21st Century Neuroscience:
Challenges and Opportunities in Neuroscience Research for Real-Time Integration of Emerging Tools, Technologies, and Techniques

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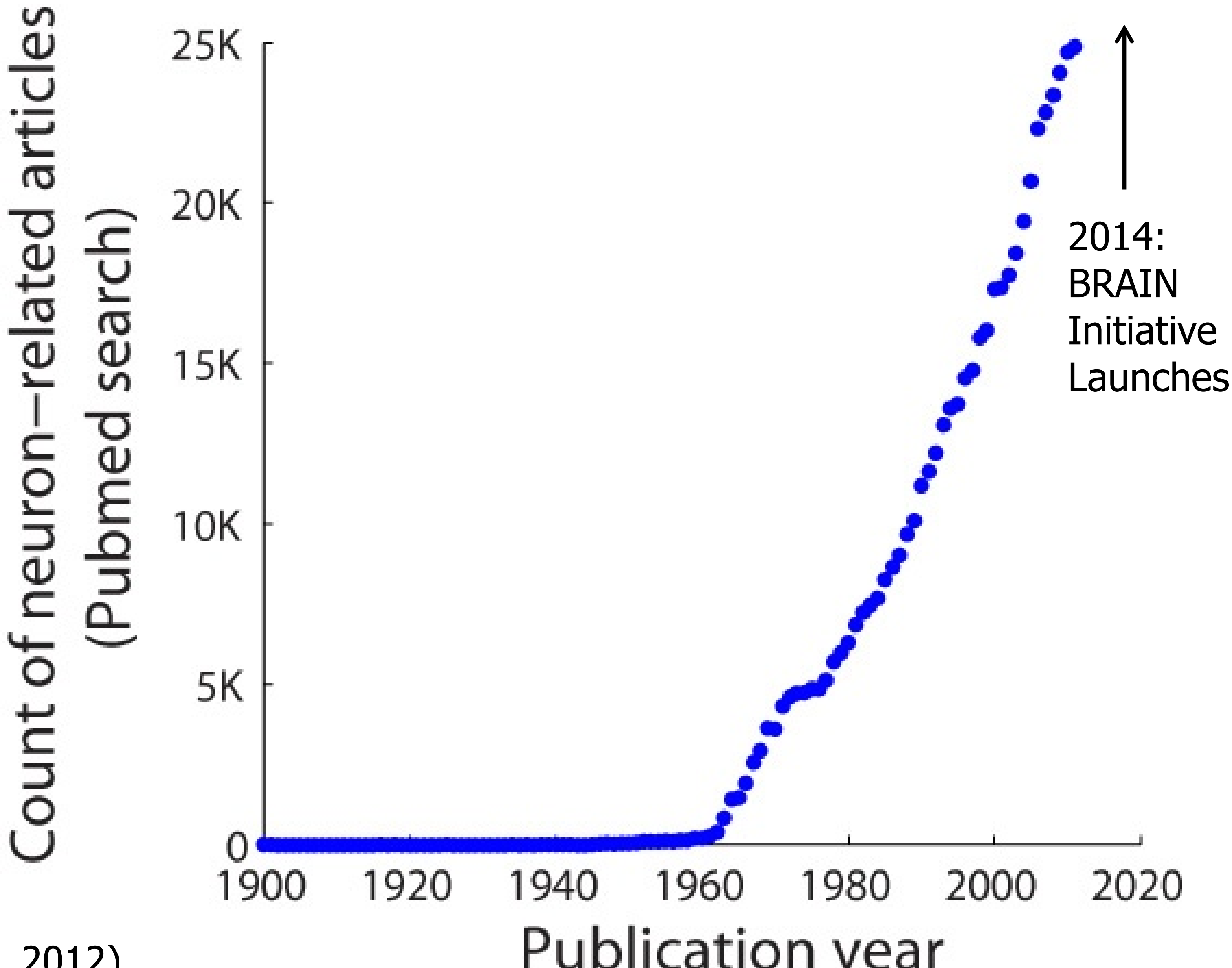
29 October 2012

DARPA

Outline

- Growth of neuroscience (and neurotechnology) in last century
- Where are we going?
  - Single-cells to neural networks; systems neuroscience
  - Challenges for the field, particularly trainees
- (My) DARPA perspective

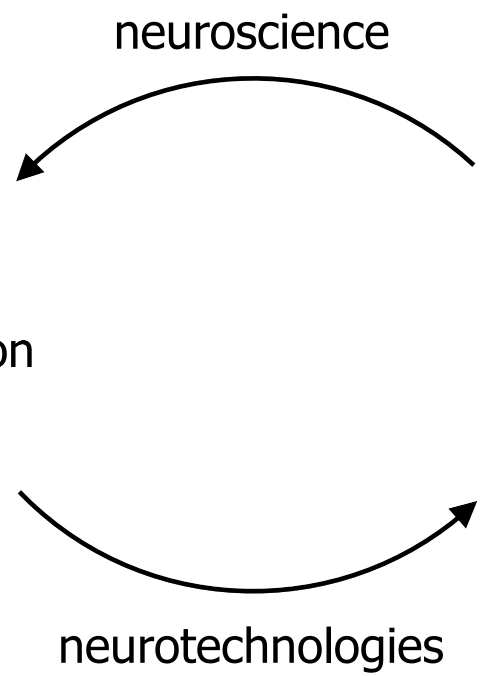
Neuroscience is Growing (and diversifying) Rapidly



(Tripathy, 2012)

Neuroscience and neurotechnologies have co-evolved in a synergistic fashion

Discoveries
- Anatomy
- Physiology
- Development/Regeneration
- Plasticity
- Network dynamics



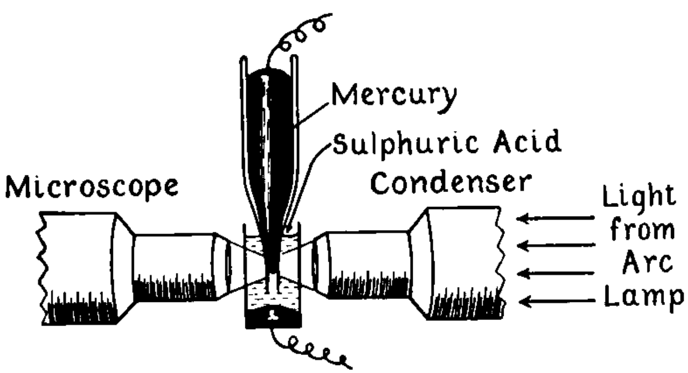
Technologies
- Micro-electrodes/electronics
- Imaging: structural and functional
- Analytics
- Immunohistochemistry
- …
- Cochlear Implants
- Brain Machine Interfaces
- Deep Brain Stimulators

Understanding function of single neurons (sensory coding)

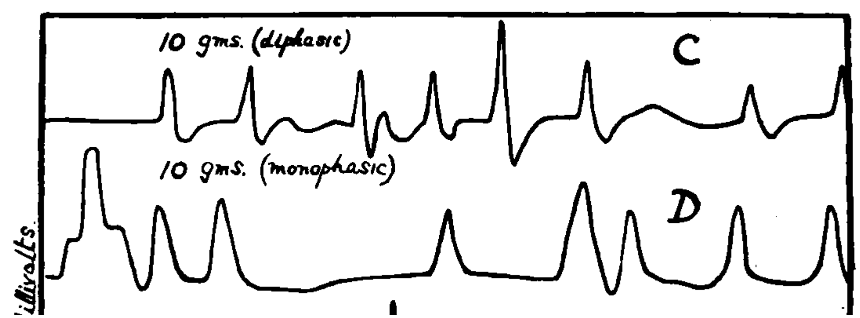
- 1928: Edgar Adrian – ‘The basis of sensation’
  - reported first ‘spike’ recordings using capillary electrometer and cathode ray tube
  - Nobel Prize in 1932 (with Charles Sherrington)

44 THE BASIS OF SENSATION

conical part of the tube must cause a reduction in the surface of separation between the mercury and the acid, and this is resisted by the forces of surface tension. Normally, therefore, the lower surface of the mercury comes to rest at a point in the tube where a balance



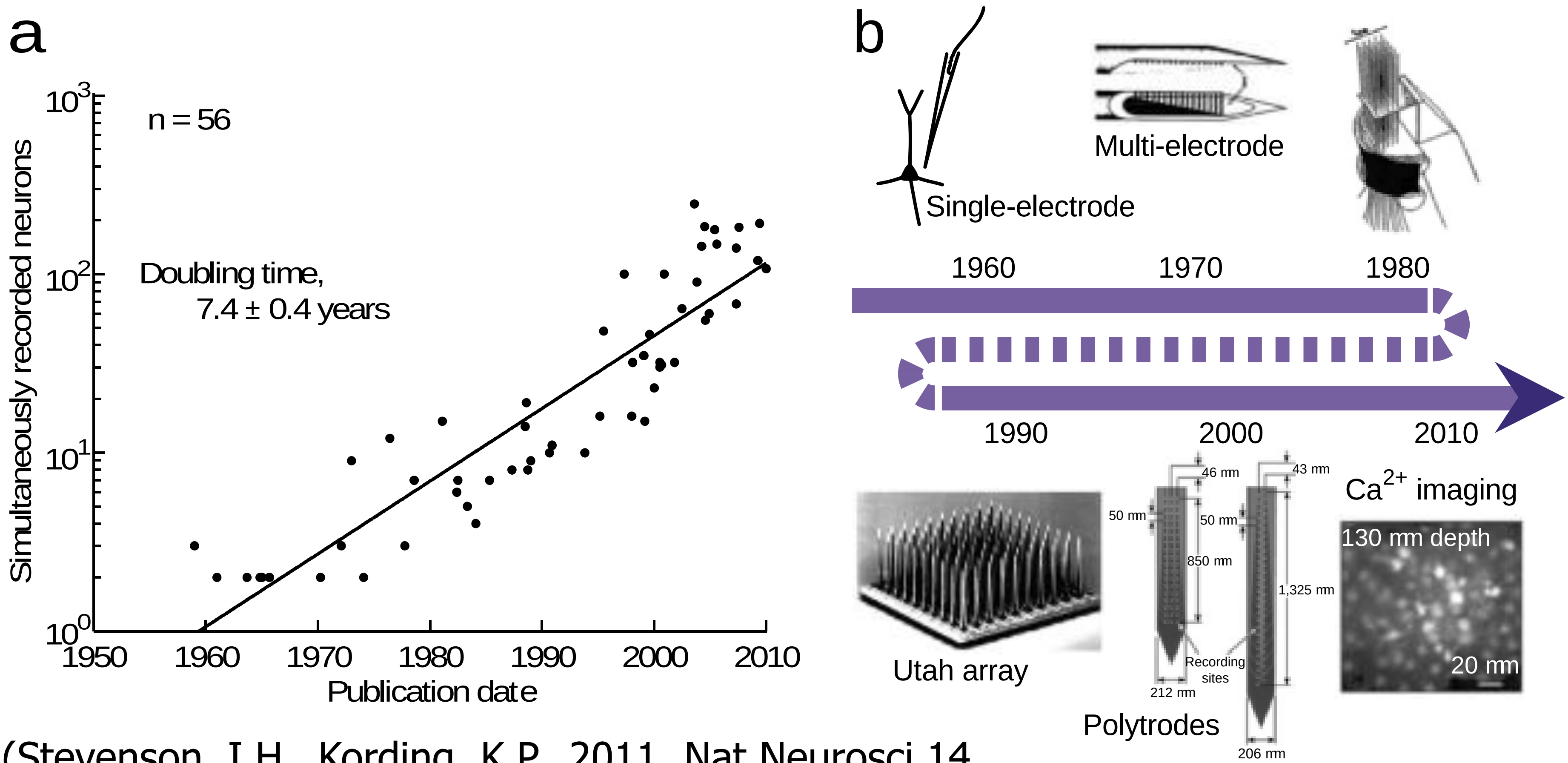
of the stimulus, but the size of each impulse does not vary; in other words there is the same “all-or-nothing” relation in the sensory fibre as in the motor. In the preliminary experiments other preparations were used as well, and discharges of the same kind were found in the sensory nerves from



(Adrian, E.D., 1928)

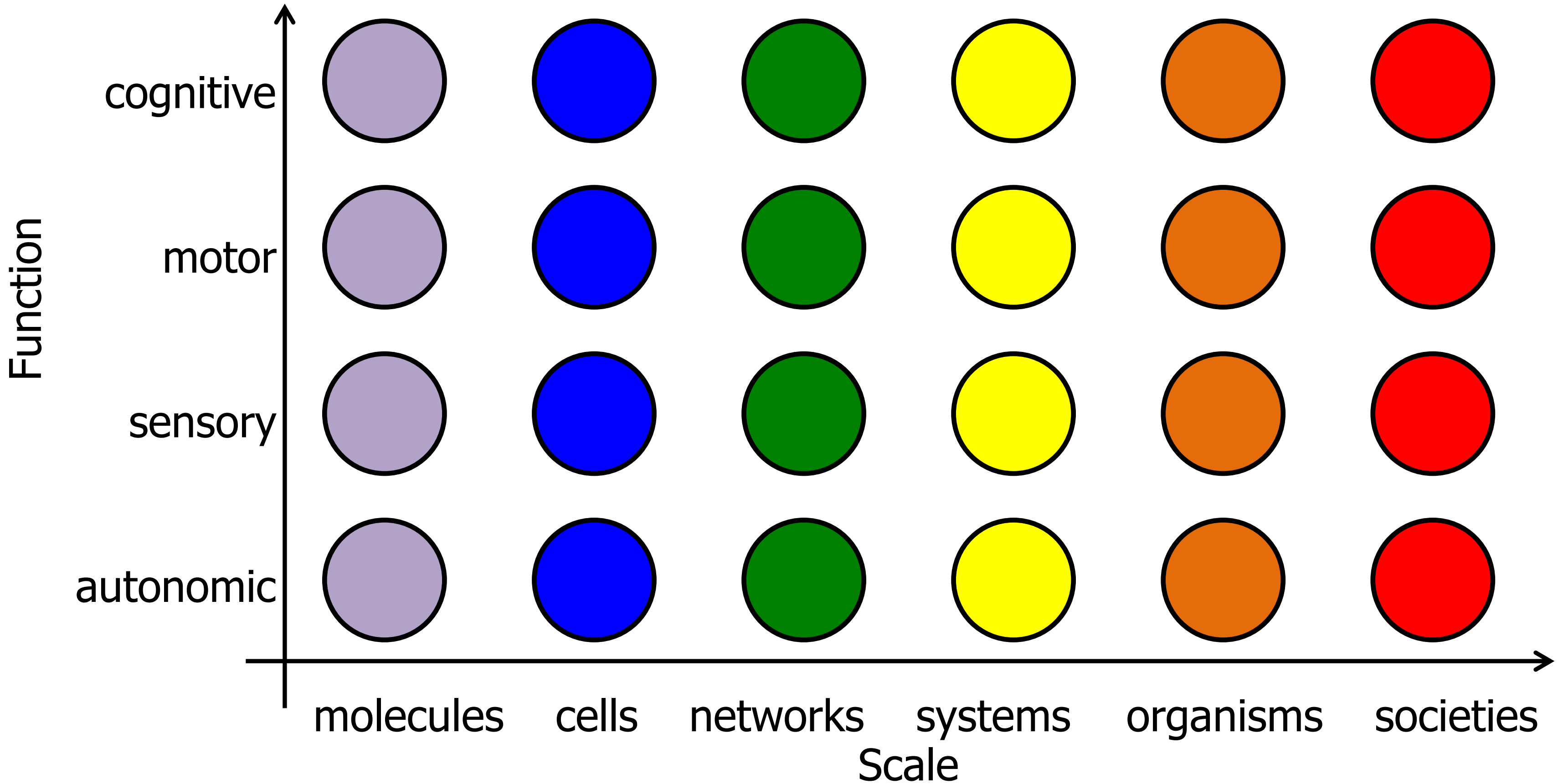
Evolution of microelectrode recording techniques

- Microelectrode and array recordings have evolved steadily since 1950's



(Stevenson, I.H., Kording, K.P., 2011. Nat Neurosci 14, 139.)

Rapid Growth and Diversification of Neuroscience has created many tall silos



"Inter-disciplinary" research and training WITHIN neuroscience is already challenging

Moving forward: Technical and Scientific Challenges

- Tools for measuring and probing neural signals at high precision (single cells) and full scale (whole networks)
  - Nanotechnologies
  - Optical and acoustic imaging tools
  - Collection and integration of data across large scales in time and space
- Data management, analytics, and dissemination
  - Standards
  - Sharing
- Rigorous, hypothesis-driven science (traditionally reductionistic) vs. Integrative Neuroscience
  - Model selection
  - Rational, theoretical, impactful
  - Inter-disciplinary

How do we create training opportunities and environments that facilitate development of 21st century neuroscientists?

DARPA: How we work

- DARPA ignores barriers that emerge as scientific disciplines mature – we find process and inspiration to solve problems in one space by mining other fields (encourage/force integration).
- We envision the world 'as it should be' … and then develop programs aimed at overcoming critical barriers to realizing that vision

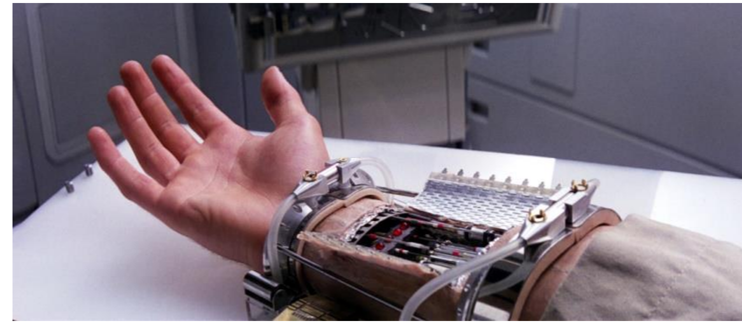
Example: Revolutionizing Prosthetics Program

- Problem: Standard-of-care in prosthetics offers limited capabilities to restore sensory and motor functions

- The solution often starts with the question: *Wouldn't it be great if …?*

Making science fiction a reality (setting and achieving audacious goals)

Transformative Capabilities



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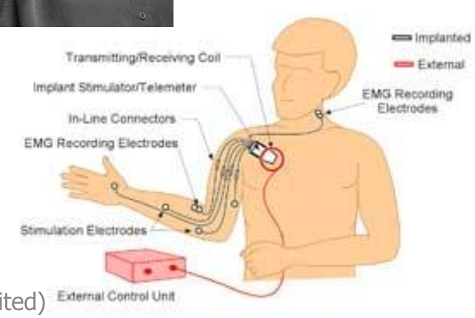
- 2 Key Requirements (DARPA-hard problems) required to create transformative capabilities for prosthetic limbs
  - Mechatronics: prosthetic limb with 22 degrees-of-freedom (state of the art is ~3)
  - Neurotechnology: An intuitive interface with the nervous system to communicate motor intention and sensory feedback
    - Brain-machine-interface science and technology

DEKA ‘Luke-Arm’ completed in 4 years

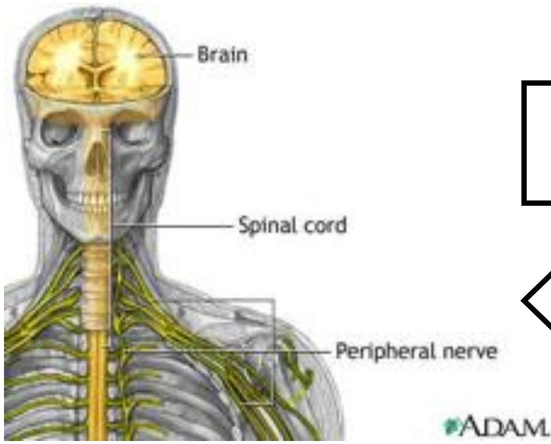
Brain-machine-interfaces for Prosthetics

Multi-channel neural recording → Signal processing and feature extraction → Decoding movement or intention → Control signal for an external device



Feedback

Advanced neurotechnologies require inter-disciplinary investments; creates unique training opportunities



Measure/decode neural signals →

← Stimulate sensory neurons

- Solutions require tight integration of neuroscience and technology to communicate information <u>in real-time</u>
- Neuroscience
  - Anatomy and physiology of sensory and motor structures
  - Computational models of neural function in coding information
  - Learning and plasticity
  - Psychology – perceptual functions and embodiment
- Technology
  - Microelectrodes and other physical interfaces with neural tissue
  - Electronics and systems that incorporate knowledge of neural communication
  - Standardized and automated processes – e.g. neural signal processing – traditionally performed by 'experts' (trained students)

Tight integration of neuroscience and technology can create amazing capabilities

Summary: Focus on creating capabilities

- Future of neuroscience will continue to depend on continued co-evolution of science and technology
- Focusing on creating 'capabilities' will ensure that knowledge is integrated into technology, and that technology will continue to facilitate progress in science
- 'Practical' applications provide a framework for integrating knowledge and technology
  - Automate, integrate and systematize
    - Trainees often spend too much time learning techniques and developing skills
    - Common workflows need to be automated to enable scientists to do science (question, reason, speculate, test)
  - Standardize
    - Terminology
    - Knowledge representation
    - Data management
  - Entice and evangelize – grow and diversify our 'critical mass' by recruiting people to join the cause; show them the potential to have impact by creating transformative capabilities

Capability driven co-evolution of neuroscience and neurotechnology

neuroscience

Discoveries
- Anatomy
- Physiology
- Development/Regeneration
- Plasticity
- Network dynamics
- Mind-body interactions
- Unknown unknowns

neurotechnologies

Technologies and applications
- Micro-electrodes/electronics
- Imaging
- Cochlear implants
- Vision prostheses
- Vestibular prostheses
- Spinal Cord Stimulation
- Deep Brain Stimulation
- Bioelectronic Medicines

www.darpa.mil