Welcome to
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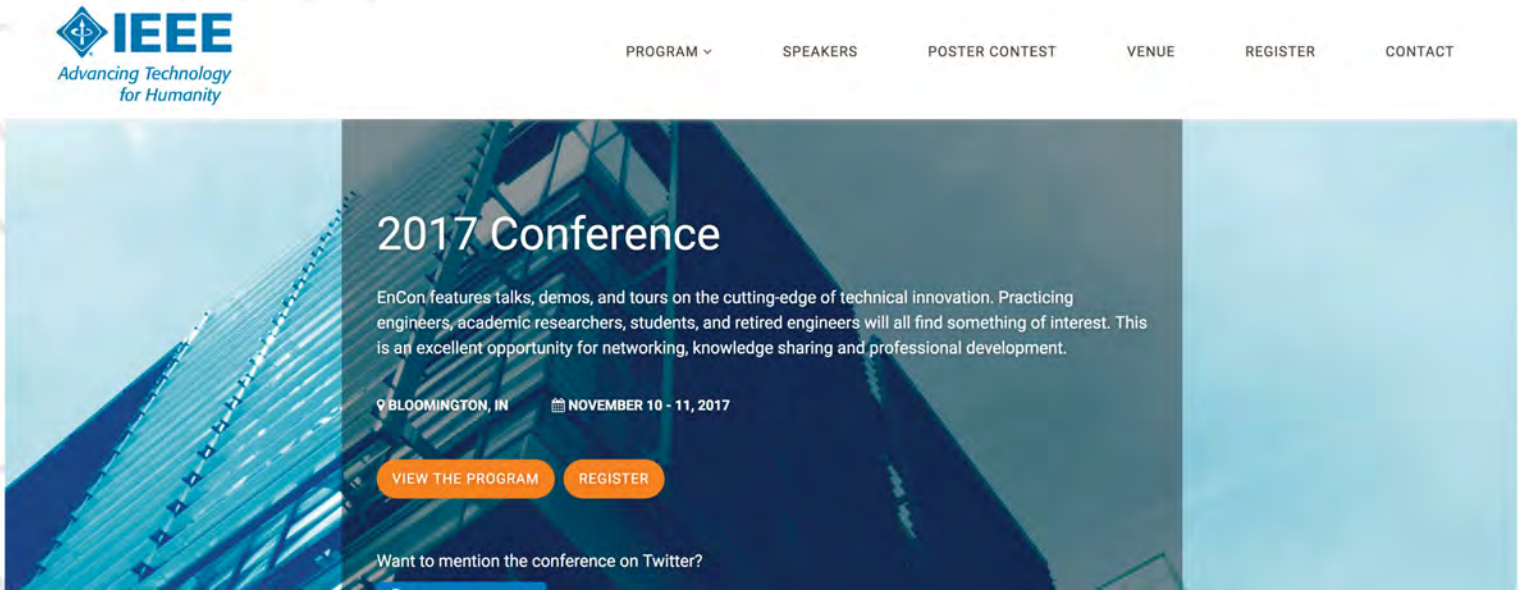
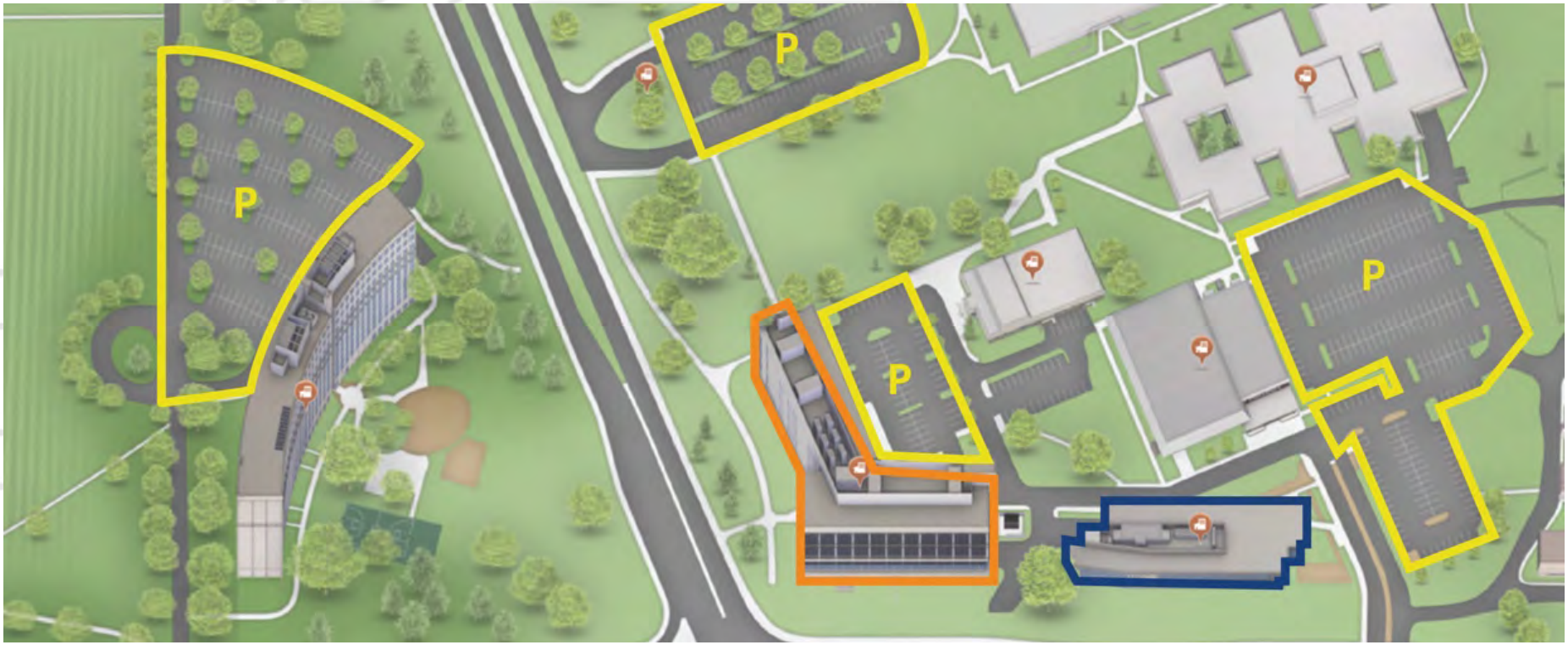


Welcome to
Indiana University Bloomington

Welcome to
Indiana University Bloomington



Program Committee

Katy Börner, Indiana University
Bob Evanich, Duke Energy
Brian King, IUPUI
Gerhard Klimeck, Purdue University
Oscar Moralez, Vision Tech
David Peter, Borg Warner
Lisel Record, Indiana University

Special thanks to...

Stephen Bird
Sara Bouchard
Tina Bradley
Jill Clancey
Dave Cooley
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Steven Egyhazi
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Contributors

Message from the Dean

Raj Acharya, Dean, Rudy Professor of Engineering, Computer Science and Informatics

"The Indiana University School of Informatics, Computing, and Engineering educates computer scientists, informaticians, and engineers who are firmly grounded in fundamental principles. Our students learn to be global, holistic, and creative thinkers who are well-versed in the liberal arts and humanities, as well as science and technology."

Raj Acharya, Dean

Welcome

Geoffrey C. Fox

Interim Associate Dean for Engineering
Chair, Intelligent Systems Engineering (ISE)
Distinguished Professor, ISE

Brad Wheeler

IU Vice President for IT
IU Chief Information Officer
Professor, Information Systems

Indiana University School of Informatics, Computing and Engineering
ISE: Intelligent Systems Engineering



INDIANA UNIVERSITY
SCHOOL OF INFORMATICS, COMPUTING, AND ENGINEERING

National Heart, Lung,
and Blood Institute

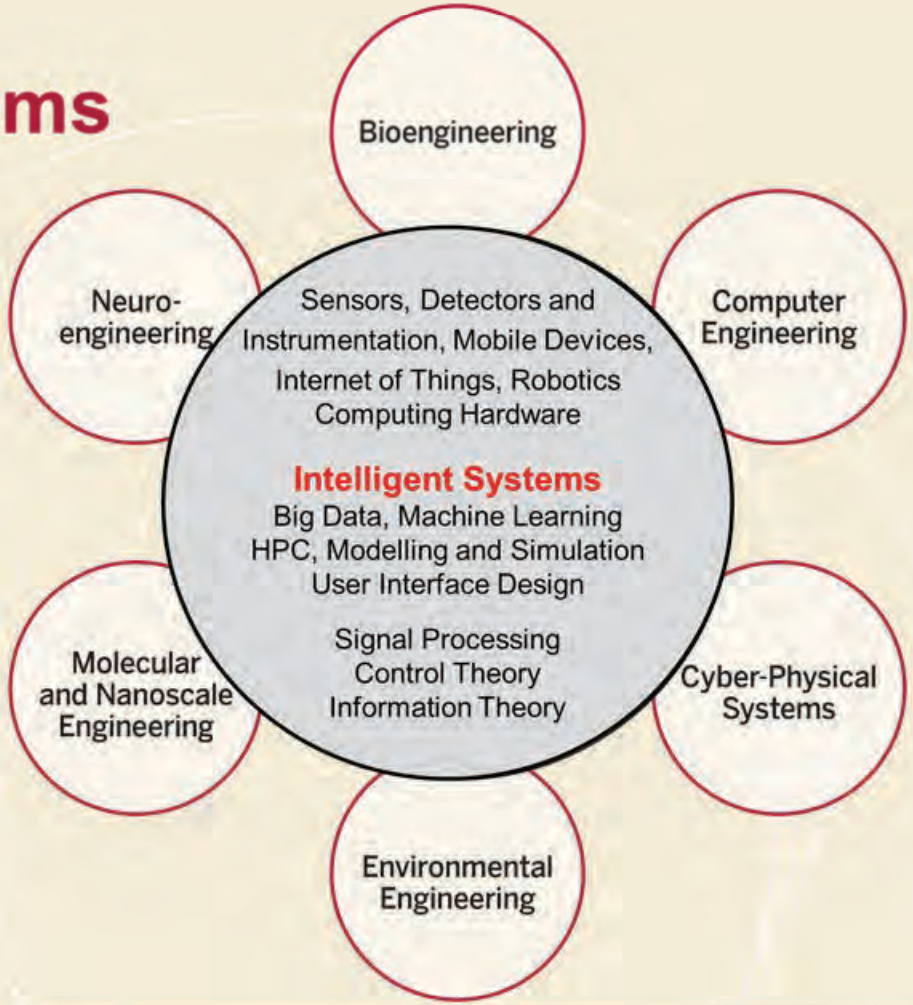
What is Intelligent Systems Engineering?

- We define "Intelligent Systems" as purpose-engineered systems
  - from the **raw hardware** and embedded systems,
  - through **data acquisition** and signal processing
  - to the **transformation of data** into decisions and/or knowledge.

- Creating a new program ab initio offers us the opportunity to focus on a modern set of engineering topics:
  - those that involve **intelligent systems**
  - as realized with **embedded, customizable** computing components
  - combined with **sophisticated data interpretation**

This program will train students in the practical engineering of systems with an emphasis on *hands-on designing, simulating ("digital twin") and building systems*. Graduates prepared with this core set of workforce-aligned skills will be in high demand for careers.

Intelligent Systems Engineering Structure



What is Intelligent Systems Engineering?

- *From the small to the large*
- **Edge Computing: Embedded Systems and Nanoscale Sensors** – computing and sensing will be ubiquitous as we move toward smart homes, smart cities and smart transportation, with computing and intelligent systems helping us lead healthier lives
- **Cloud and High-Performance computing** – behind all of these edge devices are massive systems that analyze and manage the floods of data that are being produced
  - They also allow modeling and simulation of the engineered systems
- All students have courses on edge, cloud, HPC systems, machine learning and modelling and simulation

Intelligent Systems ~ Artificial Intelligence ~ Machine Learning

- **2017 Headlines**
- The Race For AI: Google, Twitter, Intel, Apple In A Rush To Grab Artificial Intelligence Startups
- Google, Facebook, And Microsoft Are Remaking Themselves Around AI
- Google: The Full Stack AI Company
- Bezos Says Artificial Intelligence to Fuel Amazon's Success
- Microsoft CEO says artificial intelligence is the 'ultimate breakthrough'
- Tesla's New AI Guru Could Help Its Cars Teach Themselves
- Netflix Is Using AI to Conquer the World... and Bandwidth Issues
- How Google Is Remaking Itself As A "Machine Learning First" Company
- If You Love Machine Learning, You Should Check Out General Electric

- **The trouble for all of these companies is that finding the talent needed to drive all this AI work can be difficult.** **(That is where ISE comes in!)**

Intelligent Systems Engineering Areas of Study

- **Undergraduate and Graduate**
  - Computer engineering
  - Cyber-physical systems
  - Bioengineering
  - Nano-engineering

- **Graduate (Masters, PhD) Only**
  - Environmental engineering
  - Neuro-engineering
  - Intelligent systems (base ISE degree)

Structure of ISE Undergraduate Degree

- Total 120 credits of which 69 are Engineering
- University General Education: 21 credits
- University Math and Science: 30 credits

- Intelligent Systems Engineering core taken by all tracks: 30 credits
- CE/CPS core taken in CE and CPS: 15 credits
- CE Track: 18 Credits
- CPS Track: 18 Credits
- Engineering Electives: 6 Credits

- Bio/Nano differ first in semester 4 with advanced Chemistry course
- There are separate ISE Nano and ISE Bio cores of 15 credits in third year
- There are separate Nano and Bio tracks of 18 credits in third and fourth year

Typical Degree Map - CE

Eng Innovation and Design (E101)	Eng Computer Architectures (E110)	Computer Systems Engineering (E201)	Eng Cyber-Physical Systems (E210)
English Comp	Software Systems Engineering (E111)	Intelligent Systems Engineering I (211)	Intelligent Systems Engineering II (E222)
Calculus I	Calculus II	Professionalization and Ethics (E299 & E395)	Signal Processing (E250)
Physics I	Physics II	Statistics	Differential Eqn
		Science Elective	Arts&Humanities
Digital Design with FPGA's (E315)	Intro to Modeling and Simuation(E332)	Eng Capstone Design (E490)	Eng Capstone Design (E491)
Advanced Eng Mathematics (E331)	Circuits and Digital Systems (E311)	Operating Systems (E316)	Cloud Computing Eng (E416)
Modern Computer Arch (E312)	High Performance Computing (E317)	Network Eng (E318)	Deep Learning (E433)
Math/Sci Elective	Engr Elective	Engr Elective	Sci&Humanities
Language/Culture	Language/Culture	Sci&Humanities	Arts&Humanities

Accreditation and Funding Opportunities

Accreditation Information

- The curriculum has been designed to meet the ABET requirements.
- SICE can apply for accreditation after the first graduating class, which means that the first cohort of graduates' degrees will be accredited.
  - SICE will seek retroactive accreditation
  - The B.S. in Intelligent Systems Engineering is a degree from Indiana University; it is an accredited degree
  - IU holds North Central Association accreditation

Scholarship Information

- IU/SICE/ISE

Other Funding Opportunities

- Summer Camps
- Summer and Academic Year Research

19 Faculty in ISE

- **Raj Acharya; CE, Intelligent Systems:** Dean of SICE
- **Associate Dean for Engineering** (advertised)
- **Geoffrey Fox;** *Chair*, **CPS, Intelligent Systems**
- **Martin Swany;** *Associate Chair,* **CE, CPS**
- **Katy Borner; Intelligent Systems**
- **James Glazier; Bio-engineering, Bio-complexity**
- **Judy Qiu; CE, Intelligent Systems**
- **Thomas Sterling; CE, CPS**
- **Clint Whaley; CE**
- Lei Jiang; CE
- Minje Kim; Intelligent Systems
- Vikram Jadhao; Computational Nanoengineering
- Alexander Gumennik; Nanoengineering
- Eleftherios Garyfallidis; Neuroengineering
- Maria Bondesson-Bolin; Bioengineering
- Paul Macklin, Bioengineering:
- *Lantao Liu; CPS, Env*
- *Eatai Roth; Neuro, CPS*
- *Greg Lewis; Bio, CPS:*
- *Feng Guo; Bio, Nano*

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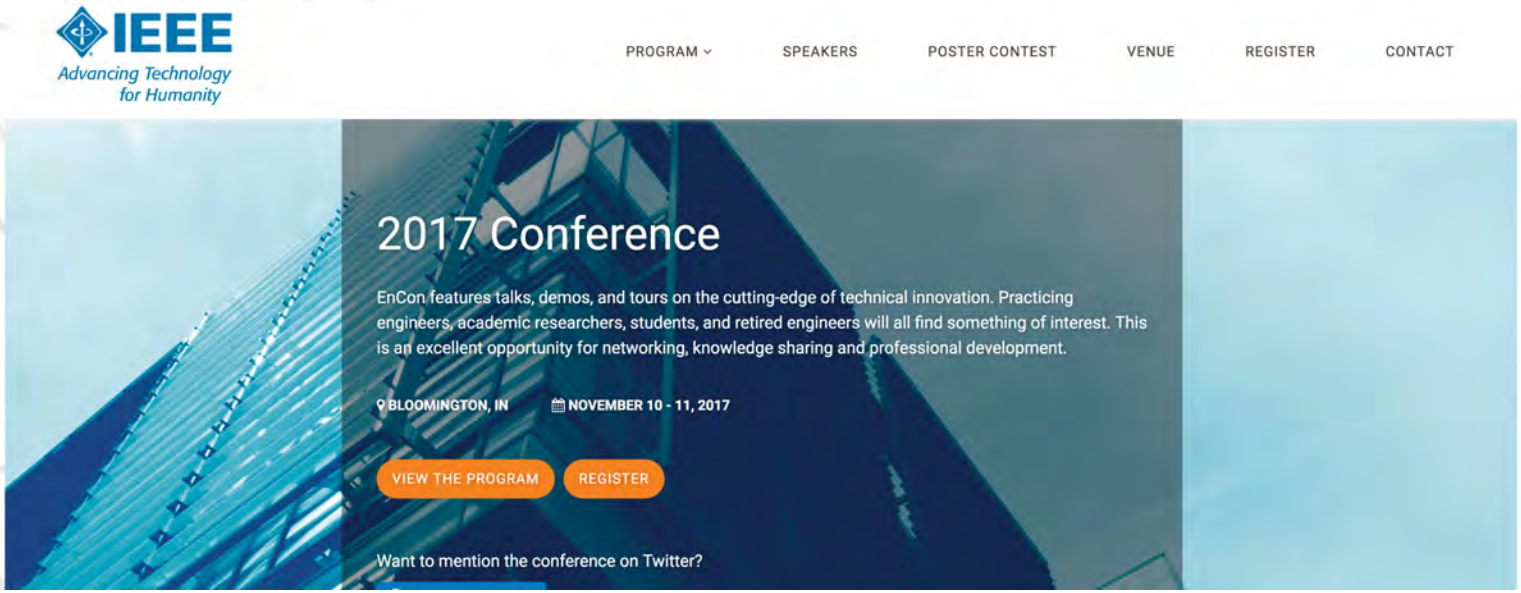


INDIANA UNIVERSITY

Information Technology at Indiana University

Brad Wheeler

IU Vice President for IT & Chief Information Officer

Professor of Information Systems
Kelley School of Business

bwheeler@iu.edu

Welcome to the Cyberinfrastructure Building – *The CIB*

8 University Campuses
9 Medical Education Centers

Indiana University, *est. 1820*

- **$3.5B** enterprise
- Partnered with **$6B** IU Health system

- **100,000** Students
- **1.3M** Credit Hours per semester
- **>20,000** Degrees per year
- **$1.1B** in Financial Aid
- **$450M** in research grants

- **20,500** Faculty and Staff
- **7,919** Acres
- **882** buildings, 36M square feet

- **>650,000** *living* Alumni

Almost completed 2009 Network Master Plan for IUB/IUPUI 360 buildings <$130M (Orig Budget $172M)

Merged into UITS
- 2011 Regional Campus IT
- 2014 Clinical Affairs IT Services
- 2017 Auxiliary IT

Broad IT responsibilities
Large shared services

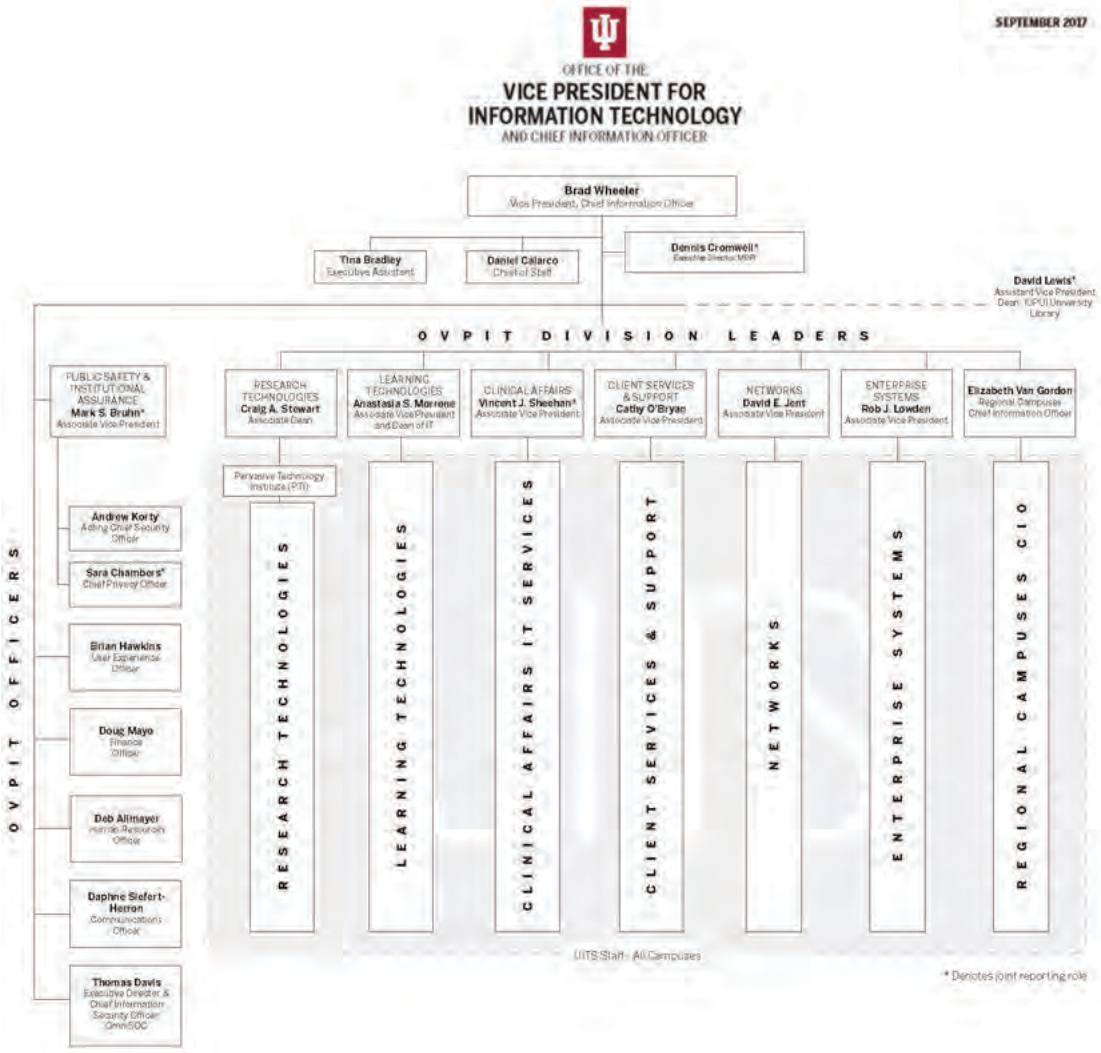
All IU IT Spend:
65% OVPIT
35% in Schools

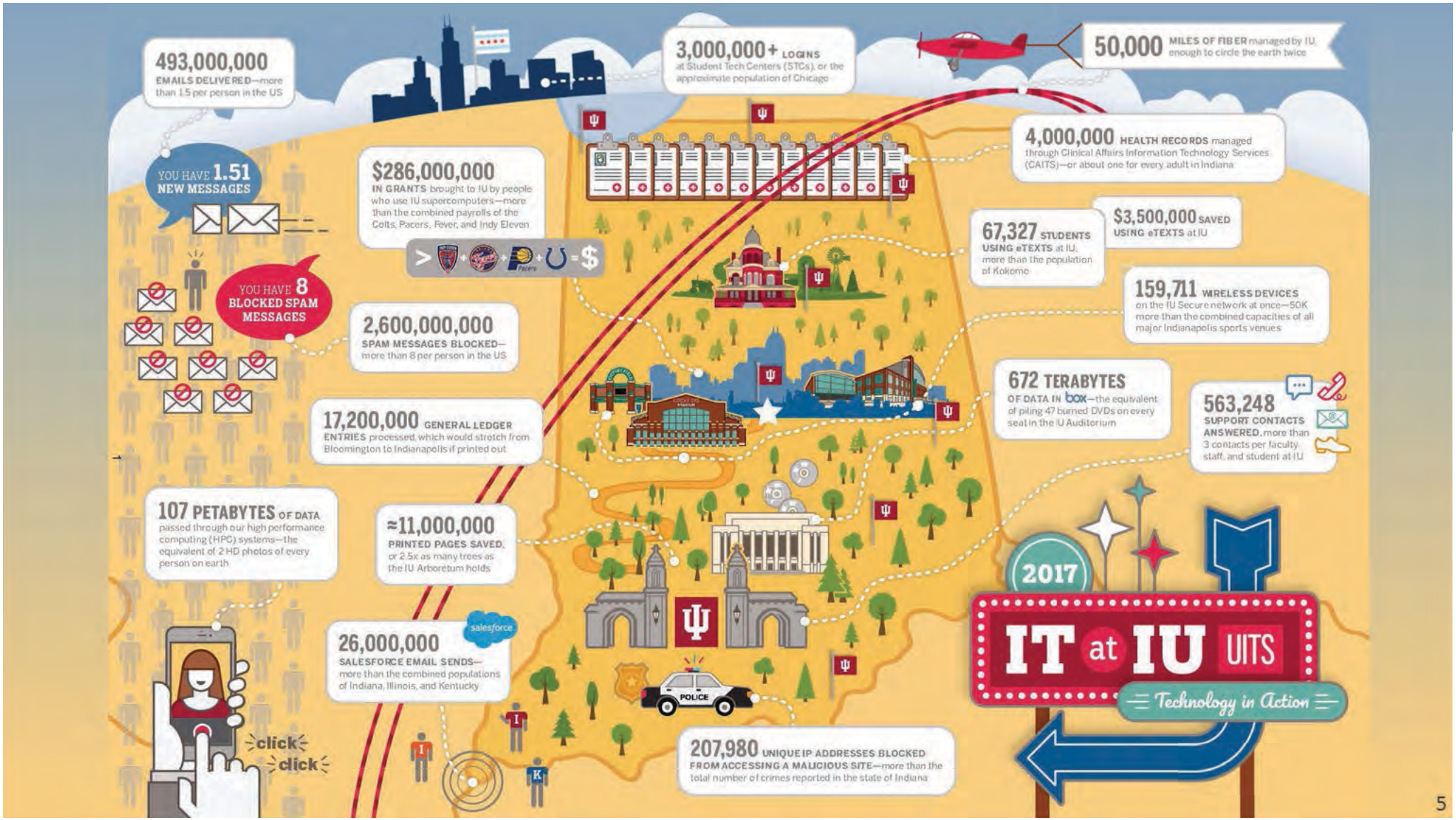
1,051 full-time staff
465 part-time

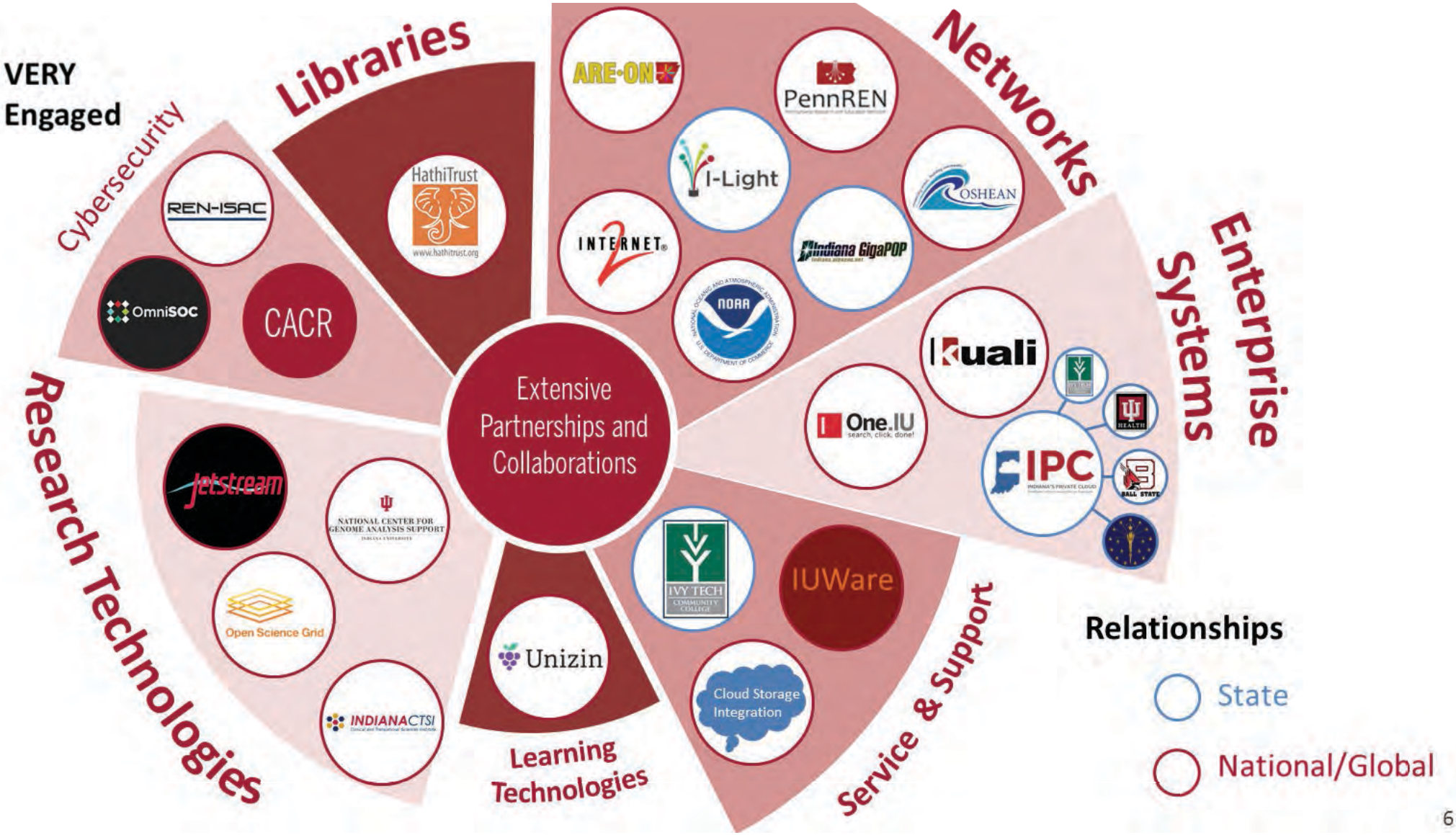
>$175M /year

$15-20M+ /year
Contracts/Grants

20 years of continuous leadership culture/capability




493,000,000 EMAILS DELIVERED—more than 1.5 per person in the US
YOU HAVE 1.51 NEW MESSAGES
YOU HAVE 8 BLOCKED SPAM MESSAGES
3,000,000+ LOGINS at Student Tech Centers (STCs), or the approximate population of Chicago
50,000 MILES OF FIBER managed by IU, enough to circle the earth twice
4,000,000 HEALTH RECORDS managed through Clinical Affairs Information Technology Services (CAITS)—or about one for every adult in Indiana
$286,000,000 IN GRANTS brought to IU by people who use IU supercomputers—more than the combined payrolls of the Colts, Pacers, Fever, and Indy Eleven
67,327 STUDENTS USING eTEXTS at IU, more than the population of Kokomo
$3,500,000 SAVED USING eTEXTS at IU
159,711 WIRELESS DEVICES on the IU Secure network at once—50K more than the combined capacities of all major Indianapolis sports venues
2,600,000,000 SPAM MESSAGES BLOCKED—more than 8 per person in the US
17,200,000 GENERAL LEDGER ENTRIES processed, which would stretch from Bloomington to Indianapolis if printed out
672 TERABYTES OF DATA IN box—the equivalent of piling 47 burned DVDs on every seat in the IU Auditorium
563,248 SUPPORT CONTACTS ANSWERED, more than 3 contacts per faculty, staff, and student at IU
107 PETABYTES OF DATA passed through our high performance computing (HPC) systems—the equivalent of 2 HD photos of every person on earth
≈11,000,000 PRINTED PAGES SAVED, or 2.5x as many trees as the IU Arboretum holds
26,000,000 SALESFORCE EMAIL SENDS—more than the combined populations of Indiana, Illinois, and Kentucky
207,980 UNIQUE IP ADDRESSES BLOCKED FROM ACCESSING A MALICIOUS SITE—more than the total number of crimes reported in the state of Indiana
POLICE
click
click
2017
IT at IU UITS
Technology in Action


VERY
Engaged
Libraries
Networks
Enterprise Systems
Service & Support
Learning Technologies
Research Technologies
Cybersecurity
HathiTrust
www.hathitrust.org
ARE·ON
PennREN
I-Light
OSHEAN
INTERNET2
Indiana GigaPOP
NOAA
REN-ISAC
OmniSOC
CACR
Kuali
One.IU
search; click; done!
IPC
INDIANA'S PRIVATE CLOUD
Extensive Partnerships and Collaborations
Jetstream
NATIONAL CENTER FOR GENOME ANALYSIS SUPPORT
Open Science Grid
INDIANACTSI
Unizin
IVY TECH COMMUNITY COLLEGE
IUWare
Cloud Storage Integration
Relationships
State
National/Global

Multi-institution Partnerships

Networks

Internet2 — National network collaboration of 375 Universities and national labs. IU acts as network operations center for the organization.

I-Light — Indiana state network for higher education with over 100 members. IU acts as its network operations center.

Indiana GigaPOP — Collaboration of I-Light, IU, Notre Dame, and Purdue providing high-speed, high-availability, feature-rich network to Indiana's higher education institutions.

Libraries

HathiTrust (www.hathitrust.org) — Began as collaboration between the Big Ten Academic Alliance and the University of California system to digitize library print holdings. Now includes over 150 universities. IU serves as primary backup site for repository.

Research Technologies

Jetstream — IU-led collaboration with Texas Advanced Computing Center, University of Chicago, University of Arizona, and University of Texas (SA) to develop cloud based tools for scientific research funded by National Science Foundation.

National Center for Genome Analysis Support — Collaboration with Texas Advanced Computing Center, Pittsburgh Supercomputing Center and San Diego Super-computing Center to analyze massive genomic data.

Open Science Grid — Over 100 institutions in the US collaborating to provide CPU core hours to researchers.

INDIANACTSI — Collaboration of IU, Purdue, and Notre Dame, with public and private partners to facilitate the translation of scientific discoveries in the lab into clinical trials and new patient treatments.

Service & Support

Cloud Storage Integration — Application developed at IU to integrate cloud storage systems into a single place. Currently has 8 university subscribers and 6 universities testing.

IUWare — System to manage software licenses developed at IU. Subscribers include University of Maryland and University of Alabama-Huntsville.

Security

REN-ISAC — Research and Education Networking Information Sharing and Analysis Center. Includes 475 member universities. One of 19 nationally recognized industry-specific ISACs.

CACR — Center for Applied Cybersecurity Research, Est. 2003, integrates applied research in cybersecurity technology, education, and policy guidance.

OmniSOC — New 2017: Shared Cybersecurity Operations Center for Big10 Universities

Enterprise Systems

Kuali — Community sourced software suite driving down cost of enterprise systems. IU co-founded and currently serves on board of directors. Includes over 50 university members.

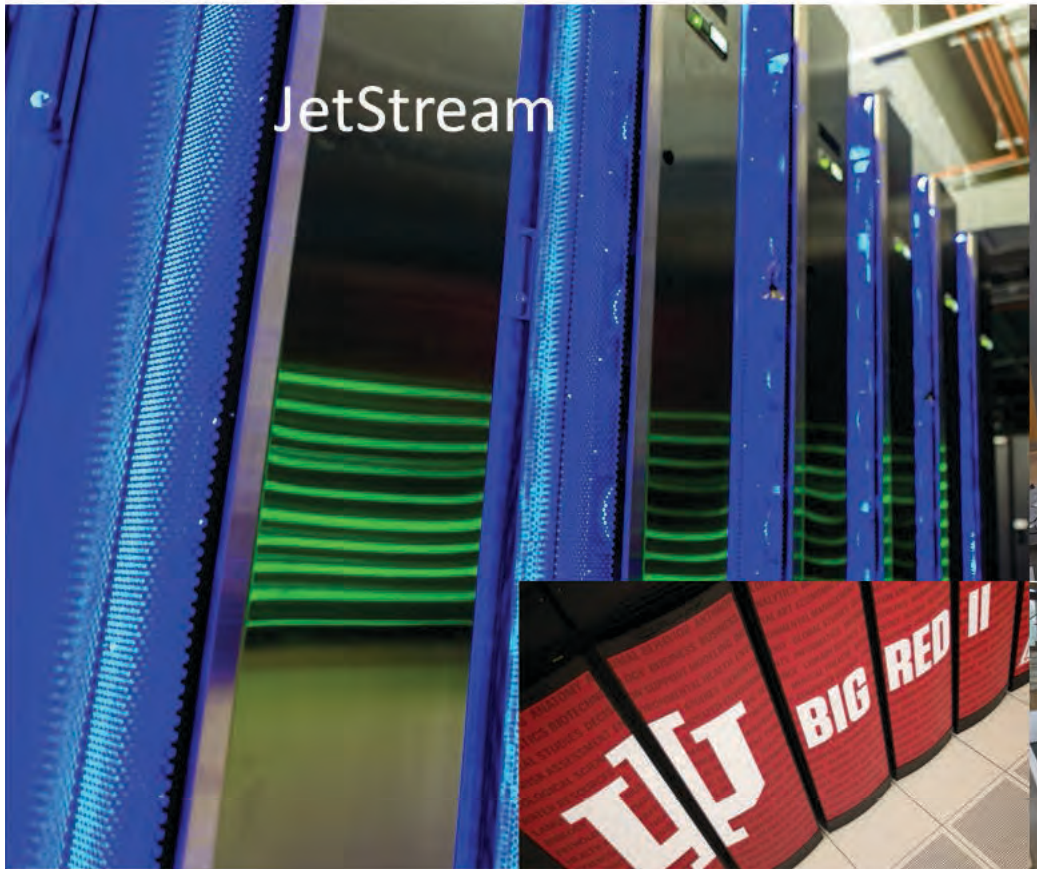
IPC — Virtual hosting for government and education institutions in Indiana. Clients include Indiana State University, Ball State University and Wabash College.

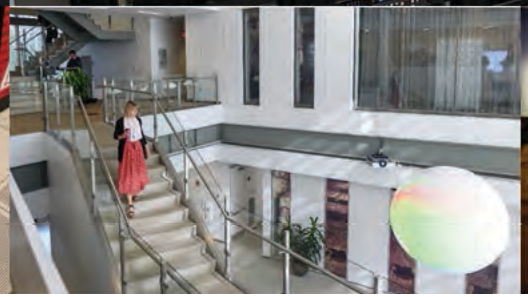
One.IU (search, click, done!) — Portal replacement service discovery application developed at IU. Currently used by 25 universities including Purdue.

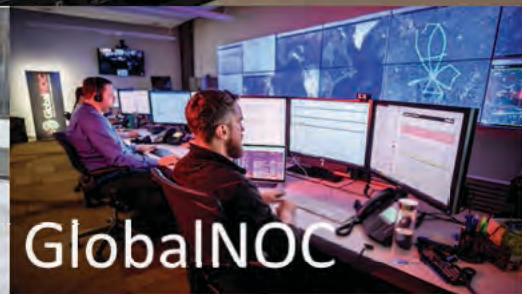
Learning Technologies

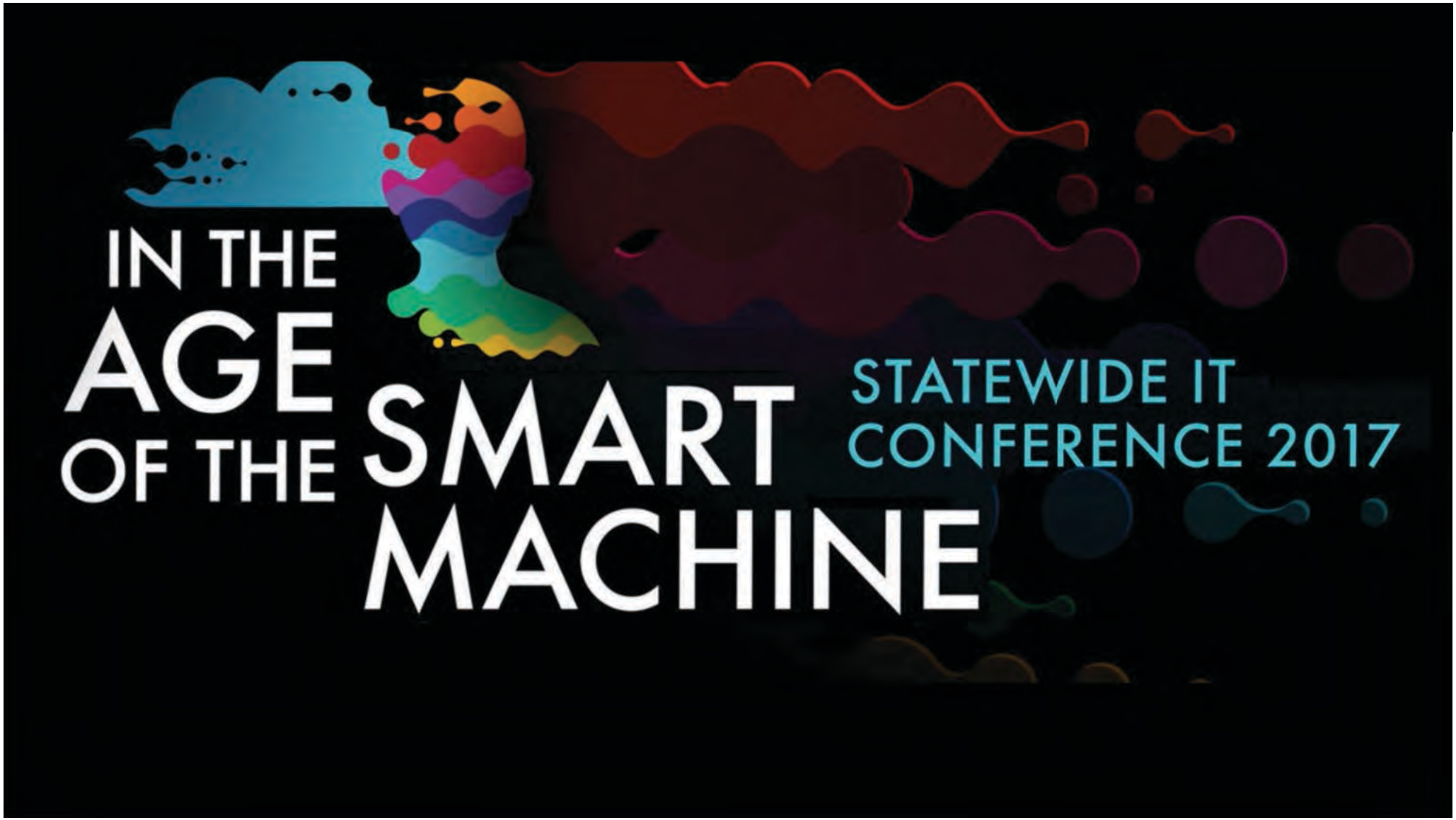
Unizin — Coalition of universities dedicated to collaborative digital education. Founded by IU, Michigan, Colorado State, and Florida. Now includes Oregon State, Nebraska, Ohio State, Iowa, Minnesota, Wisconsin, and Penn State.

What You'll See Today








IN THE
AGE
OF THE SMART
MACHINE
STATEWIDE IT
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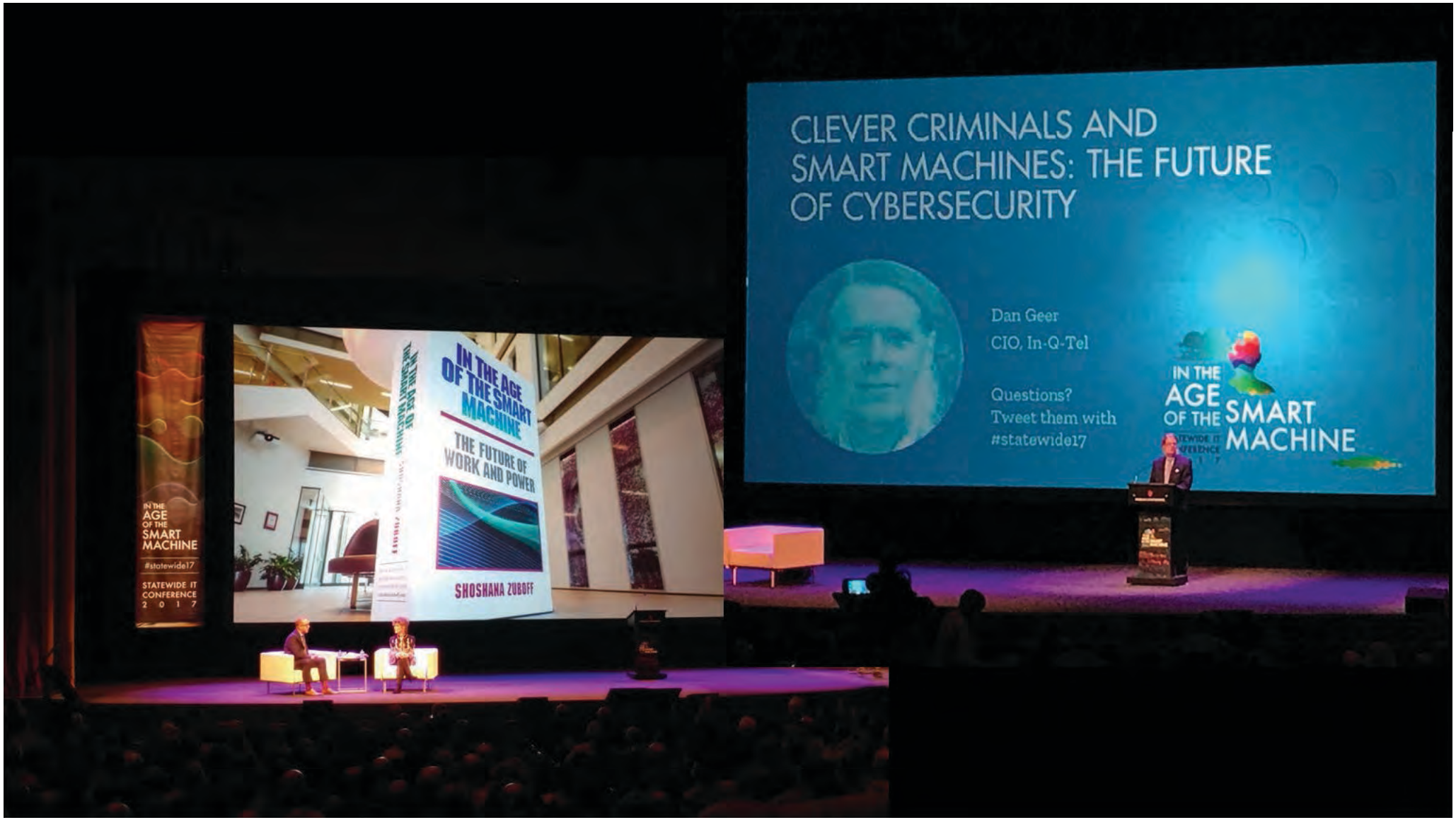
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#statewide17
STATEWIDE IT CONFERENCE 2017
IN THE AGE OF THE SMART MACHINE
THE FUTURE OF WORK AND POWER
SHOSHANA ZUBOFF
CLEVER CRIMINALS AND SMART MACHINES: THE FUTURE OF CYBERSECURITY
Dan Geer
CIO, In-Q-Tel
Questions?
Tweet them with
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IN THE AGE OF THE SMART MACHINE

COMMENTARY

Networked U.'s: This Is What Will Save Higher Ed

By Jeffrey J. Selingo | NOVEMBER 08, 2017

THE CHRONICLE OF HIGHER EDUCATION

"Today, a new type of alliance is beginning to emerge in higher education. Rather than coalitions built around geography, mission, or even athletics, these new associations are assembled around a common set of problems that multiple campuses need to address but have found they cannot solve on their own. These new alliances are less about shared purchasing or exchanging best practices, and more about developing strategic solutions, many leveraging technology, to solve some of higher education's toughest problems related to access, retention, completion, …"

INDIANA UNIVERSITY

Information Technology at Indiana University

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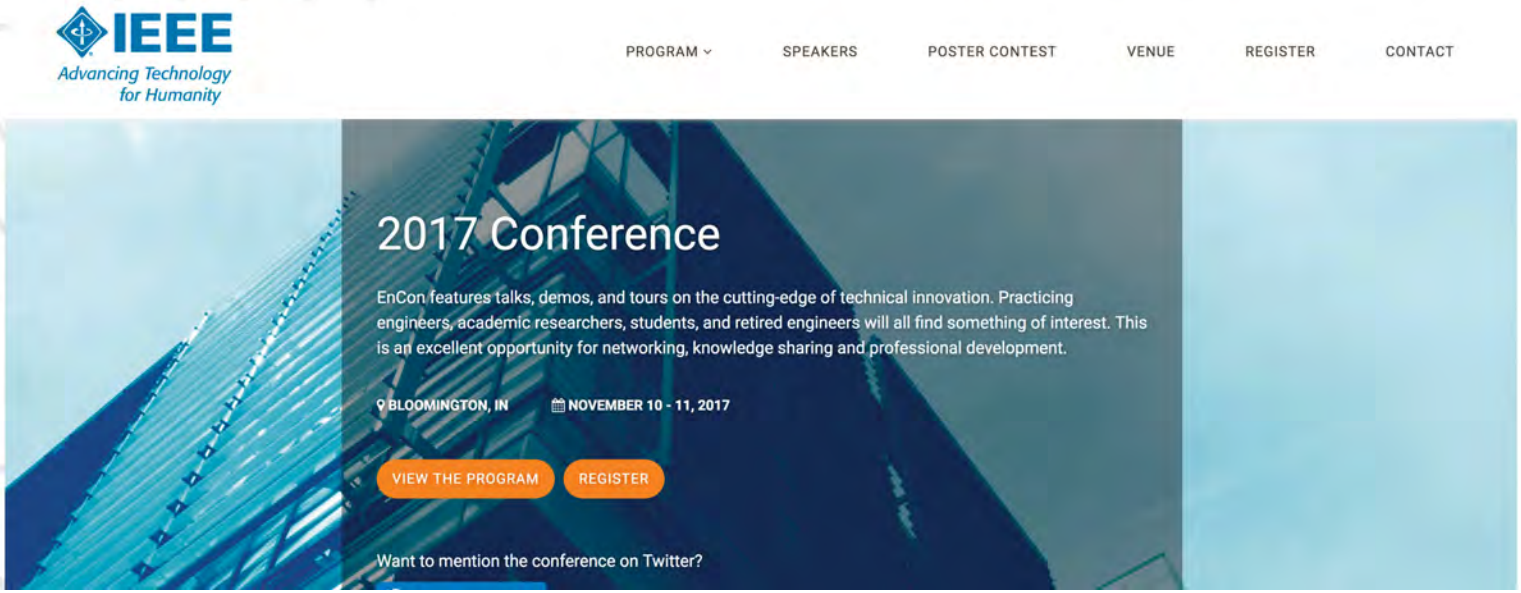
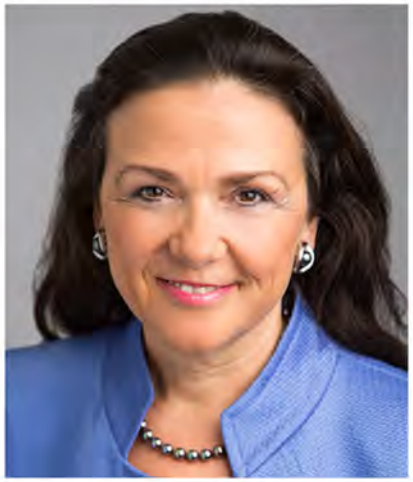


Keynote

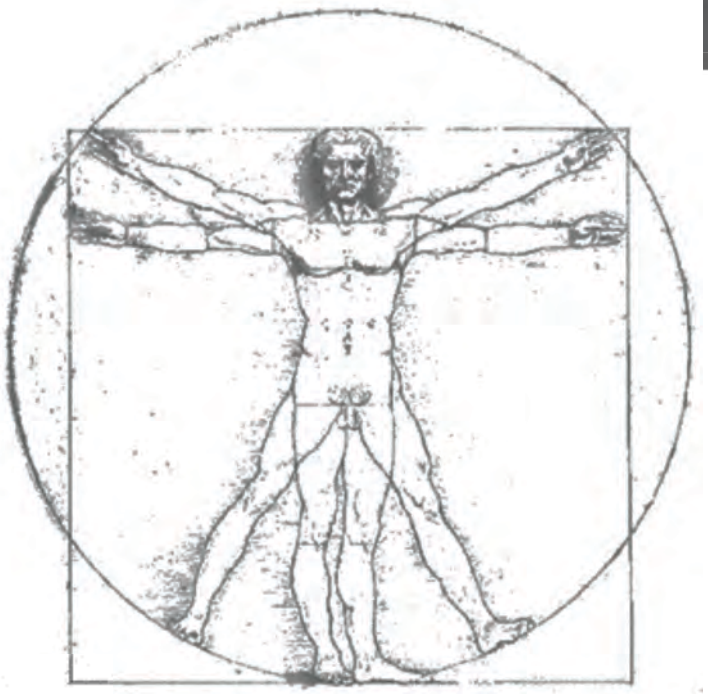
Mapping the Human Body: Splitting, Lumping, and the Rubik's Cube Dilemma



Zorina S. Galis, Ph.D.

Chief, Vascular Biology and Hypertension Branch
Division of Cardiovascular Sciences
National Heart, Lung, and Blood Institute (NHLBI)
National Institutes of Health

EnCON2017
Advancing Technology for Humanity
November 10, 2017



"Mapping the Human Body: Splitting, Lumping, and the Rubik's Cube Dilemma"

Zorina S. Galis, Ph.D.

Chief, Vascular Biology and Hypertension Branch
Division of Cardiovascular Sciences
National Heart, Lung, and Blood Institute (NHLBI)

National Institutes of Health

NIH National Heart, Lung, and Blood Institute

Conflicts And Other Disclosures

- **No** financial conflicts
- **Note**: The opinions presented are personal, they do not necessarily represent the opinions of the NHLBI.

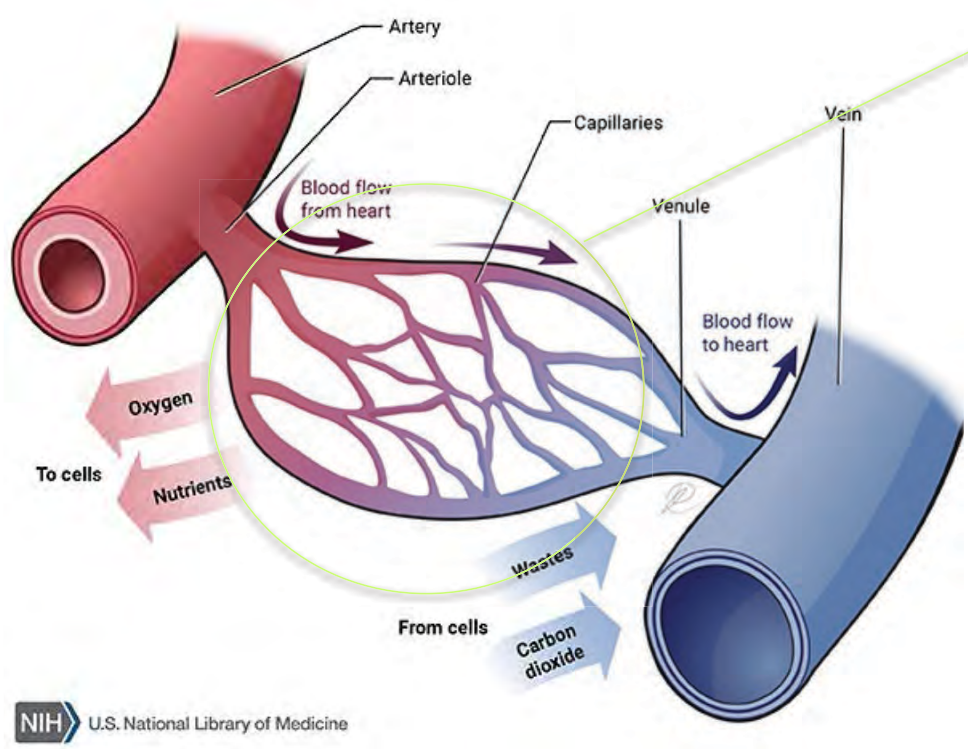
Topics

- "What is *the problem*?"
  - Example from the cardiovascular world
  - Expanding to the human body
- Some current/emerging solutions for:
  - "Splitting"
  - "Lumping"
- The Rubik Cube Dilemma?
- Challenges harbor opportunities!

Could YOU help?

The Human Vascular System

When small… gets BIG!



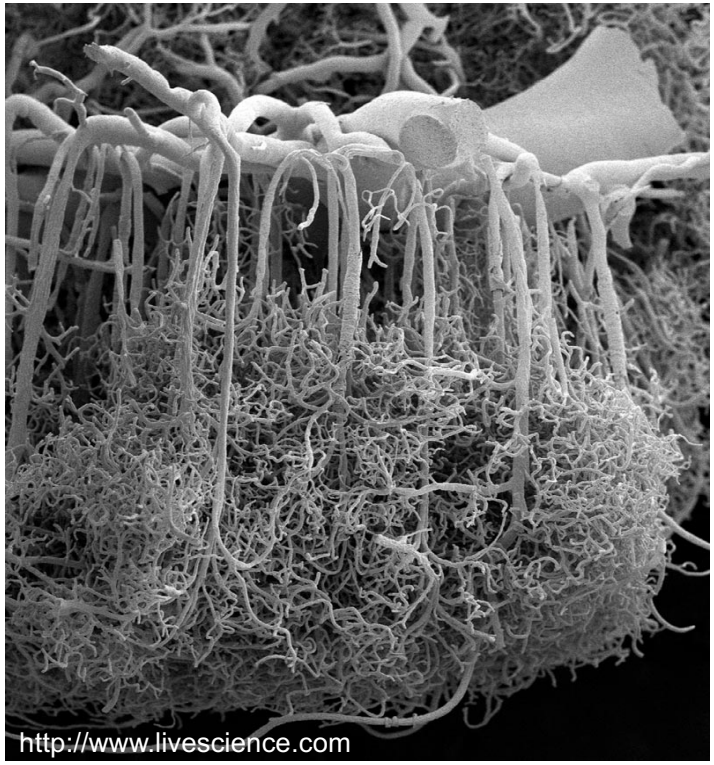
- **In Health**

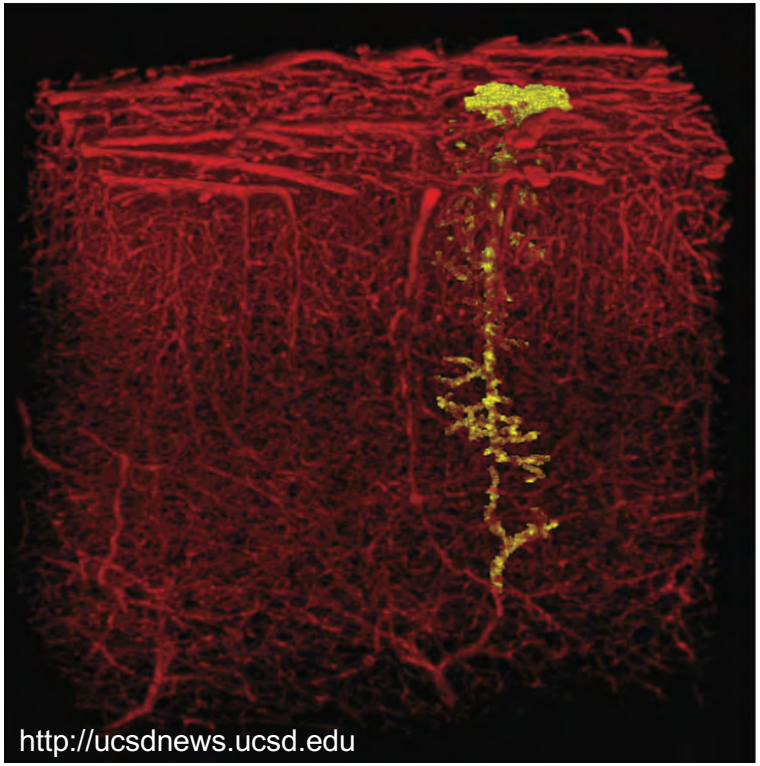
Essential for survival and normal function of ALL tissues/organs
Major site for local and systemic exchanges, sensing, integration and dynamic response to signals

- **In Disease**

Local dysfunction <=> organ and systemic diseases

Brain Small Blood Vessel Disease

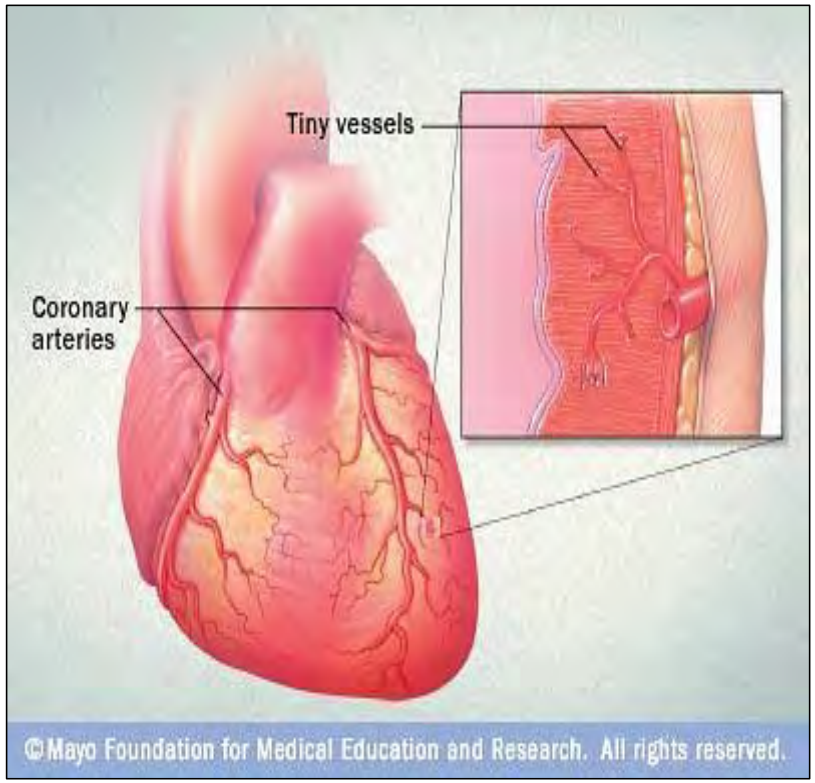




Brain infarctions/hemorrhage, associated with small strokes, vascular cognitive impairment, Alzheimer's

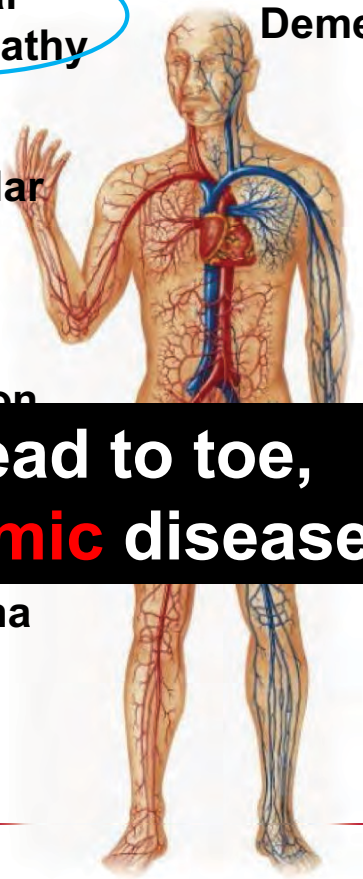
NIH National Heart, Lung, and Blood Institute

"*Small Vessel Heart Disease*"



- **Hard to diagnose, can cause:**
  - **Coronary Artery Spasm**
  - **Heart Attack**
  - **Sudden Cardiac Death**
  - **Heart Failure**
- **Risk factors:**
  - **Tobacco use, High cholesterol, High blood pressure, Obesity (body mass index of 30 or higher), Inactive lifestyle, Diabetes, Insulin resistance, Female sex, Polycystic ovarian syndrome, Age (> 45 y in men and >55 y in women)**

Small Vessels Dysfunction Implicated In…



Lacunar stroke

Lymphedema

Retinal vasculopathy

Dementia

Hemorrhage

Aging

Hypertension

Coronary microvascular disease

Diabetes

Leukoclastic vasculitis

Malaria

Pulmonary hypertension

Kidney disease

Literally from head to toe, from local to systemic diseases

Preeclampsia

Scleroderma

Wound healing

Alcohol and substance abuse

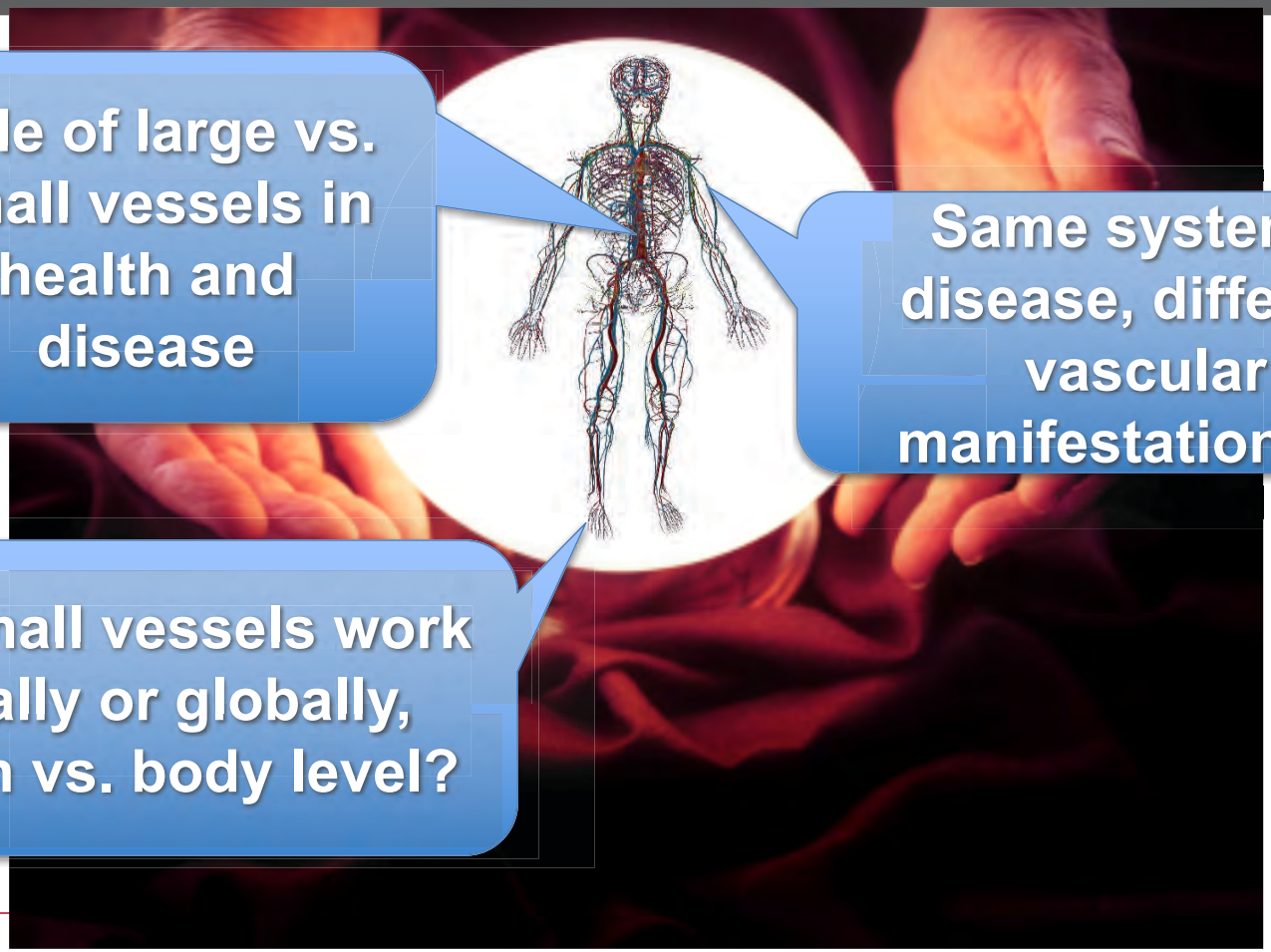
Cancer

Systemic inflammation

Sepsis

NIH National Heart, Lung, and Blood Institute

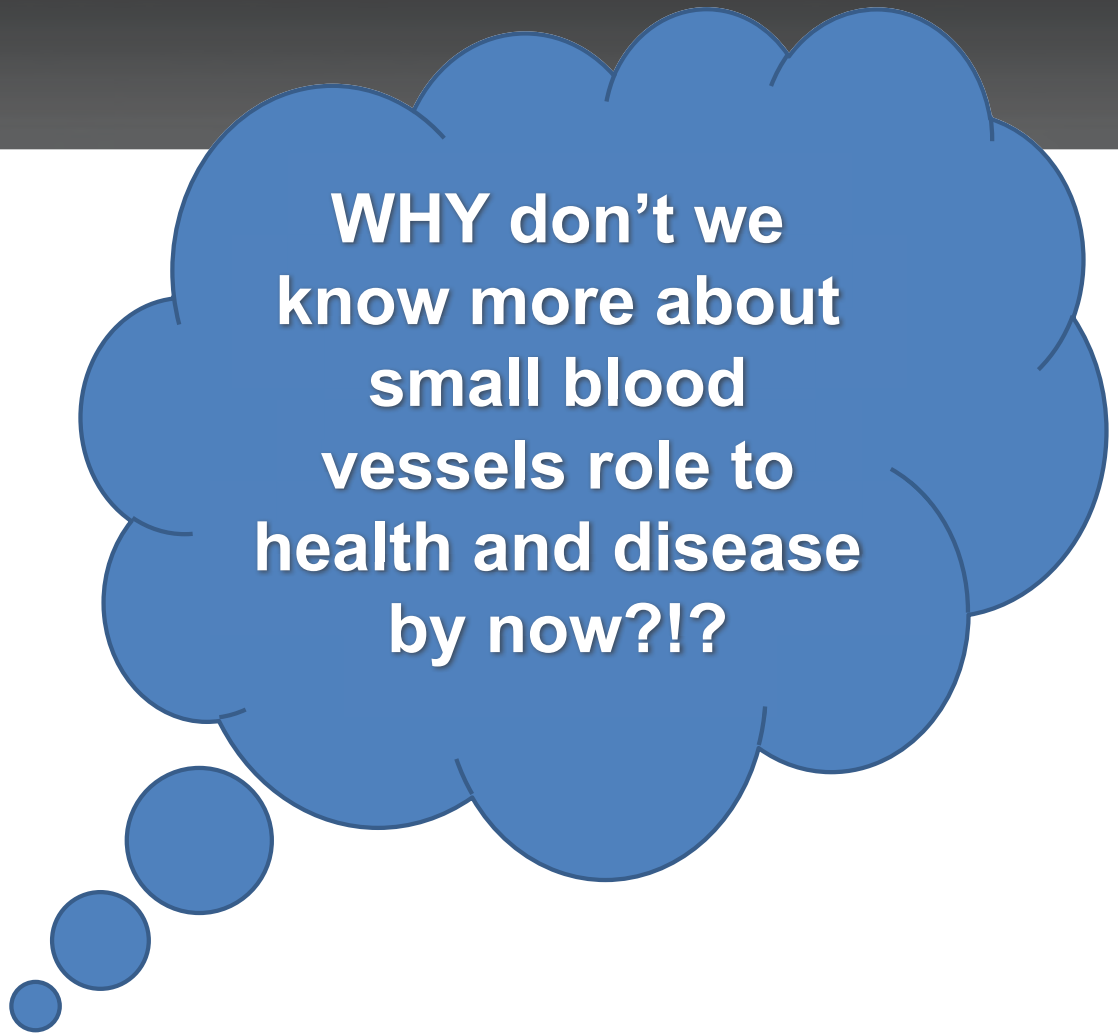
Enduring Human Health Mysteries…



Role of large vs. small vessels in health and disease

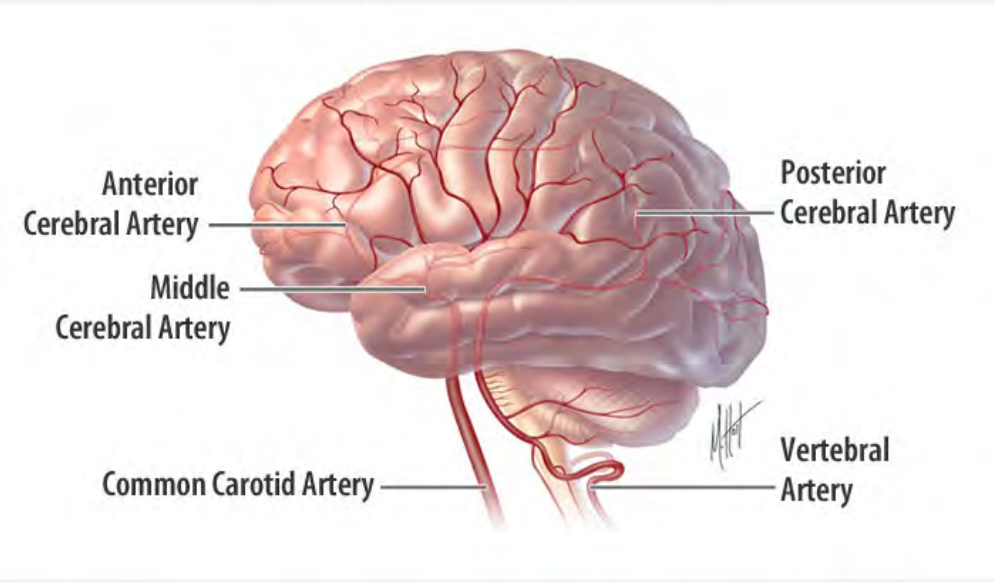
Same systemic disease, different vascular manifestations …

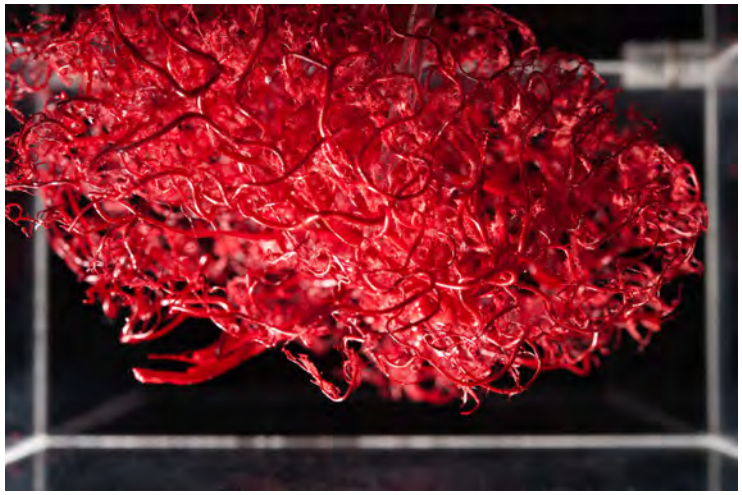
Do small vessels work locally or globally, organ vs. body level?


WHY don't we know more about small blood vessels role to health and disease by now?!?

Small Blood Vessels Have A….

SIZE problem

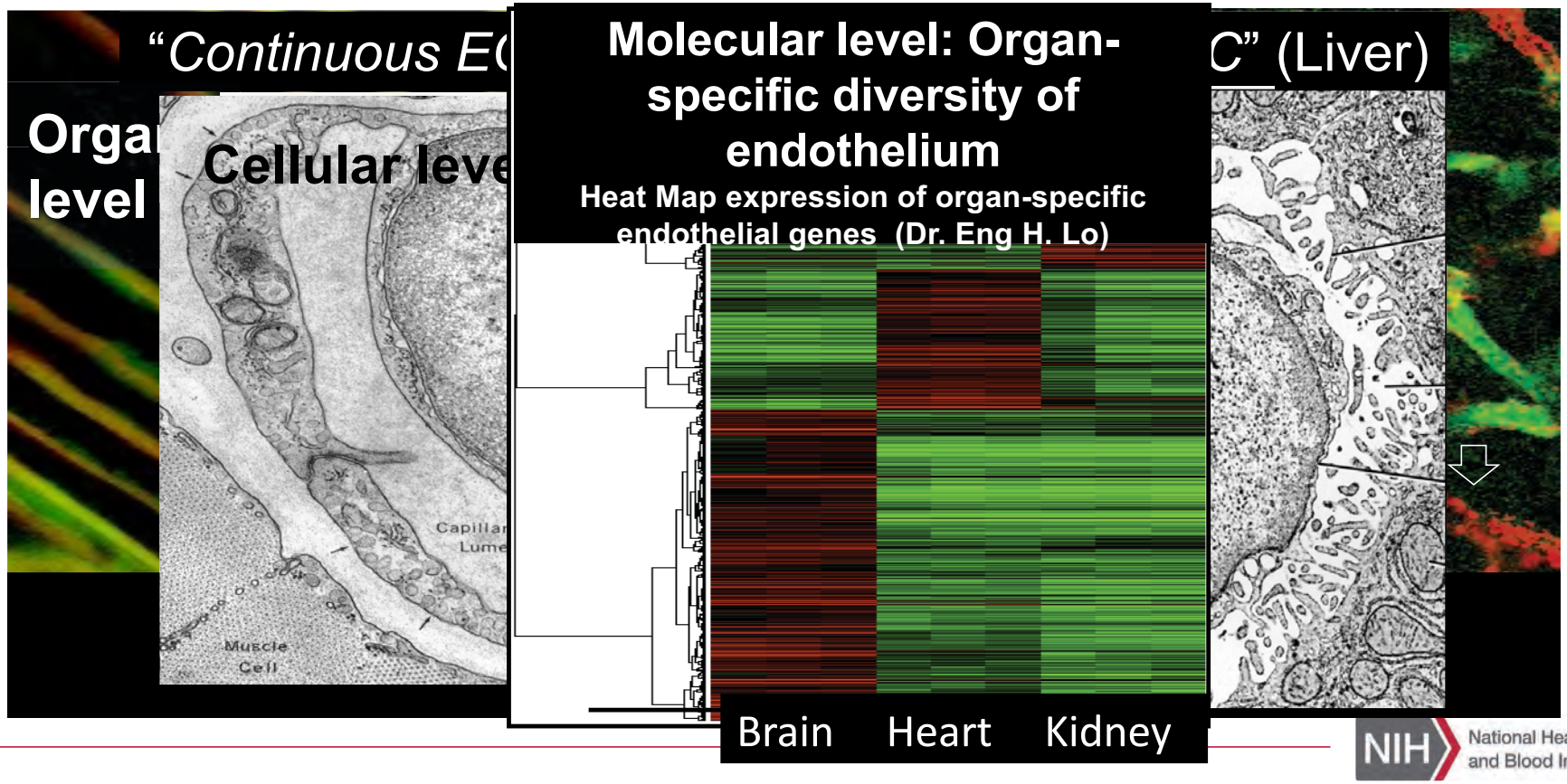




Out of sight, out of mind!

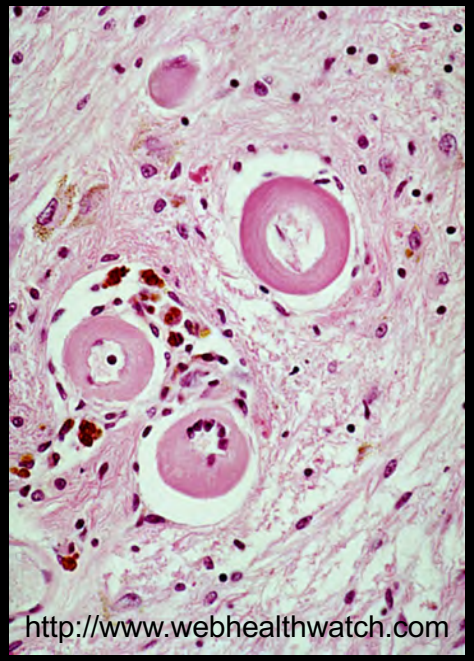
Small Blood Vessels Have a Complexity Issue

Structural/functional Diversity, e.g., Endothelial cells (EC)



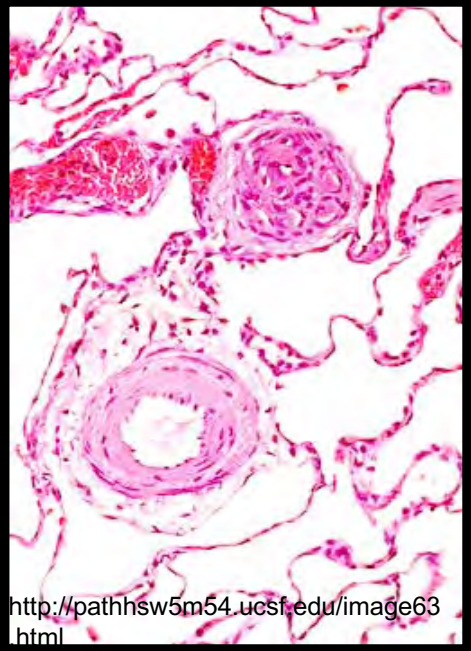
Organ-Specific Small Blood Vessel Pathology in Hypertension

Brain



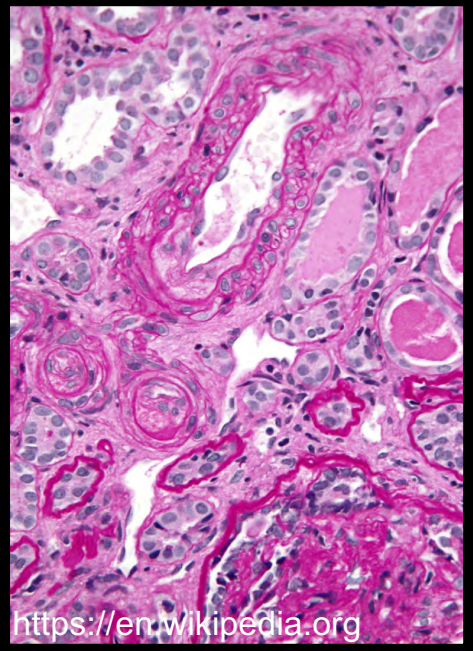
http://www.webhealthwatch.com

Lung



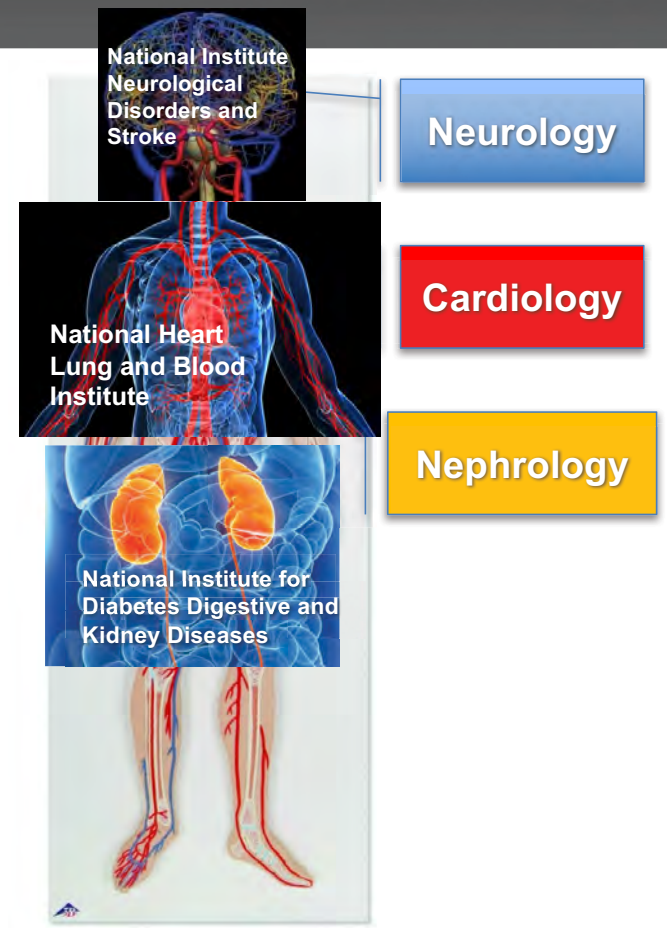
http://pathhsw5m54.ucsf.edu/image63.html

Kidney



https://en.wikipedia.org

Small Blood Vessels Have A….



Neurology

Cardiology

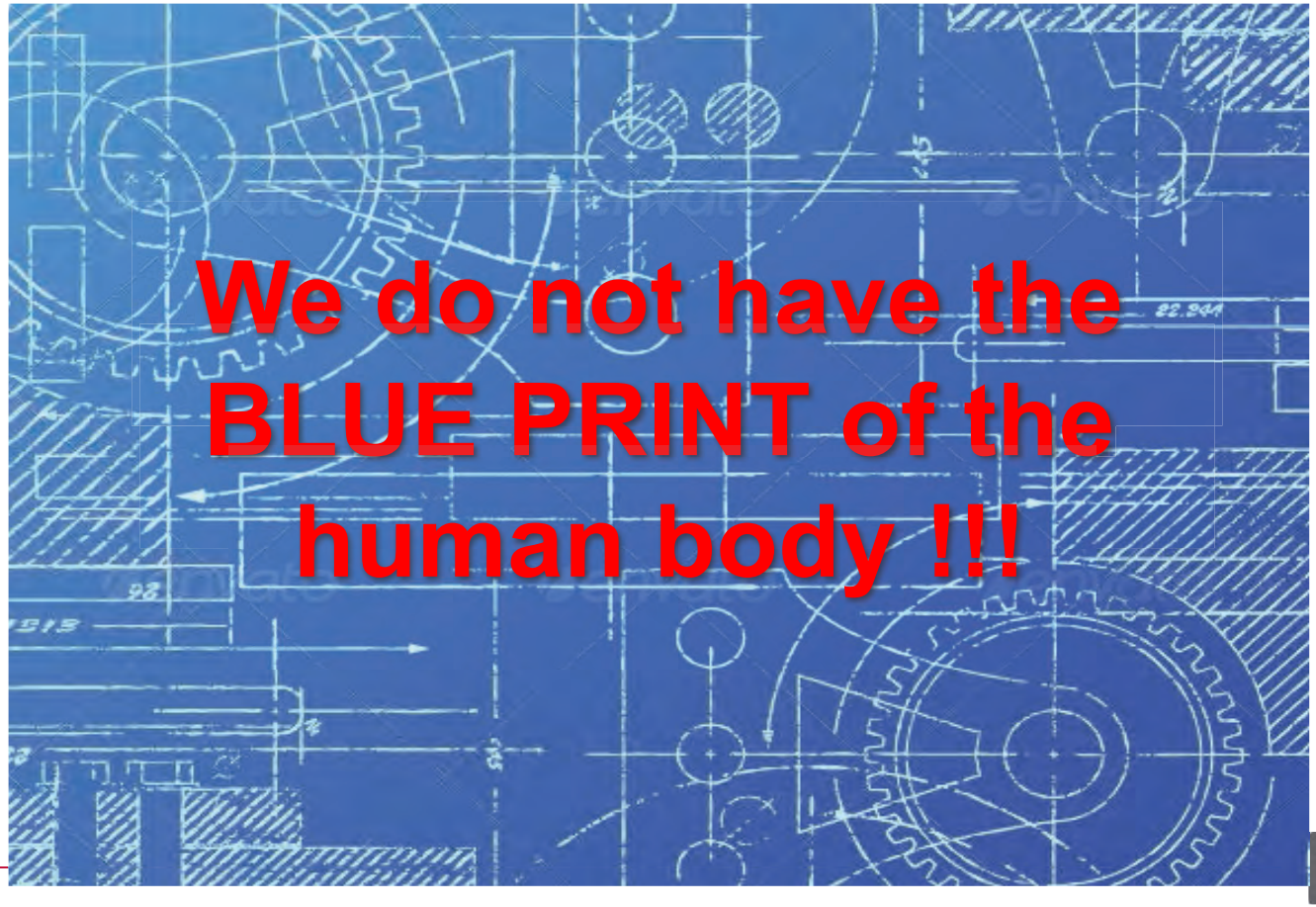
Nephrology

“KNOWEDGE FRAGMENTATION” problem!

“Knowledge silos”

- **Training, specialization**
- **Professional life**
- **Funding**

Major….“ENGINEERING” problem



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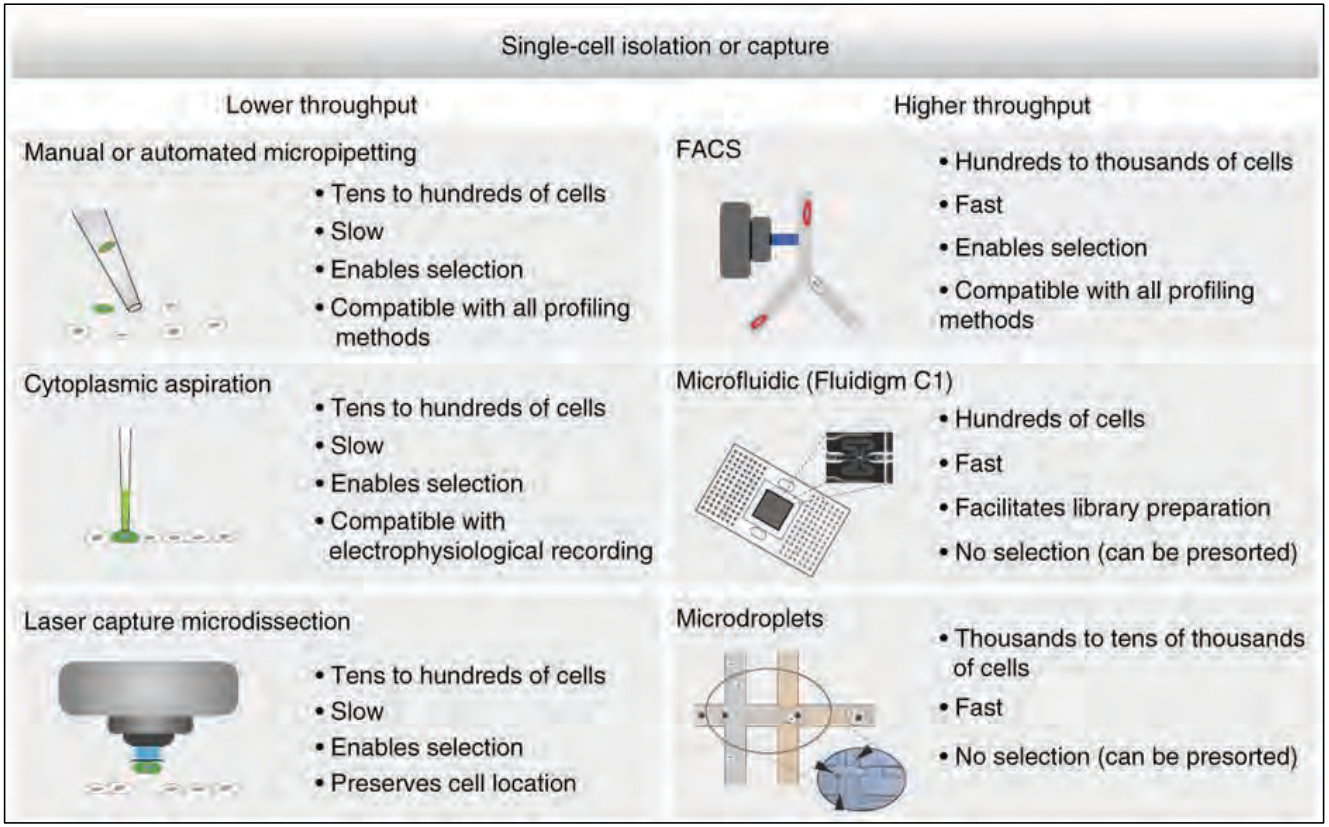
"Splitting"

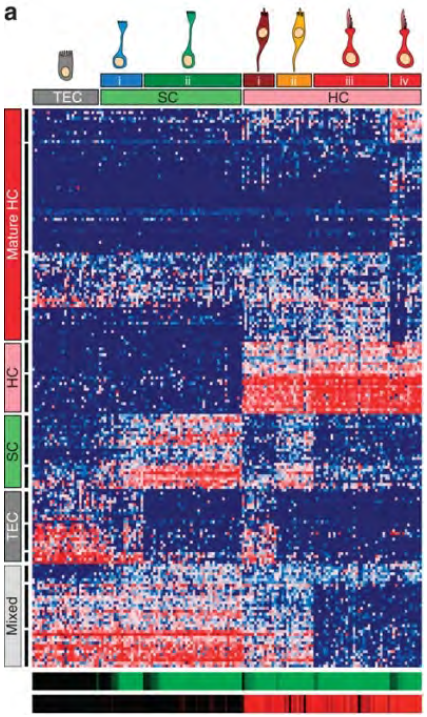
- **Individual cell = smallest functional unit**
- **Emerging opportunities:**
  - **Single cell analyses "–omics" and imaging (RNA, DNA, protein)**
  - **The "in situ" analysis challenge**



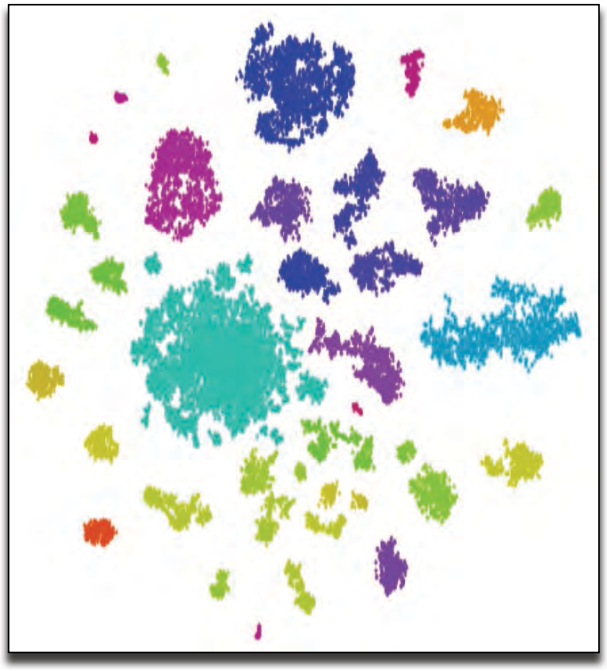
Poulin et al, Nature Neuroscience 19, 1131–1141, 2016

NIH National Heart, Lung, and Blood Institute

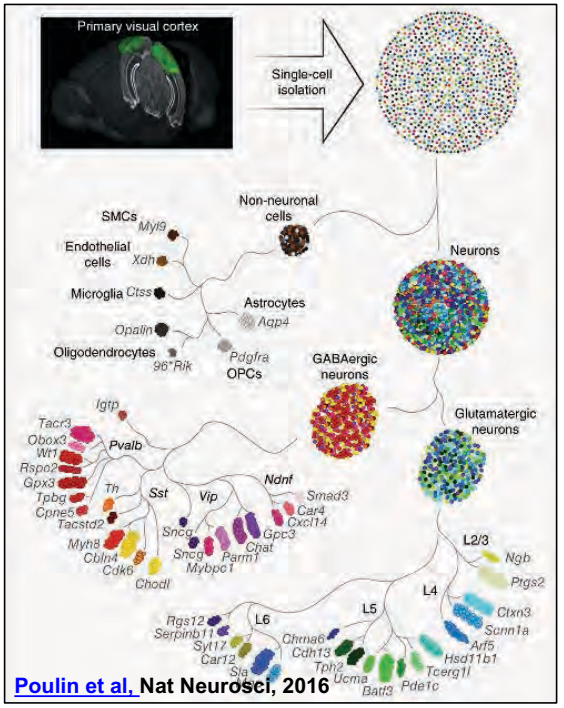
Single Cell Technologies: New Era in Human Body Exploration!



RNA-Seq identifies unique cell types in mouse utricle (Kelley Lab)



Retina Drop-Seq (48,808 cells) – Identification of 3 new cell types (Regev Lab)



Poulin et al, Nat Neurosci, 2016

Disentangling Neural Cell Diversity Using Single-cell Transcriptomics

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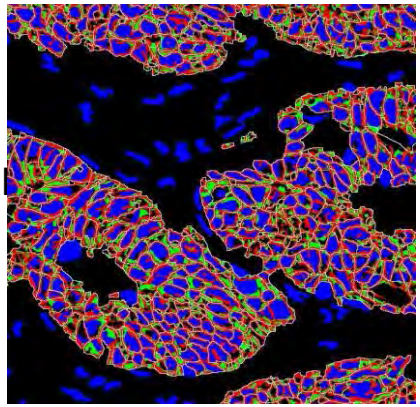
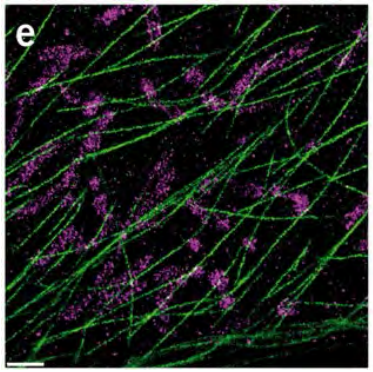
NIH Single Cell Project (SCAP)
Innovation In Single-cell Proteomics And Metabolomics

>60 Proteins then DNA FISH
Gerdes, GE Global Research
SCAP Project: R01CA173377





Multiplexed cellular super-resolution imaging using DNA-PAINT and Exchange-PAINT, Yin et al., Nat Methods. 2014 Mar;11(3):313-8.

Imaging lipid metabolism in live C. elegans using stimulated Raman scattering imaging. Cheng et al. SCAP Project: R21 GM114853

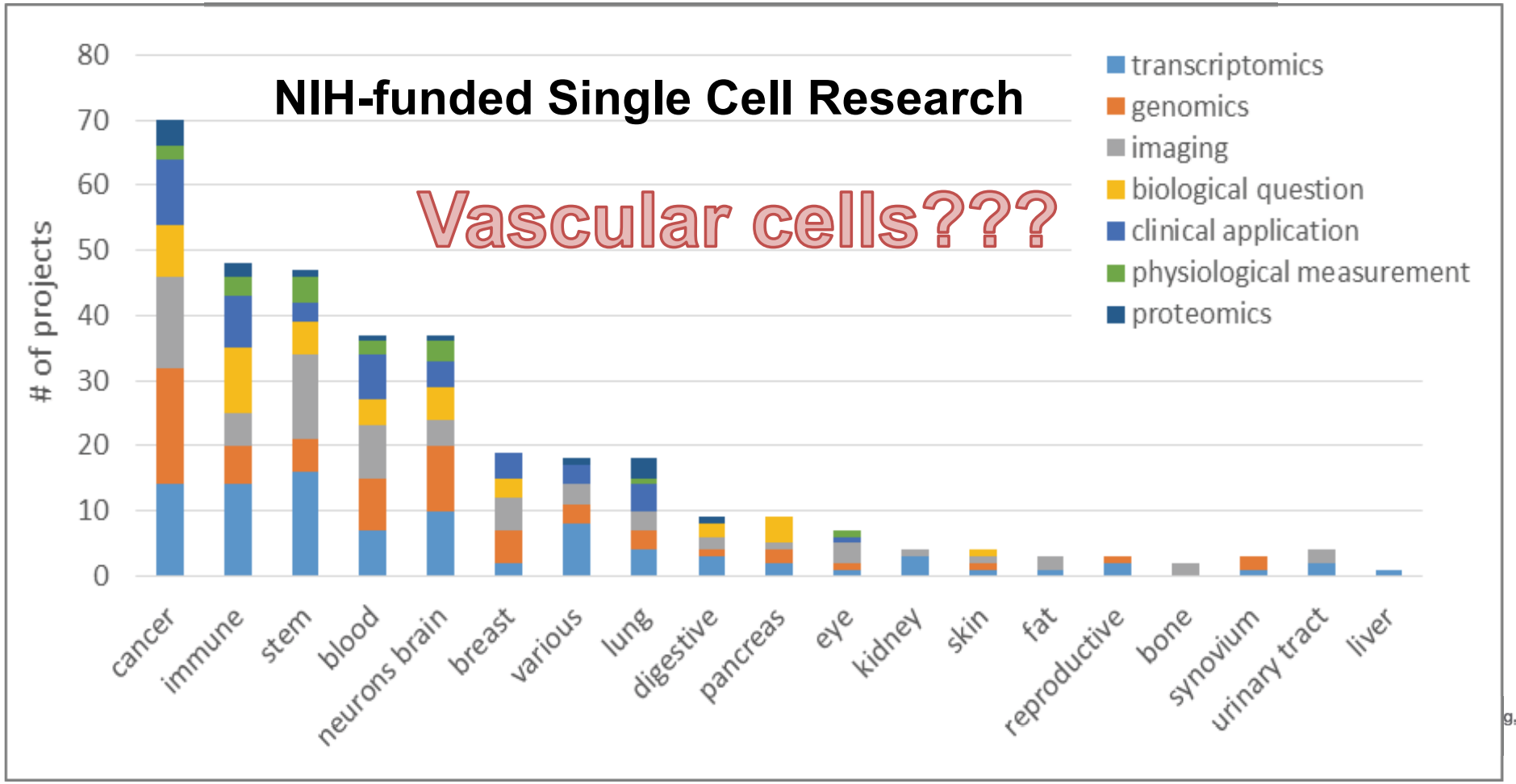
National Institutes of Health
Office of Strategic Coordination - The Common Fund

NIBIB

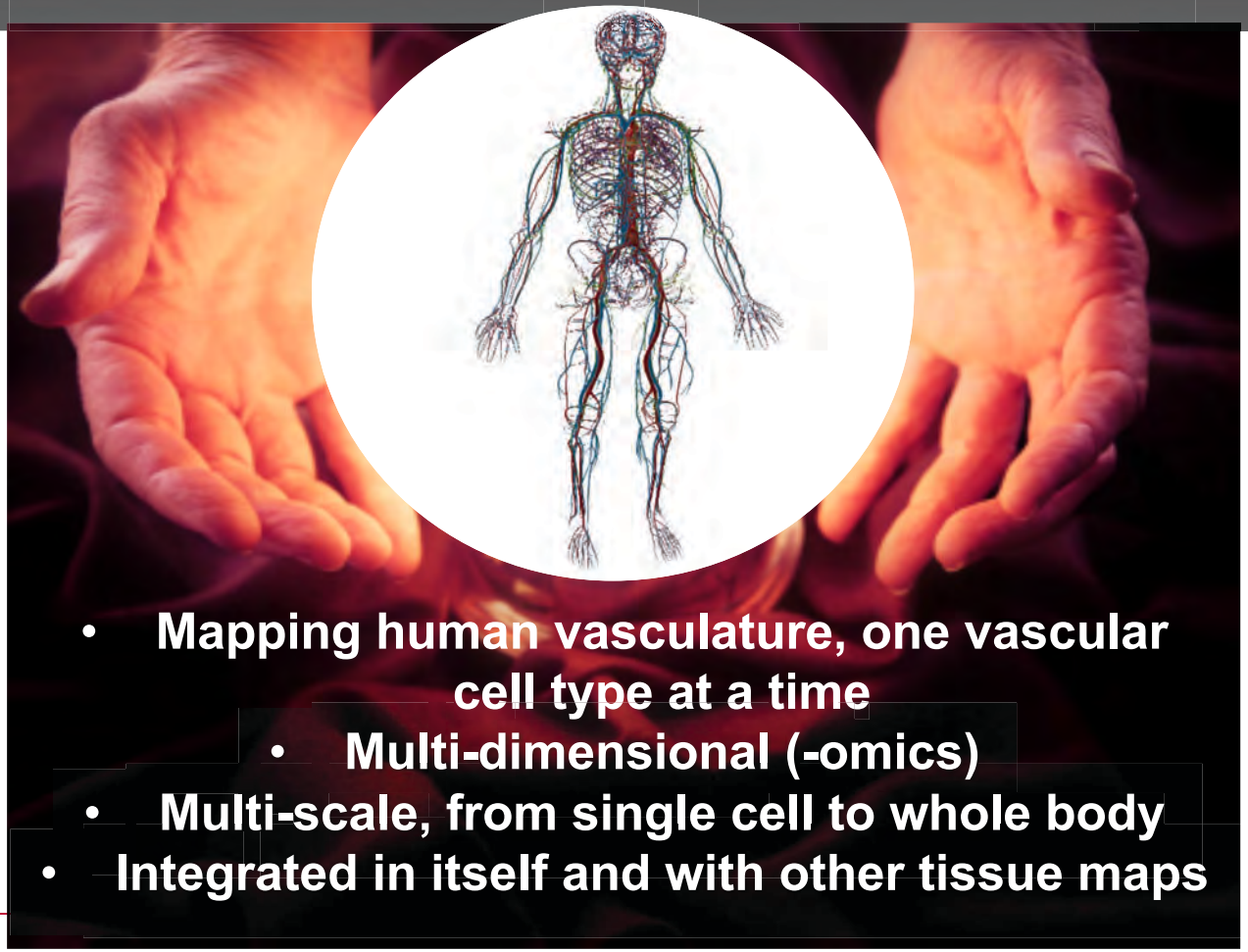
NIMH National Institute of Mental Health

NIH National Heart, Lung, and Blood Institute

New technologies > New Biology!



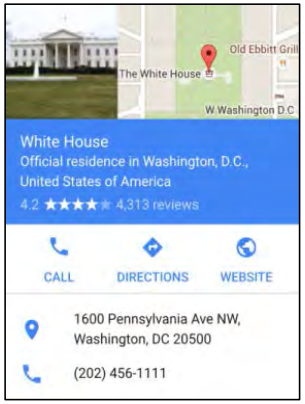
Time to Build "*The Vasculome?*"

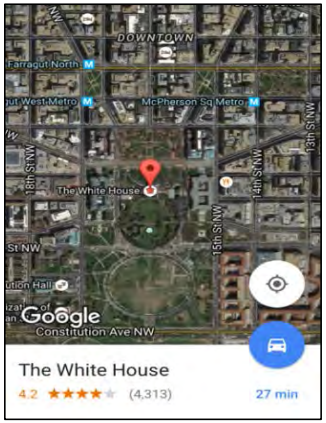


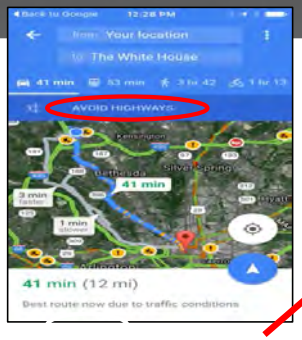
- Mapping human vasculature, one vascular cell type at a time
- Multi-dimensional (-omics)
- Multi-scale, from single cell to whole body
- Integrated in itself and with other tissue maps

A Google Map for the Human Vasculature?

Distance (Scale)





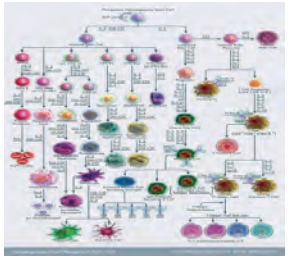


Human BODY

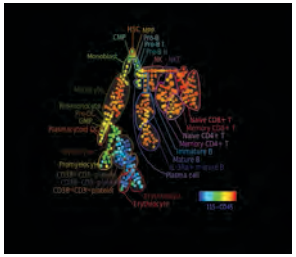
Understand Principles

Tissue

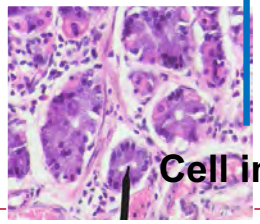
Understand Patterns



Neighborhood



Understand Relations



Cell in-situ

Amount of data (dimension)

NIH: Human BioMolecular Atlas Program "HuBMAP"

The vision: https://commonfund.nih.gov/hubmap

Catalyze development of a comprehensive atlas of cellular organization in human tissues to elucidate principles of organization-function by:

- **accelerating tool development** for comprehensive spatial tissue maps and integrating data types
- **building and generating tissue maps** from validated high-content, high-throughput imaging and omics assays
- **coordinating and collaborating** with other funding agencies, programs and the research community
- **rapidly making data findable, accessible, interoperable, and reusable (FAIR)** in standardized formats

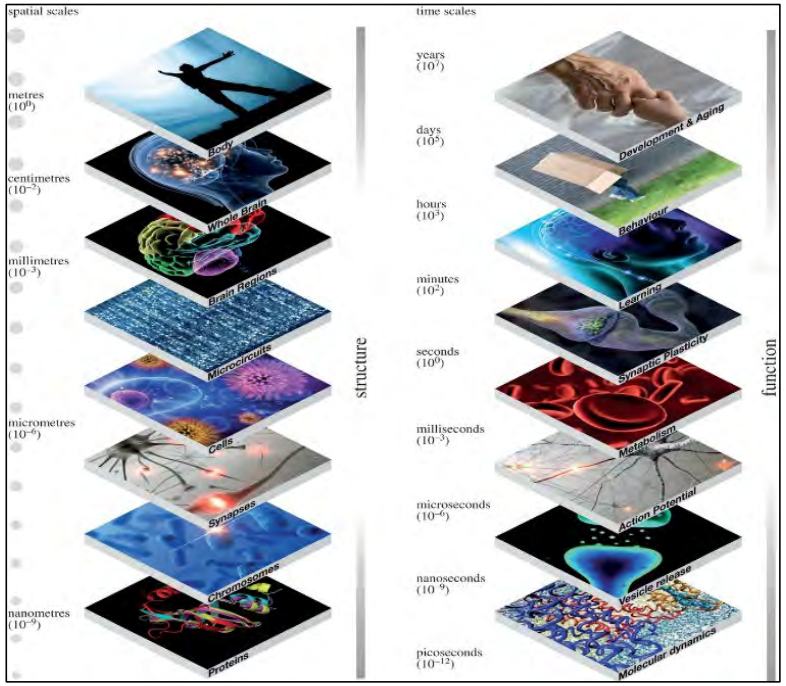
To begin funding in FY18!

NIH National Institutes of Health
Office of Strategic Coordination - The Common Fund

https://commonfund.nih.gov/

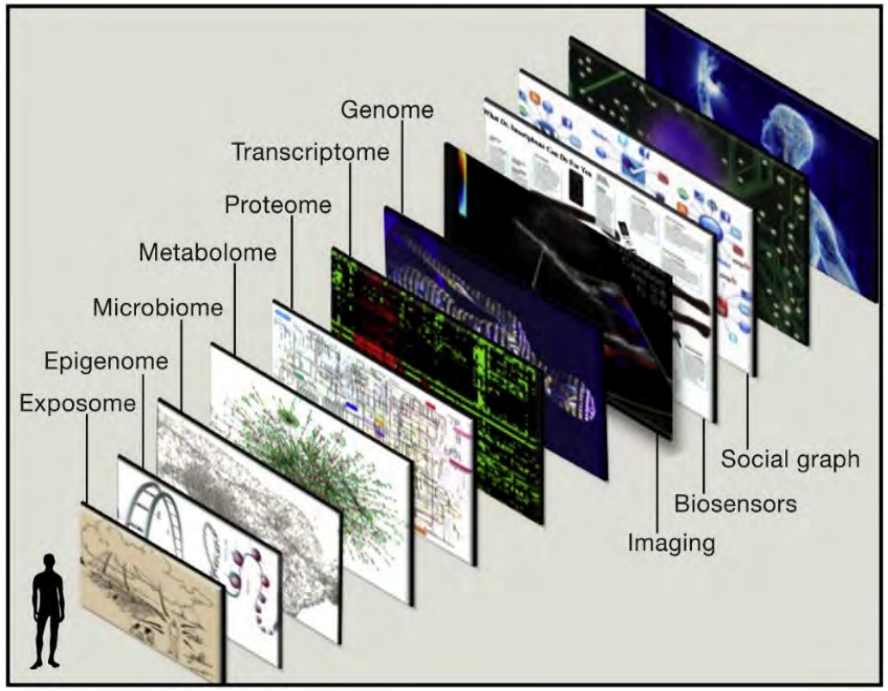
Vision for NIH HuBMAP

Multiscale



Frackowiak et al., Phil Trans R Soc B (2015)

Multimodal



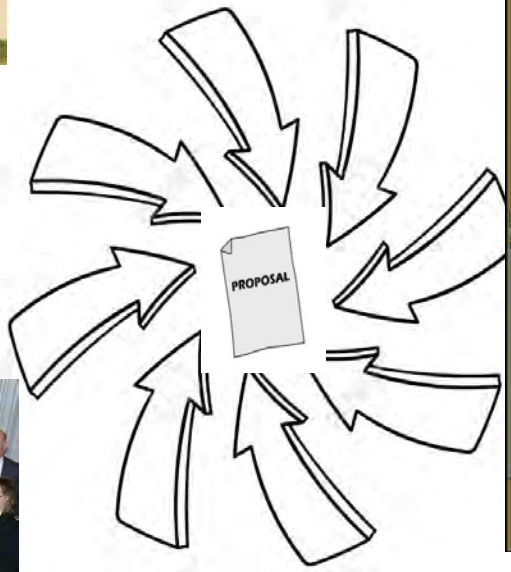
Topol, Cell (2014)

Reality check..

Identifying Key Areas in a Human BioMolecular Atlas (HuBMAP) WS, June 15, 2016

NIH RePORTER

PubMed.gov



NIH National Heart, Lung, and Blood Institute

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Roderic Pettigrew, Ph.D., M.D. (NIBIB)
Robert Star, M.D. (NIDDK)

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https://commonfund.nih.gov/HuBMAP/index

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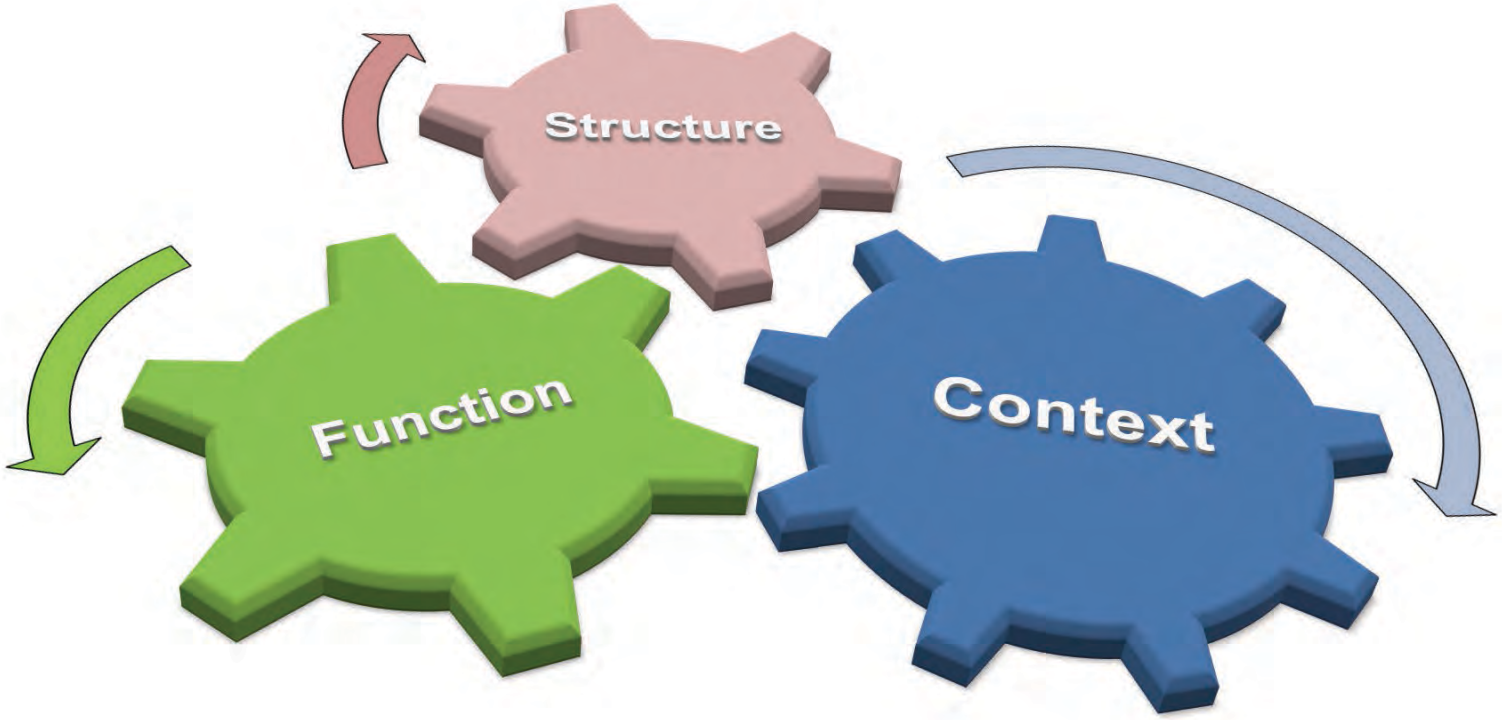
Yong Yao, Ph.D. (NIMH)

"*Lumping*"

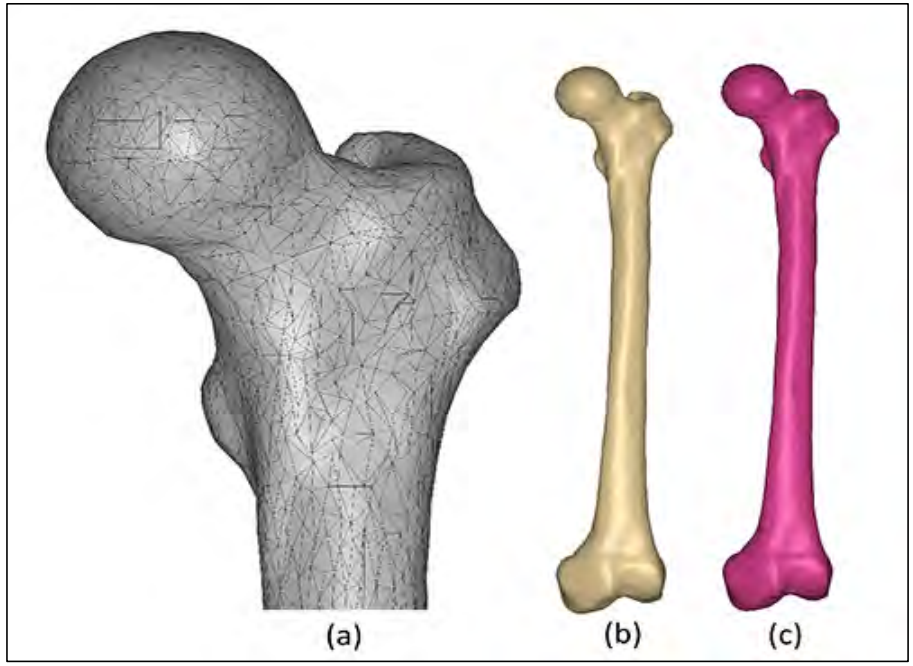
- **Assembling the puzzle pieces**
- **Integrating across scales**
  - **Individual cells > tissues> organs> human body**
  - **Key organizing principles?**
  - **Coordinates to use for the human body?**
  - **Filling in the blanks?**

Some Current/Emerging Approaches



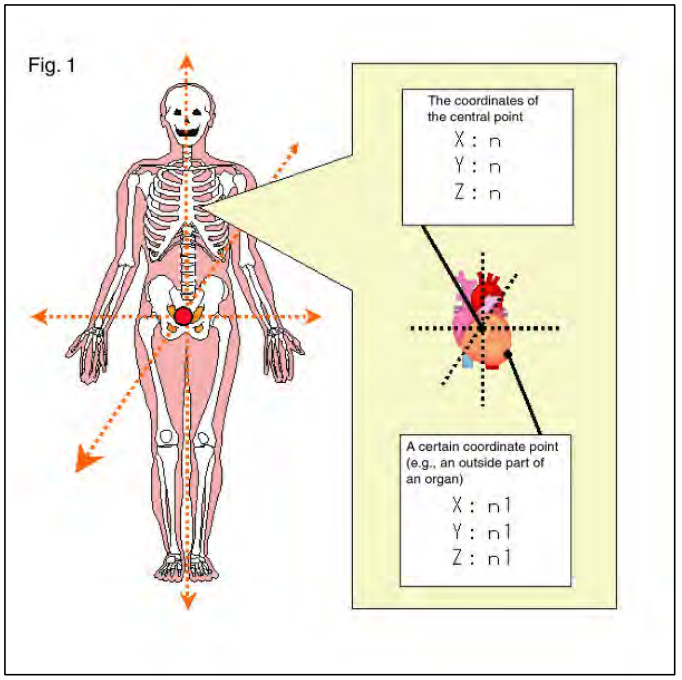
Coordinates For The Human Body Map?

Local level integration



Vector surface component of the left femur
http://www.geospatialhealth.net/index.php/gh/article/view/375/423

Central coordinates



http://www.natureinterface.com/e/ni04/P056-059/0104_058+01.jpg

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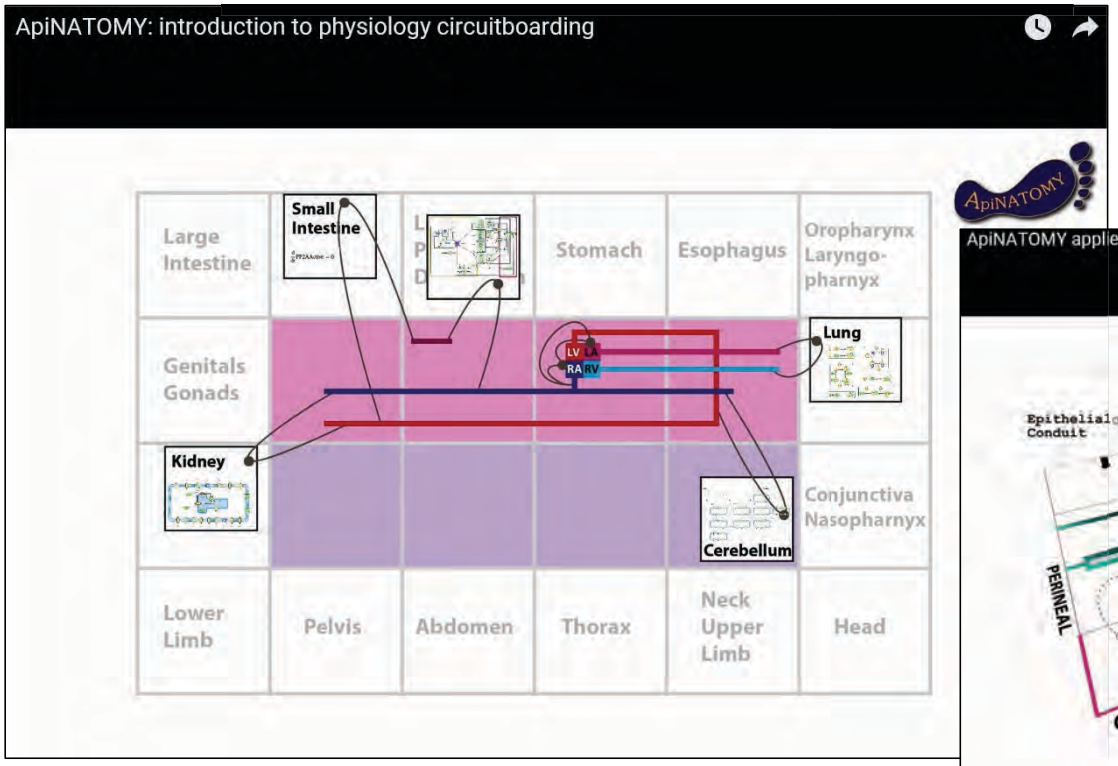
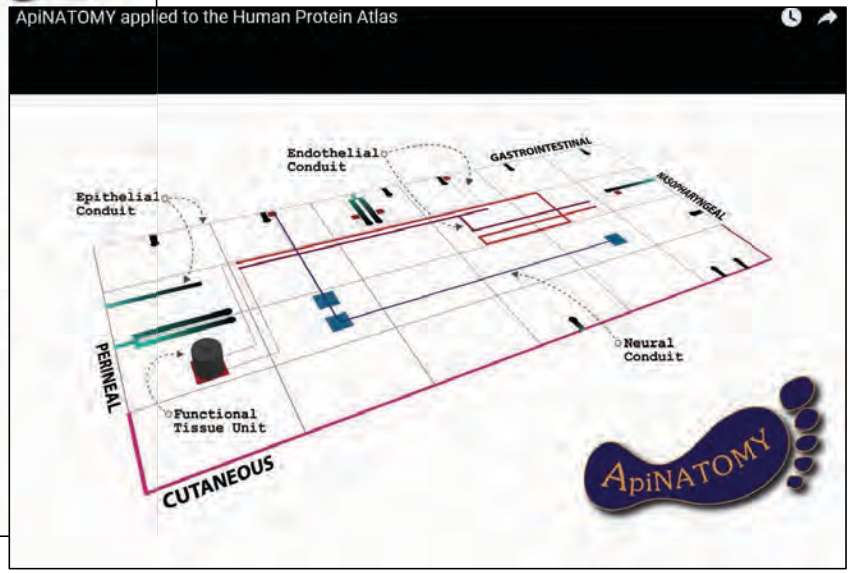
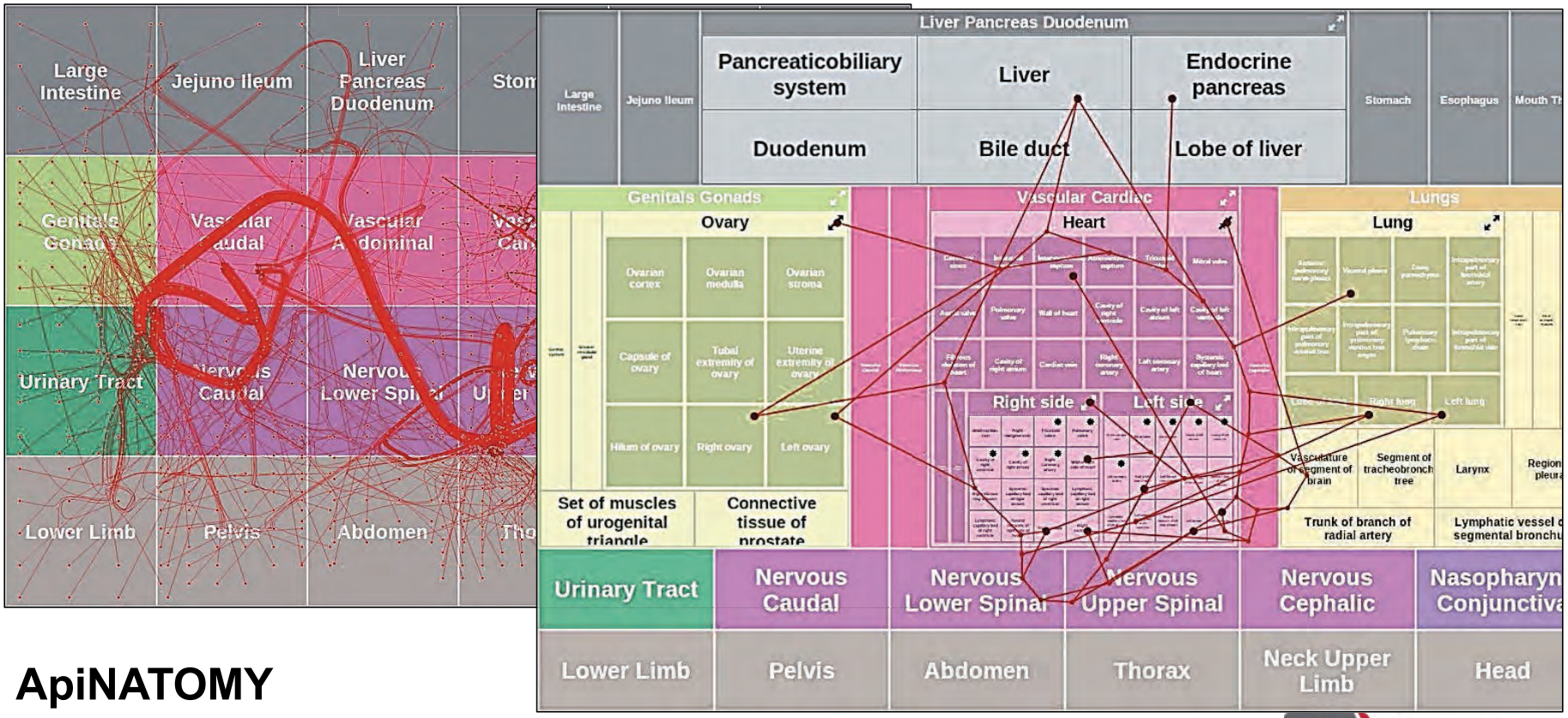
Functional Integration Of The Human Body: A Circuit Board Approach - “ApiNATOMY”



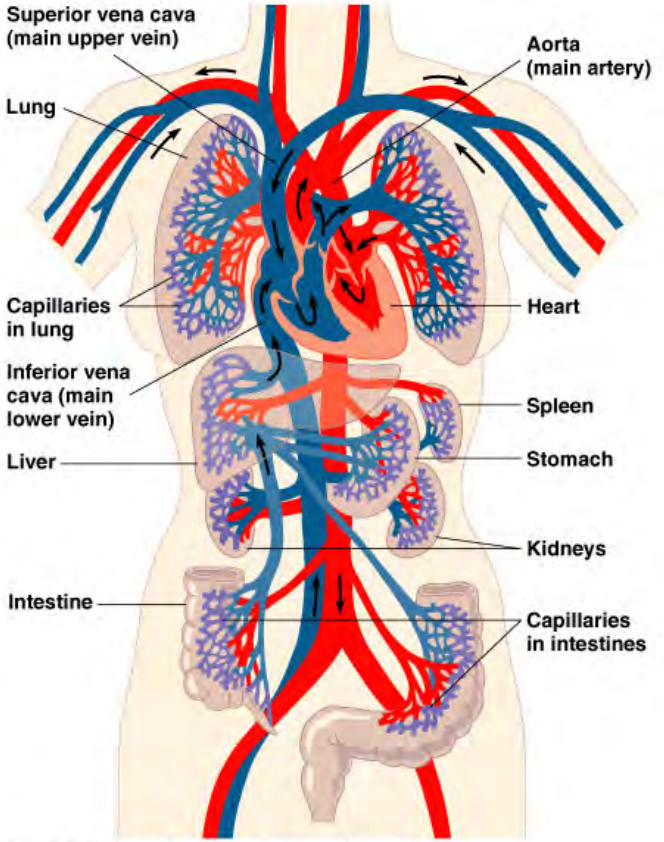


Vascular Conduits Are Used To "Wire" Together Different Organs

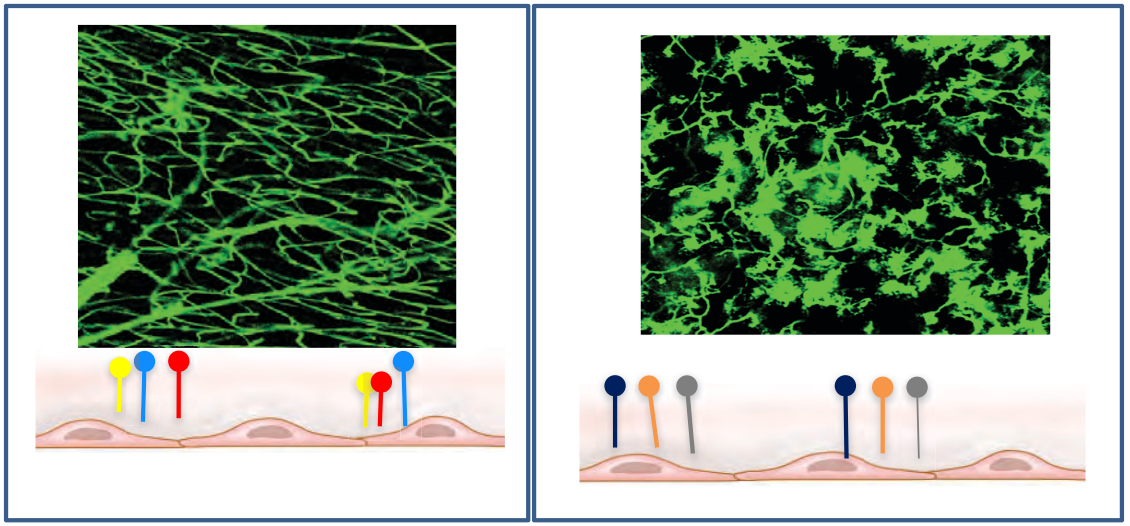


ApiNATOMY

Blood Vessels: Tissue Organization, Integration, and Navigation

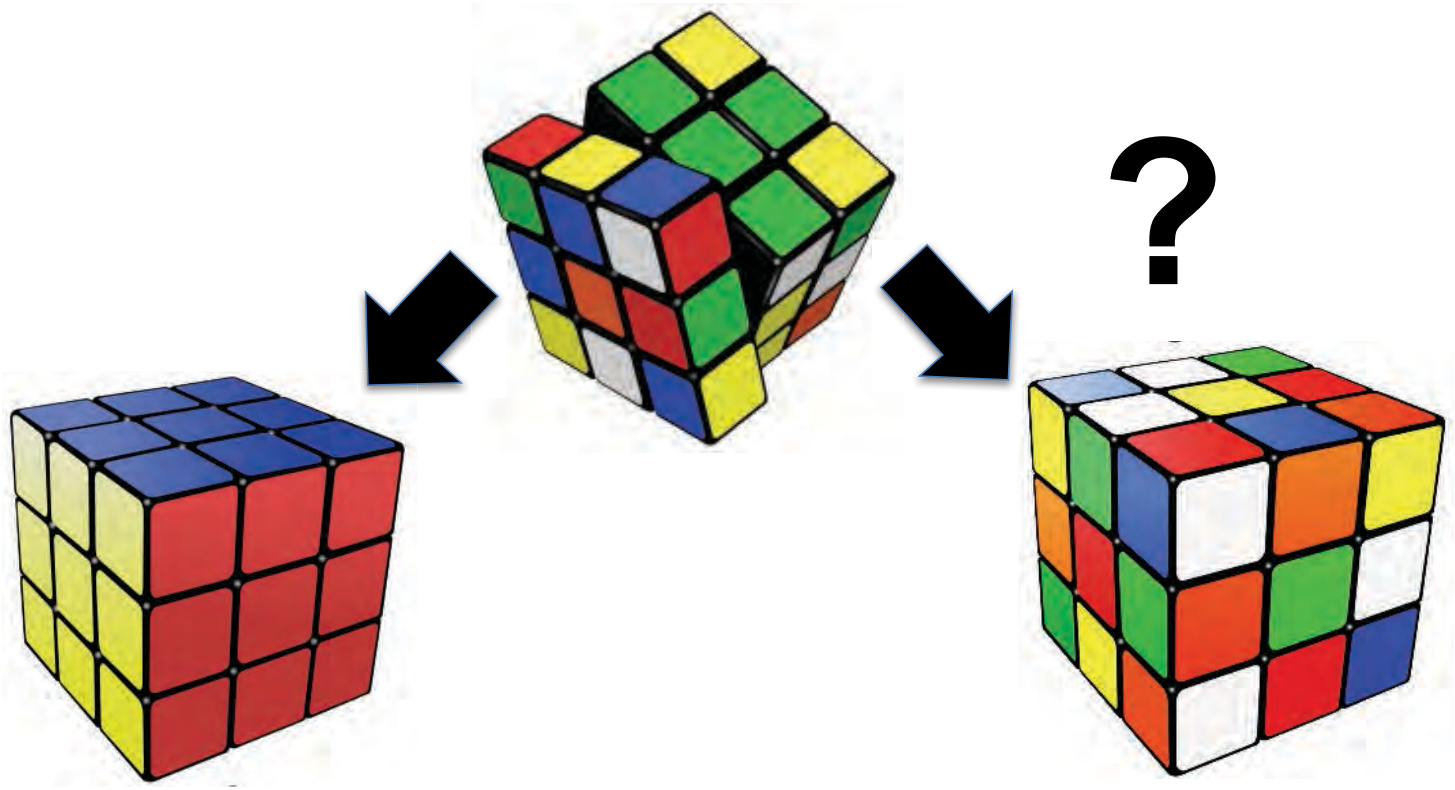


Organ-specific Vascular "Zip Codes" (Narasimhan 2002)



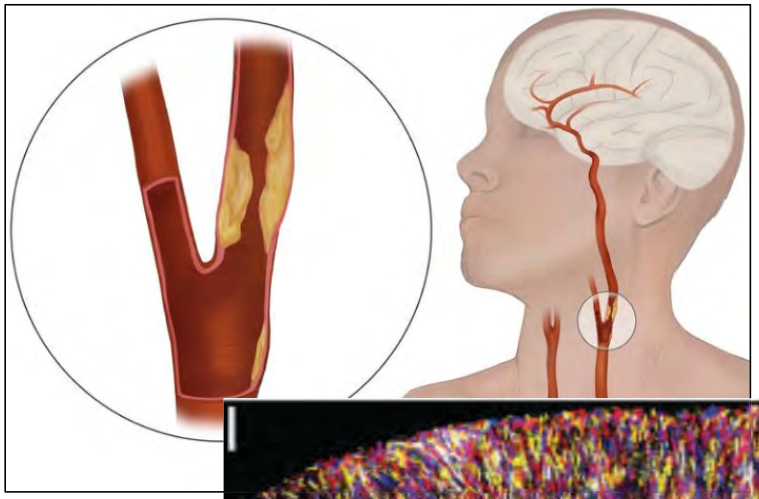
Brain: "02215" **Spleen: "10013"**

The Rubik's Cube Dilemma?

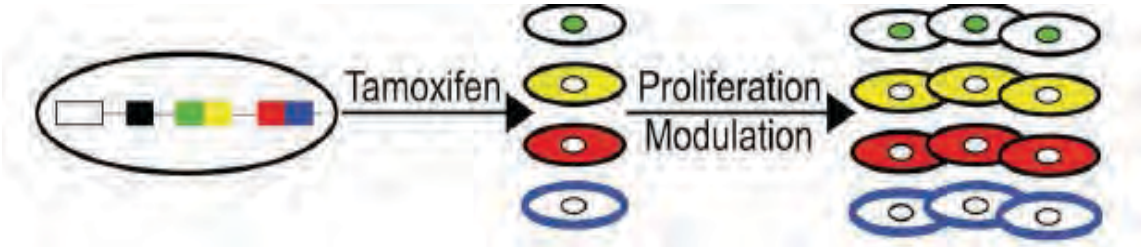


https://en.wikipedia.org/wiki/Rubik's_Cube

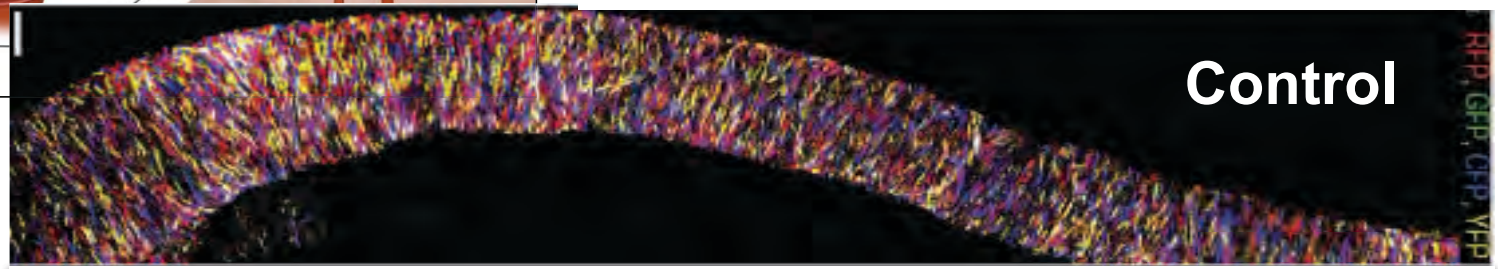
Carotid Artery: Diversity of Vascular Smooth Muscle Cells



Experimental Multi-color cell labeling in "Confetti mice"

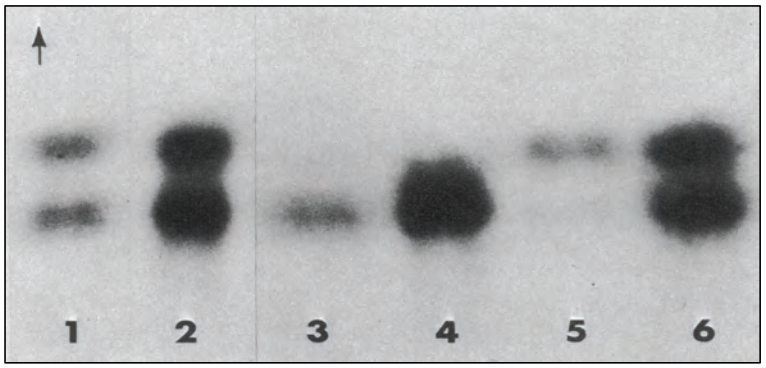


Chappell et al, *Circ Research* online, Sept 28, 2016



New Technologies Explain Previously Reported Vascular Smooth Muscle Cell (SMC) "Curiosities"

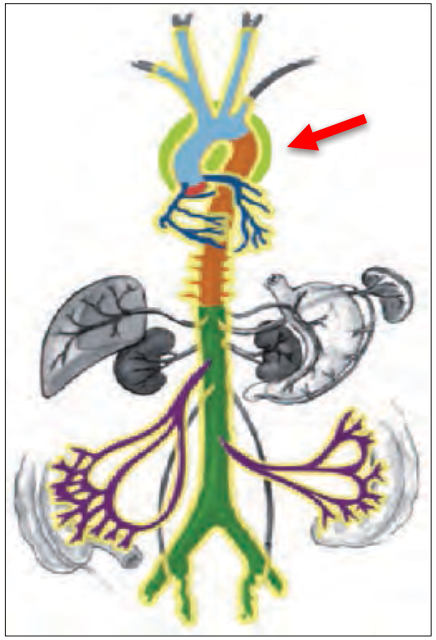
Benditt *PNAS* 1973: Discovery of SMC "Clones"



Normal artery

Atherosclerotic plaques

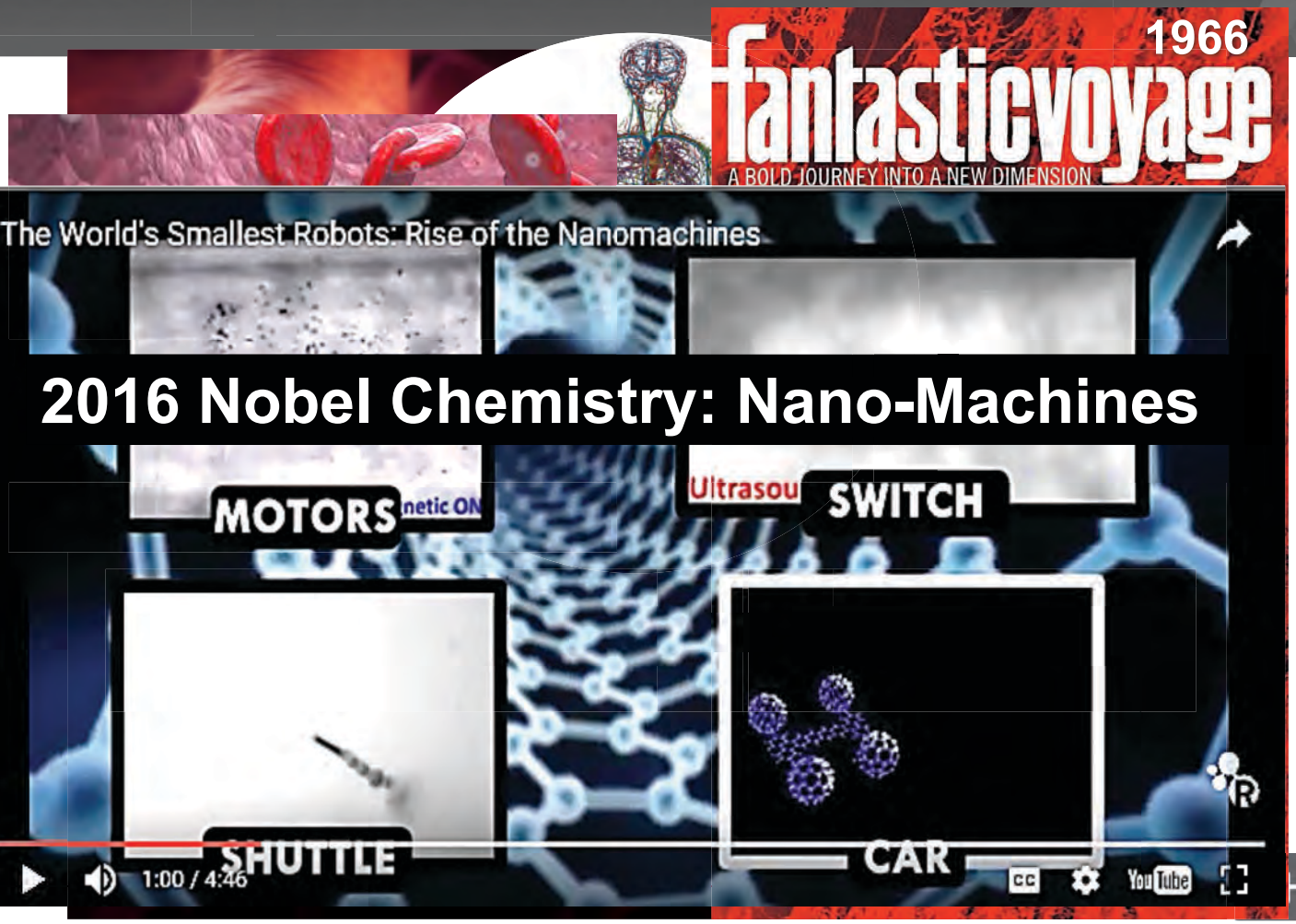
Majesky *ATVB* 2007: Different Developmental SMC Origins



Site of Aneurysms!

Understanding SMC diversity may hold the key to unsolved vascular mysteries

Vasculome-Specific Challenges and Opportunities?



National Heart, Lung, and Blood Institute

The “Vasculome” for HuBMAP Success

- Needed to complete any individual human tissue map
- May provide anatomically relevant coordinate system to organize any tissue architecture
- May serve as a prime example for body-wide integration of local heterogeneity of distributed systems
- May become the road map for the body “Google Map,” used to connect and navigate within and between tissues and organs

The Vasculome for HuBMAP…

Human

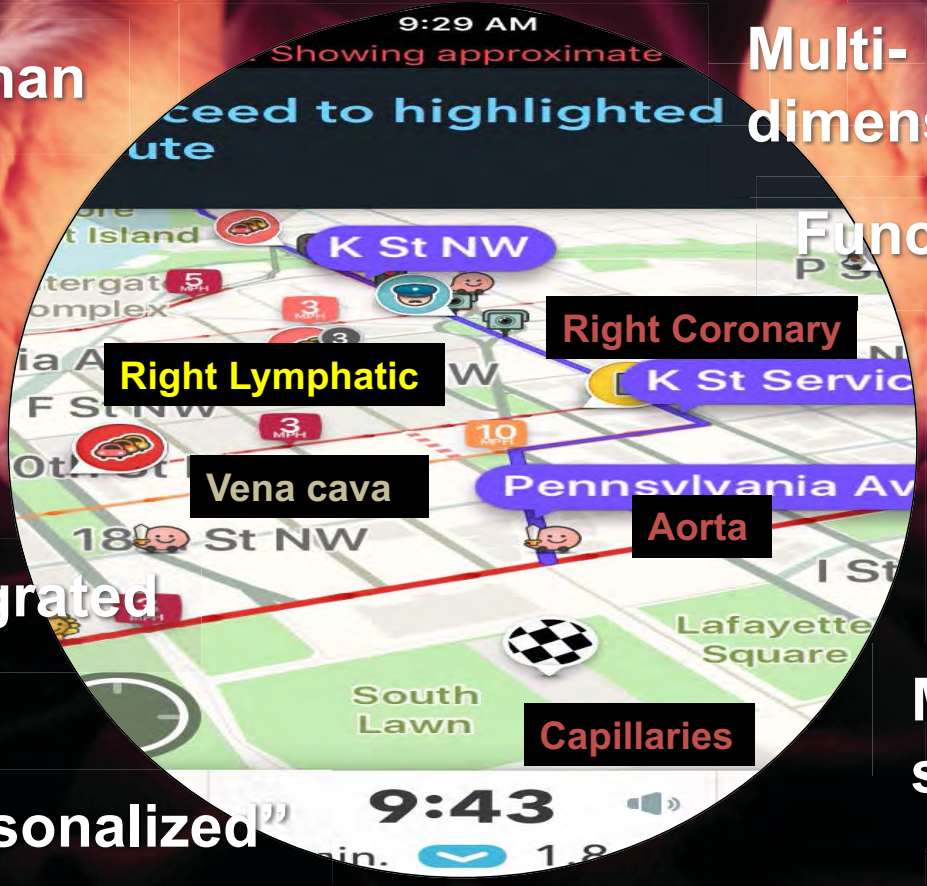
Multi-dimensional

Functional

Integrated

Multi-scale

"Personalized"



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Questions?
Suggestions?

The Human BioMolecular Atlas Program (HuBMAP)

https://commonfund.nih.gov/hubmap

NHLBI Funding Opportunities And Operating Guidelines & Strategic Visioning

NHLBI webpage: www.nhlbi.nih.gov

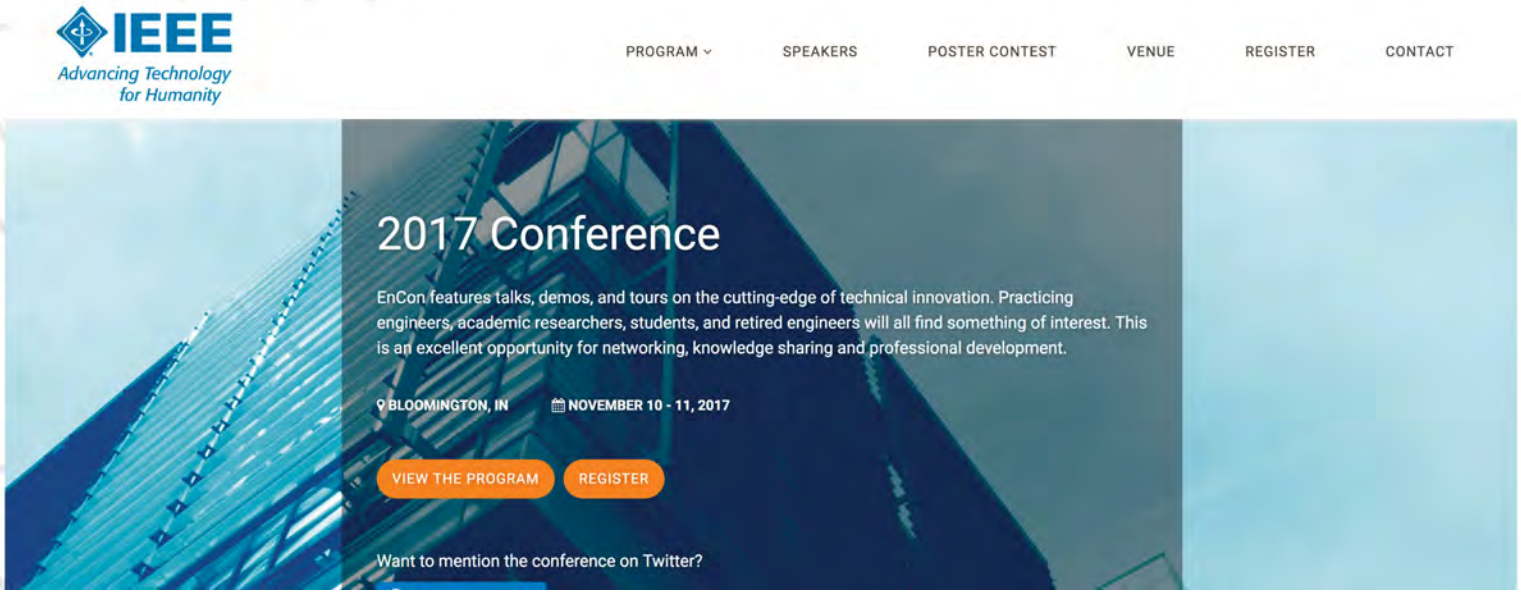
Research Portfolio Online Reporting Tools (Re-PORTER)

http://projectreporter.nih.gov/reporter.cfm

When in doubt…. Google us!

NIH National Heart, Lung, and Blood Institute

Welcome to
IEEE EnCON 2017!



Backup slides

HuBMAP Consortium Expectations

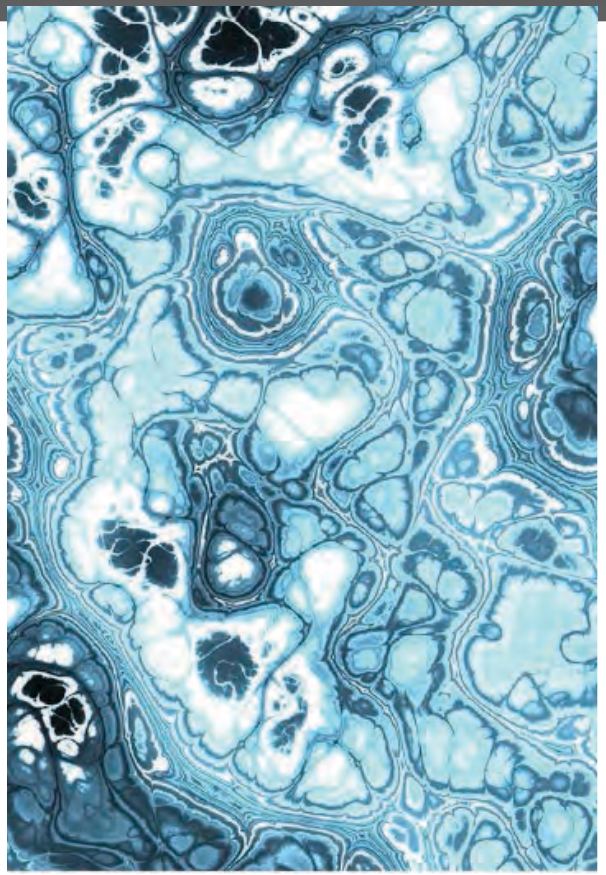
- **Membership: all successful applicants**
- **Purpose: enable groups to effectively collaborate with each other to maximize the chances of overall success of the program**
- **Expectations:**
  - **complete own research goals**
  - **work collaboratively for development of SOPs, data and metadata standards, metrics for data generation**
  - **participate in cross-site studies**
  - **engage in cross-training**
  - **guide development of data analysis and visualization tools that can be used by the broader scientific community.**
  - **attend an HuBMAP Kickoff meeting, as well as annual investigator meetings and regular teleconferences with Network members and NIH Staff for the duration of the funding cycle.**

Transformative Technology Development

Purpose: to solicit transformative technologies that will significantly expand throughput, multiplexing and discrimination of biomolecules in human tissues for comprehensive mapping of individual cells and their context in human tissues

Phases: The initial two year UH2 phase will support development and demonstration of feasibility of these emerging technologies for human tissue mapping. The subsequent UH3 phase is to support initial validation in human tissues, optimization and scale-up, and generation of production level data.

Tissue Mapping Centers



Purpose: **to solicit transformative technologies that will significantly expand throughput, multiplexing and discrimination of biomolecules in human tissues for comprehensive mapping of individual cells and their context in human tissues**

Tissue Mapping Center Structure:

- **Coordination Core: The Coordination Core will be responsible general administrative duties and for coordinating**
  - **1 core, required; 6 pages; plus 6 pages for Overall**
- **Organ Specific Projects: The Organ-Specific Projects will be responsible for generating high quality tissues maps**
  - **Can propose up to 4 projects, at least 1 required; 6 pages to describe each**
- **Data Analysis Core: The Data Analysis Core will be responsible for data annotation, curation, and analysis.**
  - **1 core, required; 6 pages**

The "HIVE"
HuBMAP Integration Visualization and Engagement

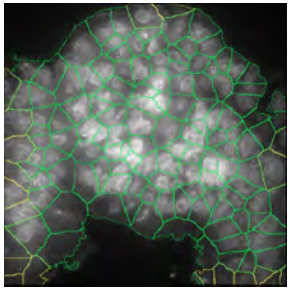
The HIVE Structure:

- Coordination Component –responsible for coordinat… collaboration with the other funded components of the HuBMAP Consortium and the wider research community;
- Infrastructure Component –responsible for building and optimizing the data ingestion and archiving platform and support the internal and external facing IT tools for the Consortium;
- Mapping Component - responsible for developing mapping pipelines and frameworks for analyzing data in the archive;
- Tools Component - responsible for developing search, analysis and visualization tools for HuBMAP data or enable adoption and usage of relevant ones from the community

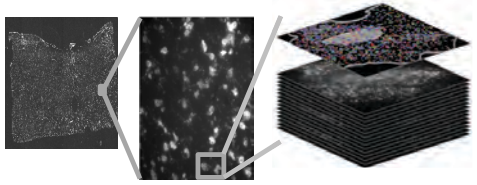
Why HuBMAP?

	HuBMAP	GTEx	GUDMAP	LungMAP	BRAIN	SGMAP	HPA
Primary Species	**Human**	Human	Mouse moving to Human	Human / Mouse	Mouse	Mouse	Human
Tissues	**Phase 1: ~10 Phase 2: ~40**	~53	Kidney / Prostate	Lung	Brain	Salivary glands	~44
Focus	**Inter-individual variability**	eQTLs	Early development	Early development	Cell census	Early development	Proteome
Tech	**FISH, RNA-Seq, IMS**	RNA-Seq	FISH, RNA-Seq	FISH, RNA-Seq, MS, CT	RNA-Seq	Microarray / RNA-Seq	60,000+ Antibody
Single cell focus?	**Yes**	No	Yes	Yes	Yes	No	Moving towards
Spatial?	**Yes**	No	Yes	Yes	No	No	Yes
Across Body?	**Yes**	**Yes**	**No**	**No**	**No**	**No**	**Yes**

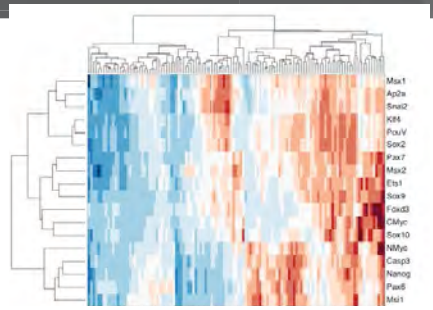
Emerging In-situ Technologies



FISH Imaging

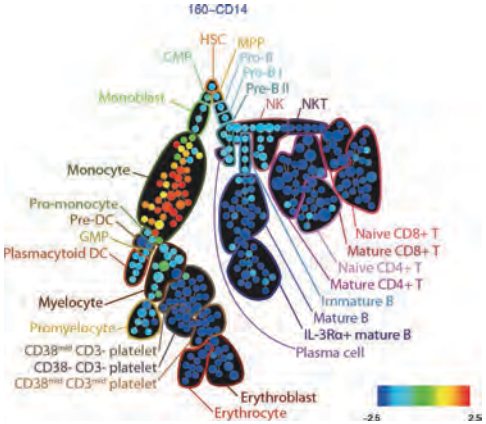


MERFISH – Imaging 1000+ genes in tissue (Zhuang Lab, 2016);



SeqFISH– Sequential barcoding, 100+ parameters, single molecule sensitivity (Cai Lab)

Mass Spec
&
CyTOF



CyTOF – 30+ parameters, high throughput, <5 Ab sensitivity (Nolan Lab)

The Human Cell Taxonomy Project ('Periodic Table' of Cells)

MIBI-TOF – up to 50 parameter imaging, down to 20nm (Angelo Lab, 2016)

	smFISH	Padlock probes and RCA	Branched FISH	LCM	Microtomy sequencing	TIVA	ISS	FISSEQ	Imagi… mass … metr…
Sample	Fixed cells and tissues; purified RNA	Fixed cells and tissues; purified DNA or RNA	Fixed cells and tissues; possibly purified DNA or RNA	Fixed tissues	Fixed and fresh tissues	Live cells	Fixed cells and tissues	Fixed c…lls and …iss…	…issues
Target	RNA	DNA; RNA	RNA	RNA; DNA; proteins	RNA; possibly DNA and proteins	RNA	RNA	NA	Proteins
Type	Targeted	Targeted	Targeted	Targeted or non-targeted	Non-targeted	Non-targeted	…rge…	Non-targeted	Targeted
Variable measured	Abundance; SNVs; fusion transcripts; splice variants; subcellular localization	Abundance; SNVs; fusion transcripts; splice variants; subcellular localization	Abundance; subcellular localization	Abundance; possibly SNVs, fusion transcripts and splice variants	Abundance; possibly SNVs, fusion transcript… and splice vari…	Ab…da…e; p…sib… S…Vs, …s… …ar…ripts …nd …plice variants	Abundance; possibly SNVs, fusion transcripts and splice variants	Abundance; possibly SNVs, fusion transcripts and splice variants	Abundance; protein modifications
Single-cell?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Spatial resolution	Subcellular	Subcellular	Subcellular (except the nucleus)	Anatomi… or cellul…	…natomical	Cellular	Cellular	Cellular	Subcellular
Morphology assessment	Yes	Yes	Yes	…s	No	Yes	Yes	Yes	Yes
Throughput (number of cells)	Low to medium	Low to medium	Low to me…	M…dium	High	Low	Low to medium	Low to medium	Very high
Throughput (number of genes or proteins)	Low to medium	Low to medium	…e…	High	High	High	Low	High	Low
Estimated efficiency	~90%	~3…	NA	NA	~5–10%	NA	NA	NA	NA
Readout	Micro…copy; flow …	M…roscopy; flow cytometry	Microscopy; flow cytometry	Microarray; RNA-seq; MS	RNA-seq; possibly MS	RNA-seq	Microscopy	Microscopy	MS
Techni… difficulty	…sy	Easy	Easy	Moderately easy	Moderately easy	Moderately difficult	Difficult	Difficult	Difficult
Refs	23,53–58, 60–63	64–68	70,71	72,74,76–78	79–81	82	83	85	87,88

FISH, fluorescence *in situ* hybridization; FISSEQ, fluorescent *in situ* RNA sequencing; ISS, *in situ* sequencing; LCM, laser capture microdissection; MS, mass spectrometry; NA, not available; RCA, rolling circle amplification; RNA-seq, RNA sequencing; smFISH, single-molecule RNA fluorescence *in situ* hybridization; SNV, single-nucleotide variant; TIVA, transcriptome *in vivo* analysis.

Crosetto, Nicola, Magda Bienko, and Alexander van Oudenaarden. "Spatially resolved transcriptomics and beyond." *Nature Reviews Genetics* 16.1 (2015): 57-66

Assays	Cell capture strategies	cDNA amplification strategies	Target RNAs	Poly(A) minus RNA detection	Number of cells	UMI
scRNA-seq	Mouth pipette or FACS	Polyadenylation followed by PCR	Full-length mRNAs	No	1–100	No
Quartz-seq	Mouth pipette or FACS	Polyadenylation followed by PCR	Full-length mRNAs	No	1–100	No
Smart-seq/Smart-seq2	Mouth pipette or FACS	Template-switch followed by PCR	Full-length mRNAs	No	1–100	No
MALBAC-RNA	Mouth pipette or FACS	MALBAC	Full-length mRNAs	No	1–100	No
PMA	Mouth pipette or FACS	Rolling circle amplification	Full-length mRNAs	No	1–100	No
SMA	Mouth pipette or FACS	Semi-random priming followed by PCR	Full-length mRNAs	No	1–100	No
SUPeR-seq	Mouth pipette or FACS	Random priming followed by PCR	Full-length mRNAs	Yes	1–100	No
Fluidigm C1	Microfluidic system	Template-switch followed by PCR	Full-length mRNAs	No	100–1000	No
Microfluidic scRNA-seq	Microfluidic system	Polyadenylation followed by PCR	Full-length mRNAs	No	100–1000	No
STRT-seq	Mouth pipette or FACS	Template-switch followed by PCR	5′ end of mRNAs	No	10–100	Yes
CEL-seq	Mouth pipette or FACS	In vitro transcription and linear RNA	3′ end of mRNAs	No	10–100	Yes

Wen, Lu, and Fuchou Tang. "Single cell sequencing in stem cell biology." *Genome Biology* 17.1 (2016)

National Heart, Lung, and Blood Institute

Assays	Cell capture strategies	cDNA amplification strategies	Target RNAs	Poly(A) minus RNA detection	Number of cells	UMI
MARS-seq	Robotics and automation	CEL-seq	3′ end of mRNAs	No	100–1000	Yes
CytoSeq	Bead-based	CEL-seq	3′ end of mRNAs	No	>1000	Yes
Drop-seq	Droplet- and bead-based	Template-switch followed by PCR	3′ end of mRNAs	No	>1000	Yes
inDrop	Droplet- and bead-based	CEL-seq	3′ end of mRNAs	No	>1000	Yes
TIVA	In vivo mRNA capture based on photo-activation	In vitro transcription	Full-length mRNAs	No	10–100	No
FRISCR	FACS or fixed cells	SMART-seq2	Full-length mRNAs	No	10–100	No
Patch-seq	Aspiration through patch-clamp pipette	STRT-seq/SMART-seq2	5′ end of mRNAs or full-length mRNAs	No	10–100	Yes/no
FISSEQ	In situ RNA sequencing	Rolling circle amplification	Full-length mRNAs	No	100–1000	No

Wen, Lu, and Fuchou Tang. "Single-cell sequencing in stem cell biology."*Genome Biology* 17.1 (2016)