molecular data and has led to discoveries regarding the regulation of protein levels and age-associated changes of the transcriptional process.

ARGYRIS PAPANTONIS is Chair of Translational Epigenetics at the University Medical Center Goettingen, Germany. He was born in 1978 in Athens, Greece, and completed his Biology degree and PhD at the National & Kapodistrian University of Athens. After a postdoctoral placement at the Sir William Dunn School of Pathology at the University of Oxford, UK, he established his own lab at the Center for Molecular Medicine, University of Cologne, Germany in 2013. In 2019, he was appointed as a Professor of Translational Epigenetics at the Medical Faculty of the University of Goettingen, Germany. His research group focuses on understanding the 3D organization of chromosomes over time and how it is impacted by aging and late-life diseases such as cancer. In addition to his scientific work, Papantonis writes and translates fiction, and his debut novella, *Karyotype* (Kichli Eds., 2014), received the prestigious "Anagnostis" First Book Award.

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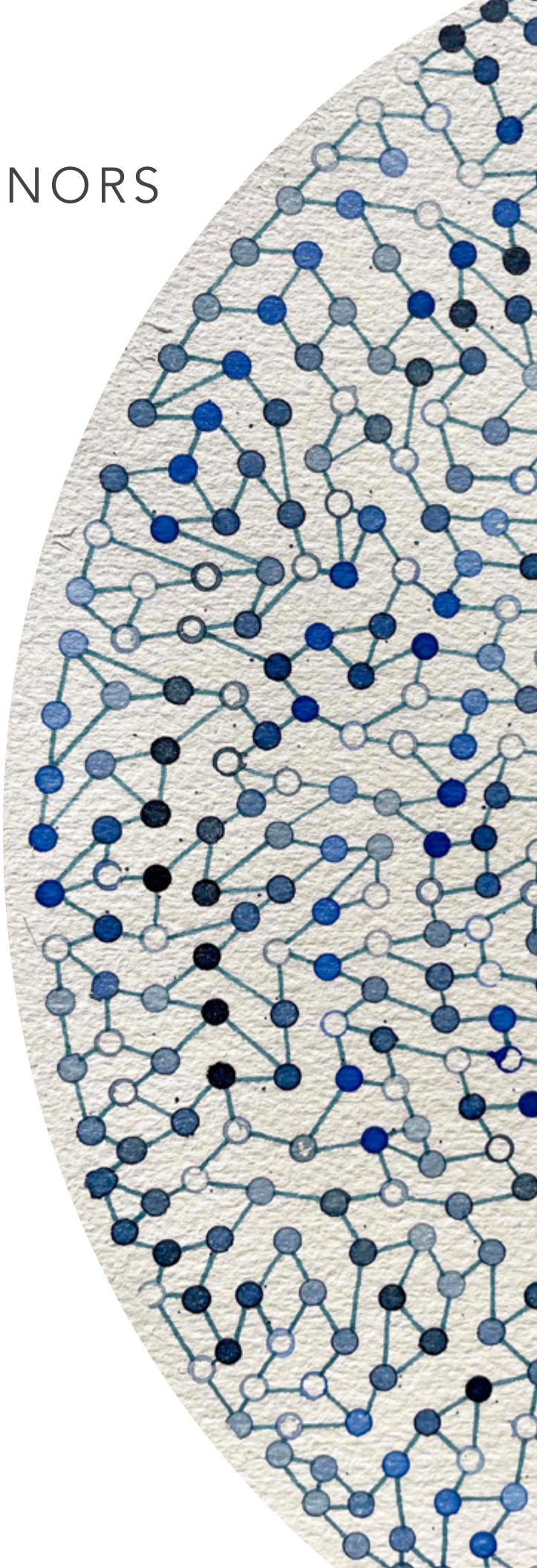

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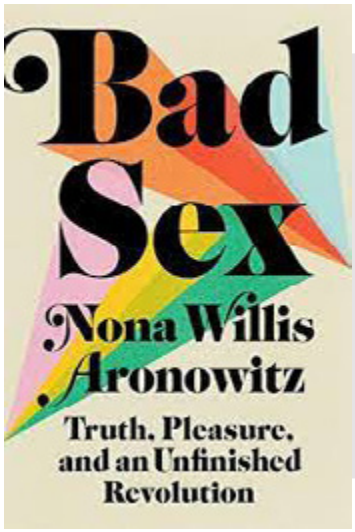


Bad Sex: Truth, Pleasure, and an Unfinished Revolution

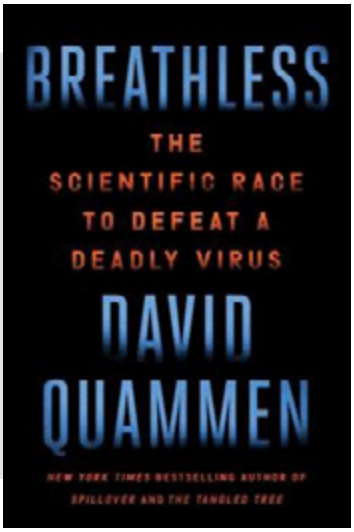
By Nona Willis Aronowitz

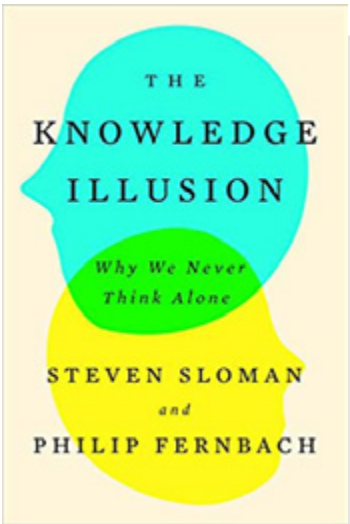
Bad Sex is a brave, bold, and vulnerable exploration of the enduring barriers of sexual freedom, which lays bare the triumphs and flaws of contemporary feminism and also helps shine a light on universal questions of desire. - GoodReads

Breathless: The Scientific Race to Defeat a Deadly Virus

By David Quammen

National Book Award finalist *Breathless* tells the story of the worldwide scientific race to decipher the coronavirus SARS-CoV-2, trace its source, and make possible the vaccines to fight the Covid-19 pandemic--a "luminous, passionate account of the defining crisis of our time." (The New York Times)

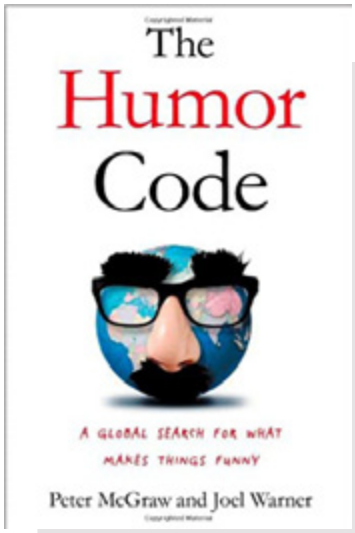




The Knowledge Illusion: Why We Never Think Alone

By Philip Fernbach

Humans have built hugely complex societies and technologies, but most of us don't even know how a pen or a toilet works. How have we achieved so much despite understanding so little? Cognitive scientists Steven Sloman and Philip Fernbach argue that we survive and thrive despite our mental shortcomings because we live in a rich community of knowledge. The key to our intelligence lies in the people and things around us. - Amazon



The Humor Code: A Global Search for What Makes Things Funny

By Peter McGraw

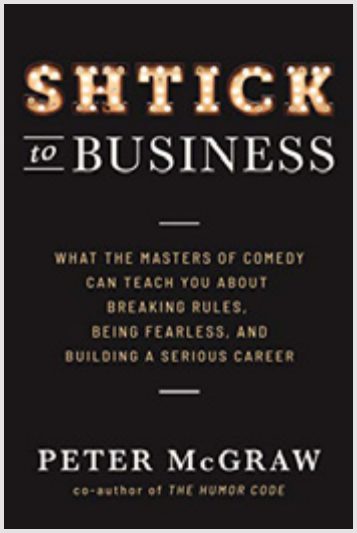
Two guys. 19 experiments. Five continents. 91,000 miles. And a book that will forever change the way you think about humor.

Dr. Peter McGraw, founder of the Humor Research Lab at the University of Colorado Boulder, teamed up with journalist Joel Warner on a far-reaching search for the secret behind humor. Their journey spanned the globe, from New York to Japan, from Palestine to the Amazon. Meanwhile, the duo conducted their own humor experiments along the way–to wince-worthy, hilarious, and illuminating results. - Amazon

Shtick to Business: What the Masters of Comedy can Teach You about Breaking Rules, Being Fearless, and Building a Serious Career

By Peter McGraw

Drawing on cutting-edge research, case studies, and his own comedy successes (and failures), Peter reveals surprising business lessons from the masters of comedy. The insights in Shtick to Business will help you improve innovation and outsmart the competition. You'll build new skills–enhanced creativity, better decision-making, and a marketing mindset–to launch a business, tackle tough management problems, and build a serious career. And you'll never have to tell a joke. - Amazon



COMING JANUARY 2024

Solo: Breaking the Rules in a World Built for Two

By Peter McGraw

DEDICATION

One person I loved deeply – Chris Walsh – died this year and one person we three love deeply – Scott Danielson – is very sick. Each of them is on our minds.

Chris Walsh

Chris was my colleague when I was a post doc at Rockefeller University from 1967 to 1969. Chris was a graduate student, studying under an actual organic chemist. What made him special was that he cared about biology in a way that was unusual for chemists at that time. Chris was ahead of his time – chemistry and biology were for him one subject, not two. Chris spoke at this symposium in 2013, warning us about antibiotic resistance. He knew everything about that topic, and gave a talk that could be followed by all of us rather than only by experts. That was a skill he had, coupled with remarkable intelligence and decency. I never met anyone, not a single person, who did not admire him.

Chris was a serious judge of great science – his standards were enormously high. He also loved to laugh about almost anything – he was without stuffiness, a remarkable quality for such an important scientist.

Scott Danielson

Scott is alive today, living with glioblastoma. Scott spoke at the first GLS in 2010 and created thought provoking etudes for the 2014 symposium. He became a great friend for Meredith, Larry Hunter, and me. He helped us make the symposia better, and he also helped us launch the Colorado Longitudinal Study (COLS). Scott was a frequent visitor to Boulder so we saw him often. Scott has been documenting his journey on his blog BeWonderNow. He has been a truth teller his entire life, a teacher, and a passionate advocate for doing useful things in the world. The project he discussed at his first moment at our symposia was about reaching out (through ads he created) to young women in Africa, teaching them that condoms were OK as an AIDS-prevention act. Scott's life has been good for all of us, a substantial achievement in a world increasingly inhabited by selfish people. We remain grateful for the time we've had with Scott and committed to continuing his legacy.

BeWonderNow blog: www.bewondernow.com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15TH ANNUAL GOLDLAB SYMPOSIUM

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