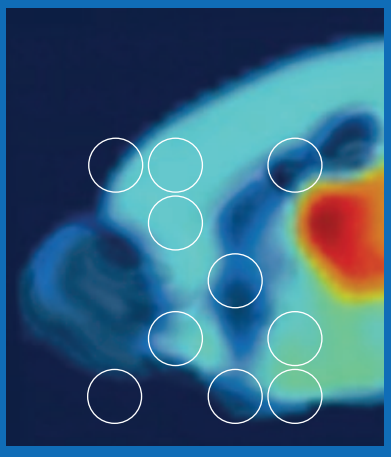
ALLEN INSTITUTE

# in mo tion

2015 ANNUAL REPORT

Our ability to interact with the world around us arises from electrical impulses moving rapidly in coordinated patterns in our brains. The pathways that underlie cognition are in near constant flux, with neurons rapidly changing shape and genetic program to process signals, create new connections and adapt to our changing environment.

At the Allen Institute, our science reflects that same adaptive motion. Building on the unique tools we created in our first decade, we now study how neuronal signatures drive the movement of signals between the brain's more than 86 billion neurons as they function in real time. We are revealing the inner workings of our body's cells as they mature. We are analyzing and modeling our data in three dimensions. We are interacting across disciplines and fields to develop new technologies, integrate large-scale datasets and move into a deeper understanding of our internal and external worlds.



**Pictured** *(cover)*
A saggital view of the mouse forebrain from our mouse anatomic gene expression atlas (AGEA).

The human brain would be complex enough if it stood still. But each of its billions of cells are in near constant motion, chattering over synapses and reaching to form new connections. The elaborate machinery of our brains drives who we are and what makes us human. In our quest to understand the brain, we are increasingly focused on deciphering its parts and how they work and move together.

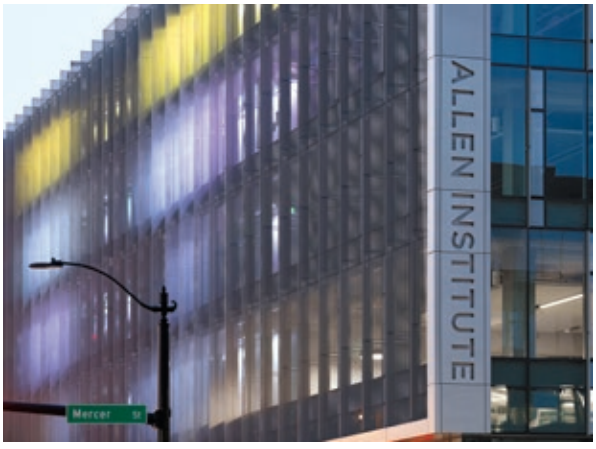
It has been an exceptional year at the Allen Institute. In May, the Allen Institute for Brain Science debuted a brand new product – the Allen Cell Types Database – which puts a powerful tool to study and catalog the cells of the brain in the hands of researchers around the world. This past December, we were thrilled to announce the launch of the Allen Institute for Cell Science to create and share dynamic and predictive three-dimensional models of cells, with an eye toward changing the way we conduct biomedical research.

All of this movement has taken place in the midst of our most literal move, as we prepare this fall to transition into our beautiful, new, purpose-built building in the South Lake Union neighborhood of Seattle.

As we continue to grow, we always come back to our goal of serving the scientific community. The Allen Institute for Brain Science has been a key driver in helping to establish the community standards that enable us to share data and analysis more easily and efficiently. The new Allen Institute for Cell Science is engaged in a fascinating conversation with the cell biology community, working to create and share tools to support science and accelerate the pace of biomedical research.

The Allen Institute has been a tremendously exciting place to watch grow and blossom. As we move into the future, I eagerly anticipate where we can go next.

**Allan Jones, Ph.D.**
Chief Executive Officer

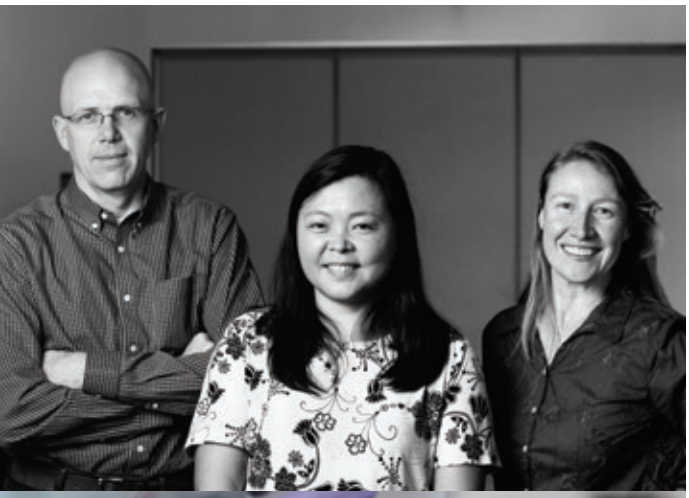



# signals in motion

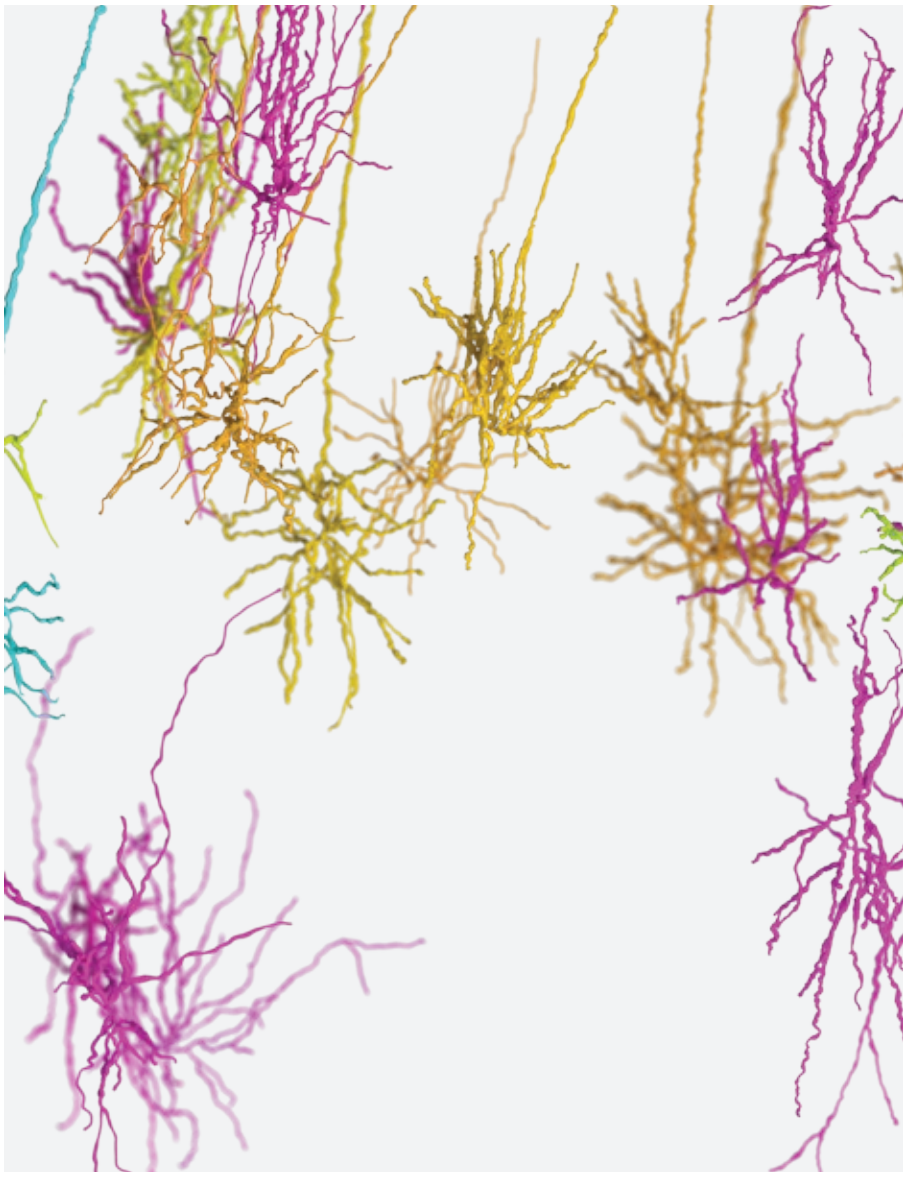
**Top** *(left to right)*
Colin Farrell, Ph.D.
Director, Manufacturing
& Process Engineering

Hongkui Zeng, Ph.D.
Investigator

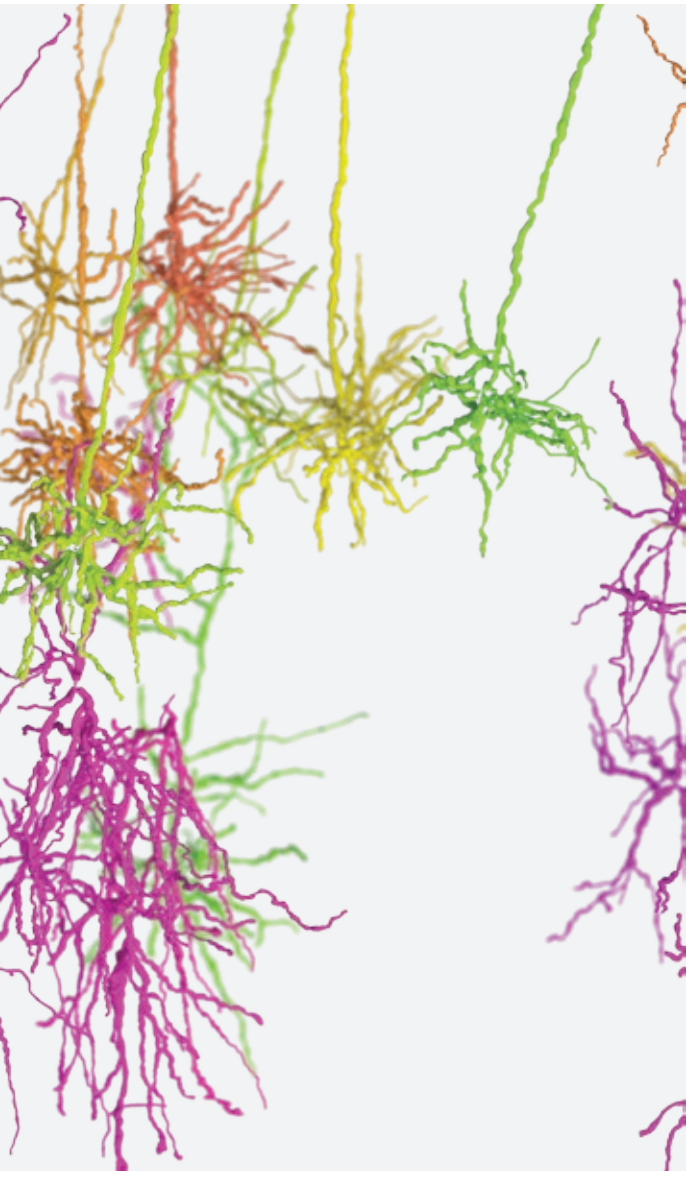
Amy Bernard, Ph.D.
Director, Structured Science




**Below**
Digitally reconstructed neurons mapped onto the Common Coordinate Framework in the mouse primary visual cortex.



The human brain has more than 86 billion neurons, and with their dizzyingly elaborate shapes, diverse signaling patterns and different gene expression, no two are quite the same. Cataloging the cells that make up the brain is an enormous task.



The Allen Cell Types Database is the first open resource of its kind to characterize the same set of cells from the mouse cortex in multiple ways, including their electrophysiological properties and shapes, and provide models of cell behavior that let users create and study their own artificial networks of cells.

The Allen Cell Types Database will help scientists create a rich list of the brain's building blocks: a key landmark on the path to understanding how the billions of cells in our brain function as a whole.

Like all the Allen Brain Atlas resources, the Allen Cell Types Database is the fruit of our team science approach that generates useful big science resources and shares them openly with the entire scientific community.

**Above** *(left to right)*
Jim Berg, Ph.D.
Manager, Electrophysiology Core

Lydia Ng, Ph.D.
Senior Director, Technology

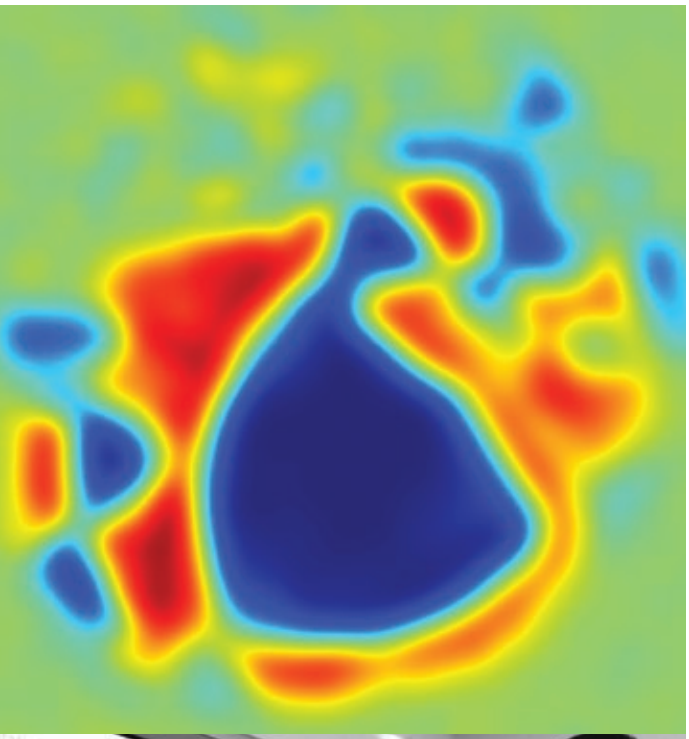
Staci Sorensen, Ph.D.
Manager, Morphology & 3D Reconstruction

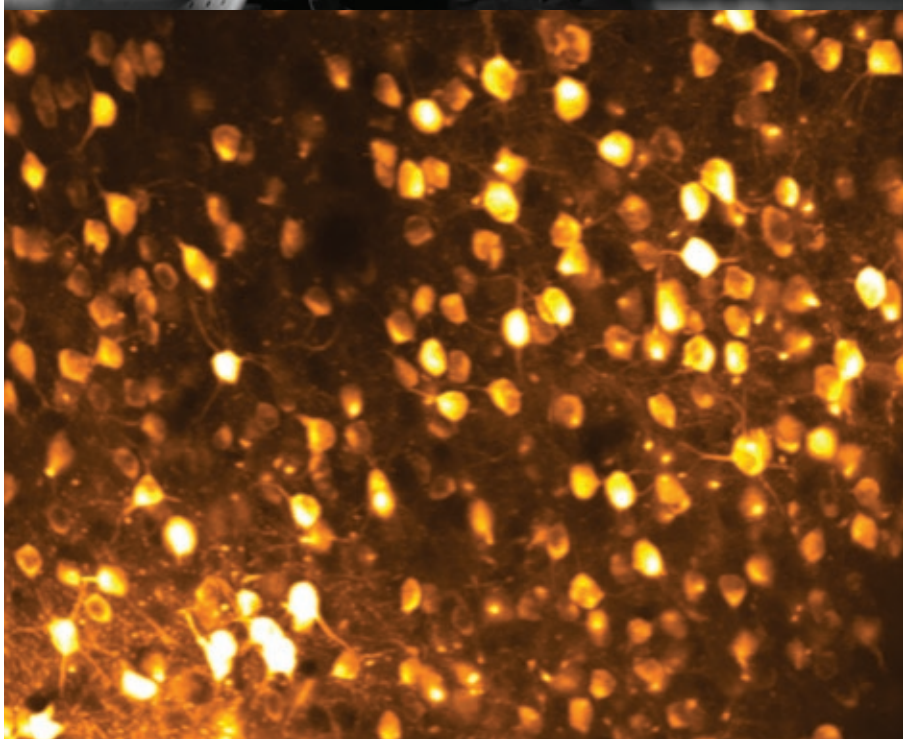
# the brain in action

**Top**
A map of visual areas in the mouse cortex generated by imaging changes in fluorescence of an activity-dependent indicator.

**Bottom** *(left to right)*
Yang Li
Software Engineer III

Quanxin Wang, Ph.D.
Senior Scientist





## What happens in our brains when we see an object?

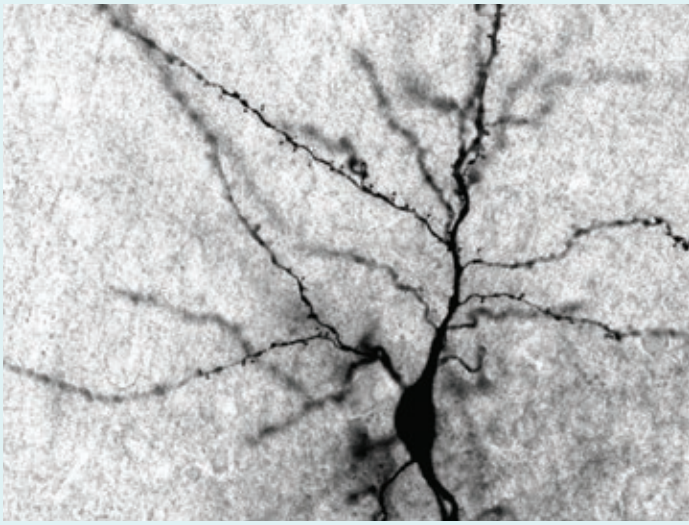
Our Cortical Activity Map program is considering this question by observing the activity of the mouse cortex during behavior and mapping which areas and which neurons are involved during different visual tasks. The aim of this complex integration of data is to ultimately create a rich map of what happens – and where – in the visual brain at the cellular level.

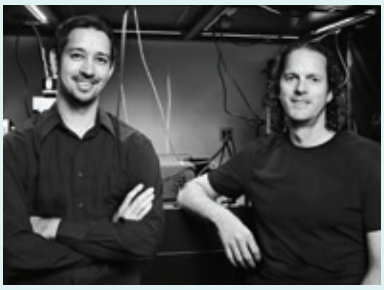
The Cortical Activity Map, built on our next generation Common Coordinate Framework, will become a valuable tool to guide how we study vision in the brain. With a map in hand, we can begin to ask which types of cells or layers of the cortex are responsible for different behaviors, or how different cells function together in circuits – all building to a more robust understanding of how vision works in real time in the brain.

**Top** *(left to right)*
Saskia de Vries, Ph.D.
Senior Scientist

Michael Buice, Ph.D.
Assistant Investigator

**Bottom**
Maximum intensity projection image of cells responding to drifting gratings of different orientations and spatial frequencies.





**Above**
A biocytin-filled human neocortical pyramidal neuron in a brain slice.

**Left** *(left to right)*
Jonathan Ting, Ph.D.
Scientist II

Ed Lein, Ph.D.
Investigator

## Human Brain Cells Up Close

In the quiet late nights of the electrophysiology lab, a small group of Allen Institute researchers is working to take recordings directly from live human tissue. This rare and exciting opportunity to learn about living human cells up close is the result of collaborations between the Allen Institute and local Seattle hospitals and neurosurgeons to acquire and study small pieces of tissue which would typically be discarded during brain surgeries. These precious cells are recorded, filled with dyes and later imaged in a light microscope – medical waste given new and invaluable life as a window directly into how the human brain works.

# moving through time and space

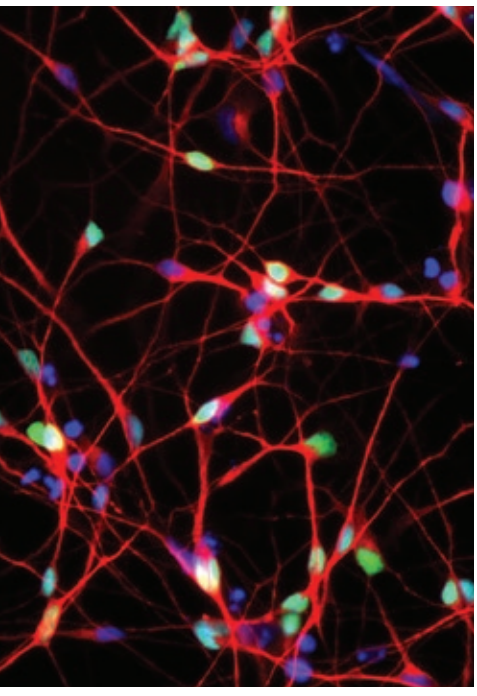
Whether charting the development of cells into neurons or navigating data in 3D, our scientists are pioneering new ways to explore the brain.

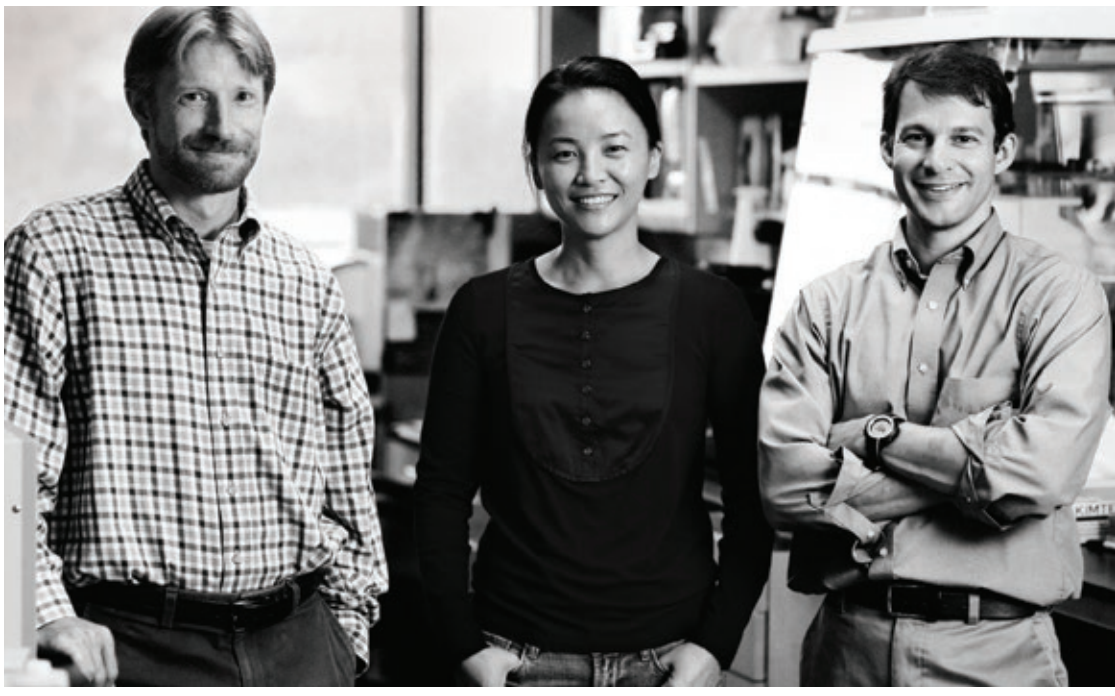
**Left**
Early-born neurons generated from directed differentiation of human embryonic stem cells.

**Right** *(left to right)*
Boaz Levi, Ph.D.
Manager, *in Vitro* Human Cell Types

Yanling Wang, Ph.D.
Manager, *in Vitro* Human Cell Types

Joshua Grimley, Ph.D.
Manager, *in Vitro* Human Cell Types



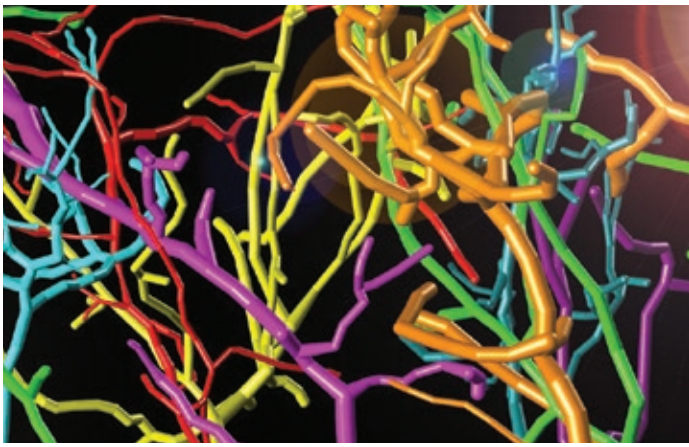


**Right** *(left to right)*
Jane Roskams, Ph.D.
Executive Director,
Strategy & Alliances

Hanchuan Peng, Ph.D.
Associate Investigator

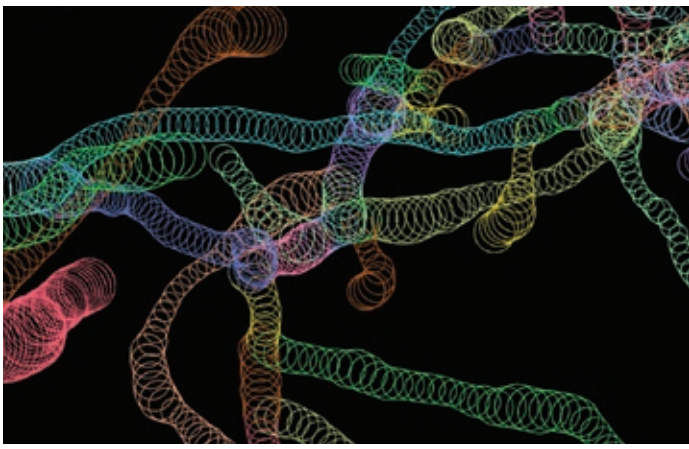
## Growing Neurons In A Dish

Much like our heritage provides insight into who we are, the lineage of our brain cells sheds light on what makes us human from the earliest moments of our development. The *in Vitro* Human Cell Types team is guiding human embryonic stem cells through early neural development, exploring how different types of brain cells emerge and mature and identifying the major molecular decision-makers along the way. They have so far fostered groups of cells in a dish up to four months old that match the milestone development of human brain tissue, creating a valuable platform to examine some of the earliest moments of brain cell growth that make us uniquely human.



## 3D Space Travel

Tracing individual neurons in three dimensions is an immense computational task. The Allen Institute is spearheading the international BigNeuron initiative: a community effort that is collecting morphological data sets from thousands of nerve cells from a variety of species, together with tracing and reconstruction algorithms, and "bench testing" the algorithms using some of the world's most powerful supercomputers. The goal is to find, compare and share the best and most accurate algorithms to help reconstruct neuron shapes from raw data and bolster our understanding of how these cells may function, based on their shape. In addition to key algorithms and tools, the project will also yield an unprecedented set of openly available single neuron reconstruction data for the entire neuroscience community.



**Middle**
A fraction of the hundreds of thousands of neuron reconstructions produced by BigNeuron.

**Bottom**
Color-coded structural elements including nodes and segments of a 3D reconstructed neuron.

# moving the needle

Creating community standards in neuroscience is one of the most important tasks to ensure that the work we do is useful and shareable. The Allen Institute is helping to drive efforts to create the common platforms that will accelerate the pace of neuroscience research around the globe.

**Neurodata Without Borders**
The Institute took a lead role in launching Neurodata Without Borders – a partnership with GE, The Kavli Foundation, NYU School of Medicine, HHMI, Caltech and UC Berkeley – which helps to establish international standards for how neurophysiology data can be represented and shared.

**Imec Neuropix**
The Institute contracted with the Belgian microelectronic design and manufacturer imec to create a very high density state-of-the-art electrical sensor array for recording neural activity in animal brains, in partnership with HHMI, the Gatsby Charitable Foundation, the Wellcome Trust and University College London.

**BigNeuron**
The Institute initiated this global community effort to identify the state-of-the-art of 3D single neuron reconstructions, standardize protocols and establish data resources.

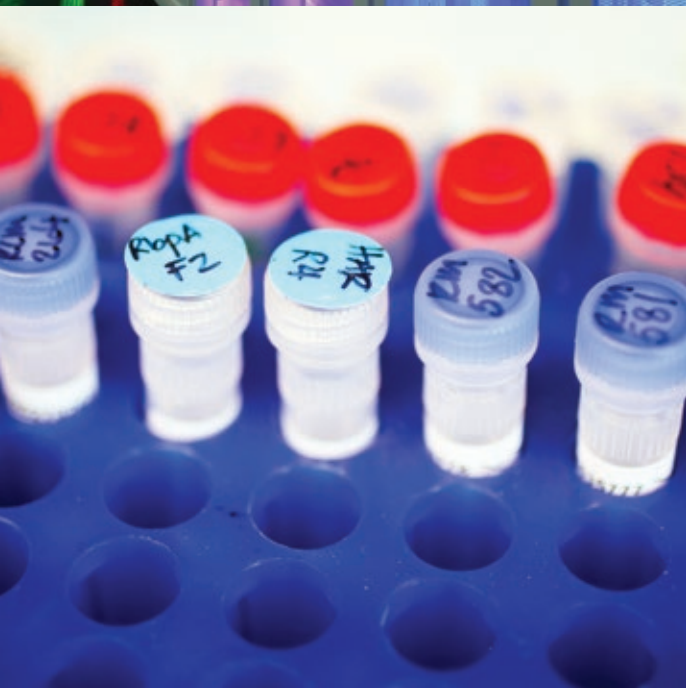
**Common Coordinate Framework**
A major feature of our Allen Brain Atlas resources, the Common Coordinate Framework is a high-resolution volumetric mapping tool for the adult mouse brain that is seamlessly incorporated into our data resources so scientists can view and quantitatively compare data from multiple sources within a common 3D anatomical reference framework.

**Left**
Scientists from around the world gather at a BigNeuron hackathon hosted at the Allen Institute.

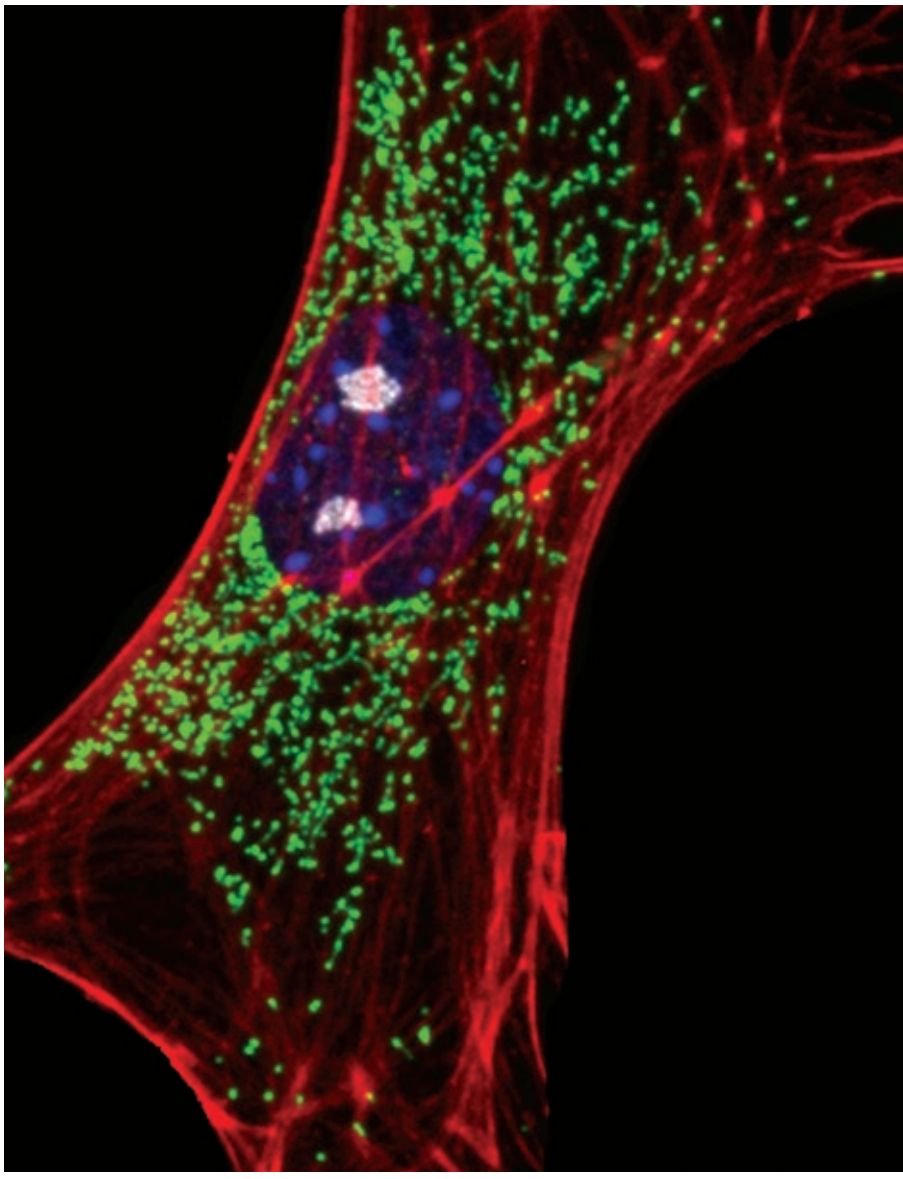
**Right**
Christof Koch, Ph.D.
President & Chief Scientific Officer

**Above**
Imec probes, used to detect extracellular electrical activity from 300 cells in the brain.

# cells in motion



**Below**
Intracellular architecture of a primary mouse embryonic fibroblast.



# Introducing the Allen Institute for Cell Science

The cell is the fundamental unit of life, and each one is a microcosm of complex, living machinery. While we understand the basic functions of most cells, how a cell's genes and environment work together to perform those functions remains largely a mystery. The Allen Institute for Cell Science was founded with the goal of better explaining and predicting the behaviors of our cells, whether healthy or diseased.

Harnessing the power of visual tools, the first project of the new Institute is to create a dynamic, animated, three-dimensional model of a cell that shows how its parts integrate to determine a wide variety of behaviors as it differentiates from an induced pluripotent stem cell into heart and epithelial cells. This rich and predictive model will become a valuable tool to cell scientists around the globe to investigate the fundamental properties of cells, and will galvanize the cell science community to combat disease in meaningful ways.

**Below** *(left to right)*
Sean Palecek, Ph.D.
Fellow, Stem Cells & Gene Editing

Nikki Bialy, Ph.D.
Associate Director

Winfried Wiegrabe, Ph.D.
Director, Microscopy & Image Analysis

Ruwanthi Gunawardane, Ph.D.
Director, Stem Cells & Gene Editing

Graham Johnson, Ph.D.
Director, Animated Cell

Susanne Rafelski, Ph.D.
Director, Assay Development

Rick Horwitz, Ph.D.
Executive Director

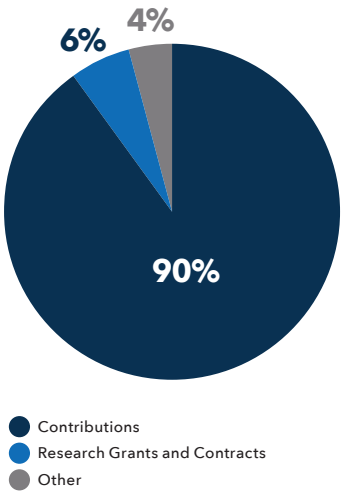
# financial summary

## Allen Institute
## Fiscal Years 2014 and 2013

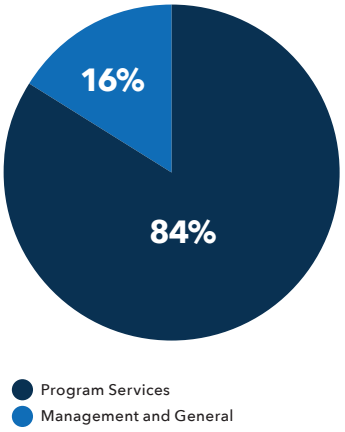
*(In Thousands)*

| | 2014 (Audited) | 2013 (Audited) |
|---|---|---|
| **Support and Revenue** | | |
| Contributions | **$ 52,878** | $ 126,894 |
| Research Grants and Contracts | **3,498** | 3,923 |
| Other | **2,671** | 553 |
| **Total Support and Revenue** | **59,047** | 131,370 |
| | | |
| **Expenses** | | |
| Program Services | **43,534** | 36,548 |
| Management and General | **8,451** | 7,983 |
| **Total Expenses** | **51,985** | 44,531 |
| | | |
| **Change In Net Assets** | **$ 7,062** | $ 86,839 |
| **Net Assets, Beginning of Year** | **164,070** | 77,231 |
| **Net Assets, End of Year** | **$ 171,132** | $ 164,070 |

## Funding Sources 2014




## Expenses 2014



# our team

*Includes 2014 and 2015 members*

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Paul G. Allen
Jody Allen

**Leadership**
Allan Jones, Ph.D.
Chief Executive Officer

Chinh Dang
Chief Technology Officer

Christof Koch, Ph.D.
President & Chief Scientific Officer, Allen Institute for Brain Science

David Poston
Chief Operating Officer

Rick Horwitz, Ph.D.
Executive Director, Allen Institute for Cell Science

Tom Skalak, Ph.D.
Executive Director for Science and Technology for the Paul G. Allen Family Foundation

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