The power to...
Use computation and engineering to solve biology’s biggest challenges

Salk science isn’t a relay race during which basic lab researchers hand off their work to applied scientists, who in turn hand it off to technology developers. Rather, it’s a dance—an iterative process that sends ideas and discoveries back and forth, enabling the most profound innovations.

The challenge
All living systems—cells, brains, whole organisms, even societies—follow certain fundamental rules for survival. Though they can apply these rules in different ways, they all need to use energy efficiently and maintain resilience in the face of change.

These fundamental rules must be better understood to uncover new ways to slow aging and prevent cancer, neurodegeneration and other conditions. And to do that, researchers must increasingly rely on the unique integration of information theory, computer science, engineering and experimental biology.

The Salk approach
In many ways, computational tools are like putting on a new, more powerful set of reading glasses: information that was once fuzzy is now clear, and patterns that have evaded detection emerge from the background.

But we are now taking these efforts further, embracing a discipline called biological computation. Whereas computational biology uses algorithms to find patterns in biological data, biological computation seeks to understand how naturally occurring biological systems store, process and use information to achieve complex goals in their environments. Since the experimental biology programs at Salk range from molecules to cells to neural circuits, the Institute is uniquely positioned to interpret fundamental principles of biological computation.

The beauty of these approaches is that they can be applied to any type of research: cancer, immunology, metabolism, neuroscience, aging and plant biology. Better computation lifts all boats.

See the Salk approach at work: Using machines to improve data collection and analysis
Merging machines with biology to understand movement.
Reaching for a glass of water seems simple, but it requires an integrated array of complex brain inputs and outputs that are constantly changing. Associate Professor Eiman Azim combines machine learning, computer vision and engineering theory to study how the nervous system makes real-time adjustments to enable coordinated movement.

Azim’s lab studies brain signals and body motion to develop a more complete understanding of how they interact. But to understand how the brain controls the body, he needs to record actual motions and train deep learning algorithms to recognize how body parts, like arms and fingers, move in 3D space. Working with engineers and computer scientists, Azim is pioneering new, automated ways to collect motion data at a resolution that the traditional cumbersome process of manual human labeling cannot achieve. Once vast amounts of movement data are gathered, he leverages machine learning and other techniques to explore how circuits in the brain govern motion.

This work is providing new insights into how injuries and movement disorders, such as Parkinson's disease and ALS, can have such devastating effects on motor skills. He hopes that by illuminating these processes, we can find innovative ways to restore healthy movement.

Decoding genetic variation. Human genomes are highly similar to one another, but they still contain millions of genetic differences in the DNA—genetic variants—that affect traits such as eye color and disease risk. While some genetic variants affect gene sequences directly, most of them are noncoding, meaning they lie outside of genes and have unknown functions. Scientists hypothesized that most noncoding genetic variants affect gene expression—how much a gene is turned “on” in different cell types or conditions—but it is currently incredibly challenging to pinpoint which variants are functional and which genes they affect.

Assistant Professor Graham McVicker is tackling this problem by developing methods to interpret noncoding human genetic variation. He is particularly interested in illuminating how noncoding variants in immune cells affect human traits such as autoimmune diseases.
To determine the function of genetic variants and reveal the molecular underpinnings of human traits and diseases, his laboratory uses a combination of computational and high-throughput experimental techniques. The team develops computational and statistical methods to analyze naturally occurring genetic variation in human populations, performs high-throughput genome perturbation experiments using CRISPR technologies, and develops machine learning algorithms to predict the function of genetic variants.

**Mapping plant growth to mitigate climate change.** Professor Joanne Chory has pioneered the study of how plants respond to their environments. Her work has detailed the complex signaling networks that control plant growth in response to environmental change. Combining computer vision, statistical approaches and functional genomics, Professor Wolfgang Busch has pioneered the understanding of how different gene variants that occur in natural plant populations influence and shape the way roots grow and respond to the environment. Busch is also working with information theorist Professor Tatyana Sharpee to distill large-scale measurements into a manageable set of coordinates that help determine how genes control behavior—one of the central challenges in biology.

The team is now leveraging this vast knowledge and experience to develop plants with desirable traits. For example, working with Salk geneticists, epigeneticists, computational biologists and others, Chory and Busch are deciphering how roots grow and what genes and signals determine traits such as length. The ultimate goal is to create plants with deeper roots that resist decay and sequester more atmospheric carbon—Salk Ideal Plants®.

Salk Ideal Plants have great potential to thrive in harsh environments, improve soil fertility and even mitigate climate change.

**Learning from biology to improve computing systems.** Scientists are increasingly turning to computational biology, using machine learning and other tools to learn more about biological systems. Sharpee and Salk Fellow Talmo Pereira’s work is part of a discipline called biological computation that does the opposite. In biological computation, scientists unravel how biology solves complex problems then they use that information to create more effective computing systems.

Pereira invented a deep learning technique called SLEAP, which precisely captures the movements of organisms, from single cells to whales, using conventional videography. This technology has enabled scientists to describe biological system behavior with unprecedented quantitative precision. This precision is now being leveraged to build biological computation models for systems that were thought to be too complex to study, such as the neural circuitry that underlies cognition.

Deep learning systems, powerful as they are, still suffer from many weaknesses not present in the brain. For example, tiny changes in an image can make a deep learning system mistake a panda for a bus. Sharpee’s group has been analyzing the system of local checks and balances that the brain employs not to be fooled in this way. Adding these checks to the current generation of deep learning systems may significantly increase their reliability.

These examples only scratch the surface—Sharpee is in high demand to collaborate with many of Salk’s research teams, across just about every discipline. Learning how biological processes work will revolutionize how we design advanced computer systems, how we understand biological functions, and how we fix them when they go awry.

**Why Salk**

For more than 60 years, the Salk Institute has pursued Jonas Salk’s vision of fearless, interdisciplinary science tackling some of the biggest challenges facing humankind.

**Some of our past computational biology advances include the following:**

- 1980s – Terry Sejnowski helped pioneer the field of computational neuroscience, and his work on neural networks formed the foundation for deep learning.
- 2003 – The Institute became an early technology adopter with the founding of the Crick-Jacobs Center for Theoretical and Computational Biology. Researchers in the Crick-Jacobs Center, and around the Institute, have been identifying better ways to interpret complex data for decades.

We recognize that the future of biological research—and its translation into meaningful therapeutic interventions—lies in our ability to acquire, manage, interpret and disseminate big data. Ultimately, the goal is to develop theories that both explain the data and lead the field into the future. On the other side of the coin, we are embracing biological computation, studying how cells, circuits and organisms make decisions, both to understand the biology and to replicate it in our own computers.

These interdisciplinary interfaces are complex, and we are building new tools every day to better probe them. This is a challenging endeavor, and Salk scientists are rising to this challenge.

**Why now**

In 2019 the Salk Institute launched the Campaign for Discovery—a seven-year, $750 million effort to accelerate Salk’s critical research.

The Campaign is focused on driving discoveries in six Centers of Excellence: Cancer Center, Center for Healthy Aging, Center for Plant Biology, Center for Neuroscience, NOMIS Center for Immunobiology and Microbial Pathogenesis, and Crick-Jacobs Center for Theoretical and Computational Biology.

To continue to lead the field in these areas, Salk is recruiting new faculty and other experts, investing in new technologies, and creating new collaborative spaces, including construction of the Joan and Irwin Jacobs Science and Technology Center.

As it has always been at Salk, there will be no barriers between disciplines. New ideas from multiple areas can mix and flourish, generating the most innovative, multipronged approaches to solving the greatest global challenges.

**Join us**

Science is a collaborative pursuit, and we invite you to join us in accelerating life-changing discoveries: [www.salk.edu/campaign](http://www.salk.edu/campaign).