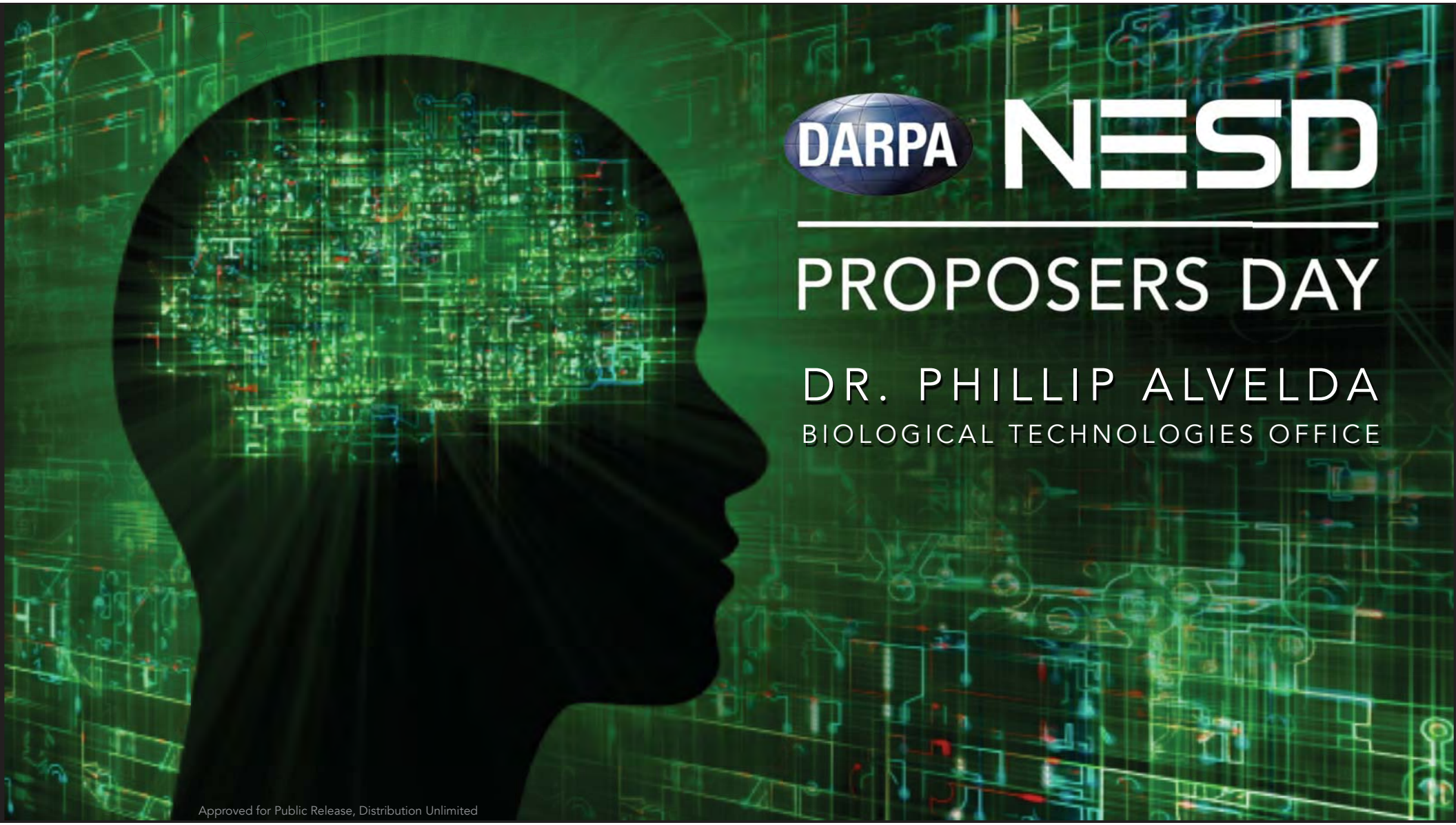
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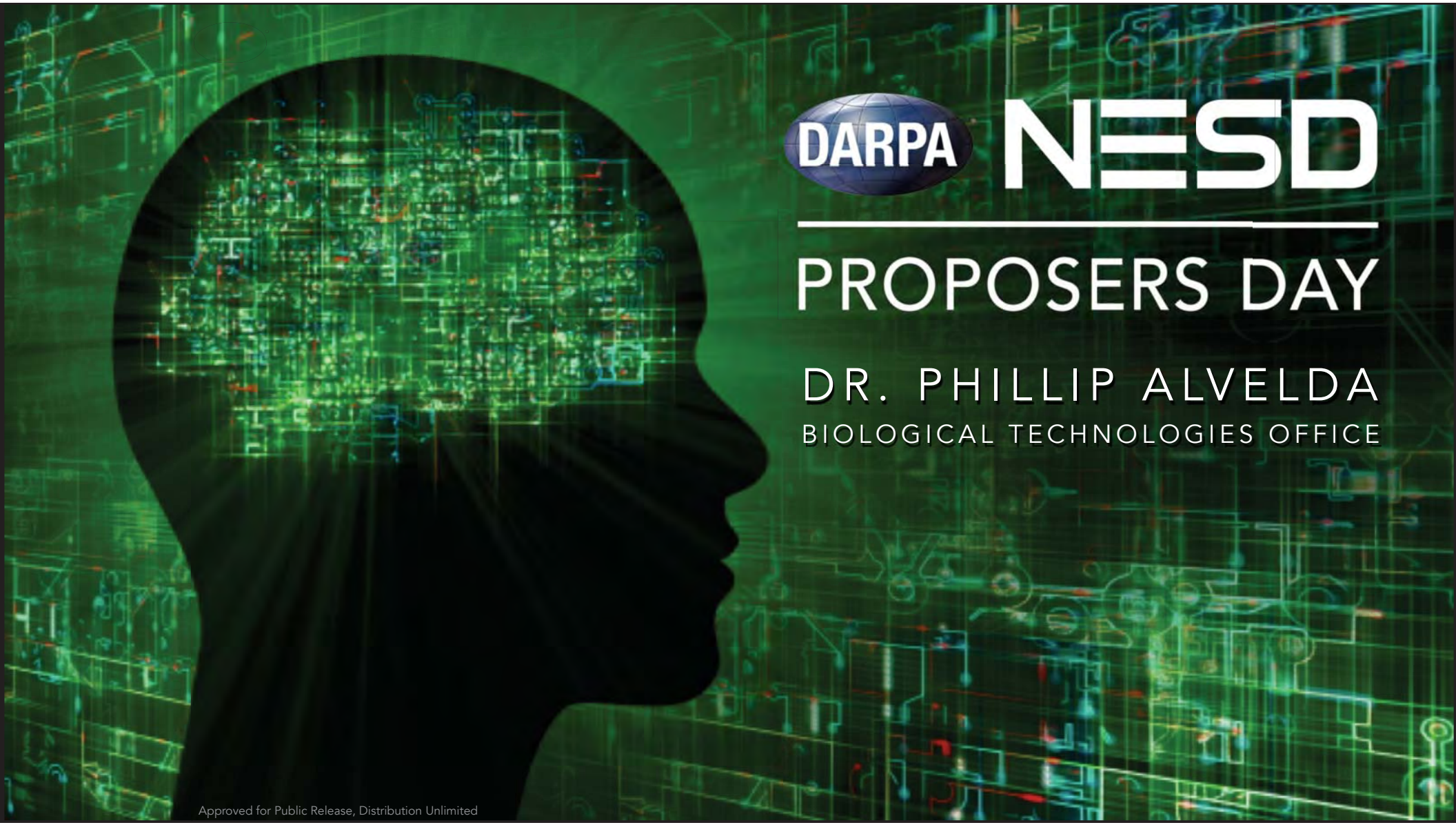
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BAA INBOX & FAQ

Direct ALL questions & communication to BAA Inbox

DARPA-BAA-16-09@darpa.mil

Dr. Alvelda, any member of his team, or the BAA Inbox cannot provide feedback or guidance on any aspect of your proposal, they can only clarify the content of BAA-16-09

DARPA will update the NESD FAQs on a regular basis

https://www.fbo.gov/spg/ODA/DARPA/CMO/DARPA-BAA-16-09/listing.html

Submit question(s) at least 15 days before the proposal submission deadline

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PM Presentation Outline

BAA Walk-Through: Key Program Requirements

1. Program Vision: Next-Gen Neural Interface ***Systems*** *for Human Use*
2. Interdisciplinary Teaming Requirement to Produce State of the Art Systems
3. Sensory Cortex Focus
4. Proposer-selected Human Therapeutic Application
5. Fundamental Challenge & Opportunity of Precision Neural I/O at Scale
6. Improve Transformation Algorithms that Leverage New Precision & Scale
7. System Design, Integration, Packaging, Telemetry and POWER
8. Regulatory, Clinical, ELSI Requirements
9. Looking Beyond Therapy: Engineering Platforms for Future R&D
10. The NESD Industry Group: IP, Fab, Prototyping, and Test Support

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1. NESD Program Vision

Next-generation
Neural Interface Systems

Anywhere that this presentation conflicts with the BAA 16-09 document, the BAA document shall be considered to hold the final definitive terms that supersede all others.

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1. NESD Program Vision

Next-generation
Neural Interface Systems

for use in humans

Anywhere that this presentation conflicts with the BAA 16-09 document, the BAA document shall be considered to hold the final definitive terms that supersede all others.

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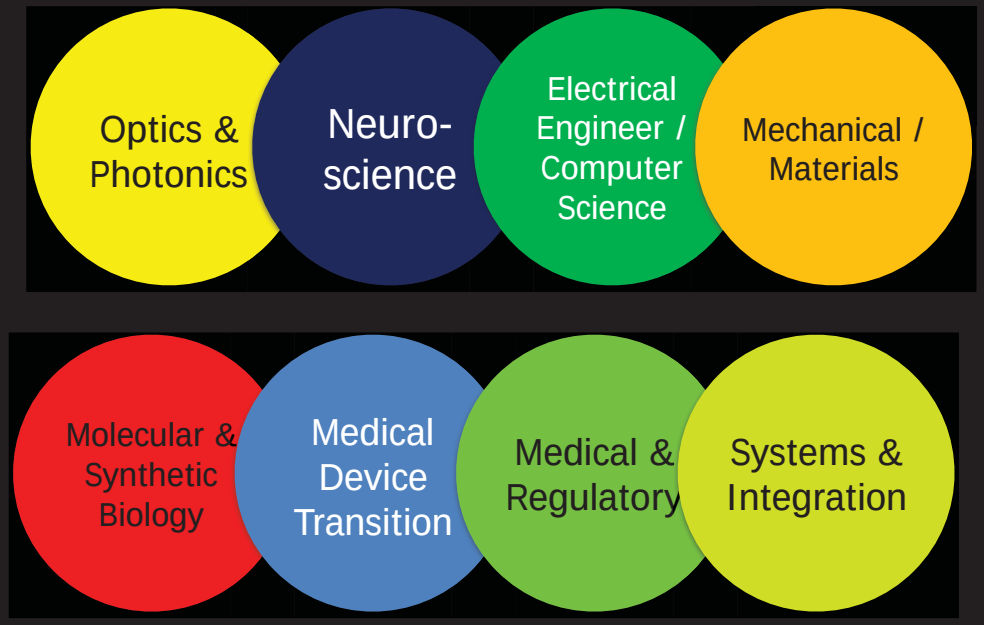
2. Critical Teaming Requirement



Recruit state-of-the-art expertise across all necessary disciplines

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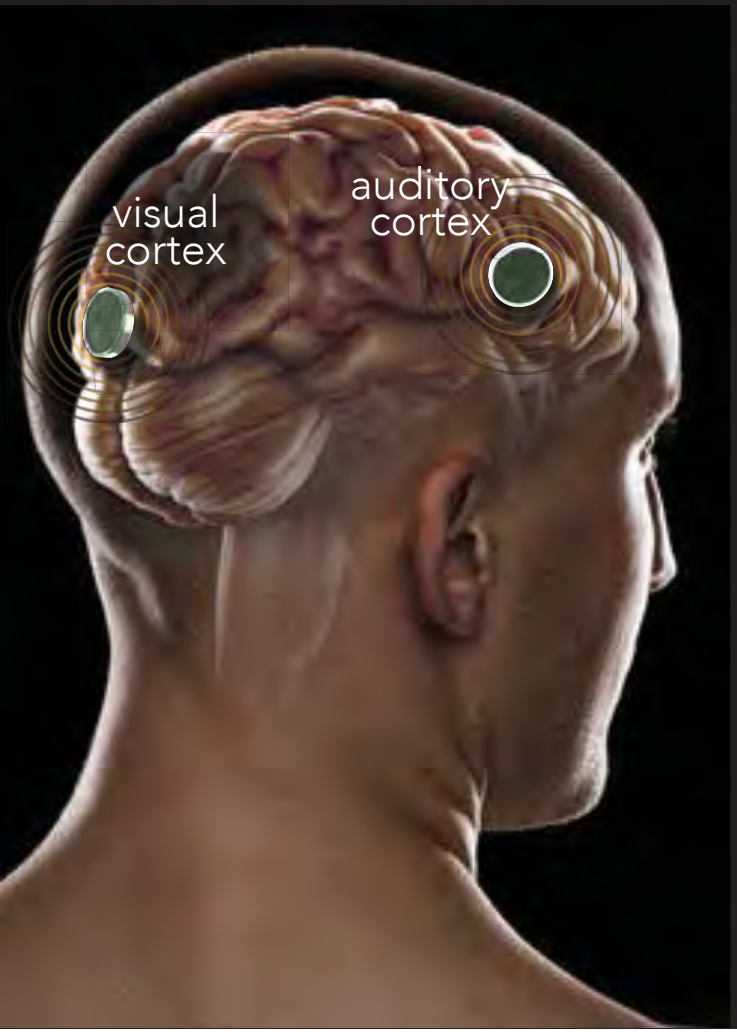
3. Sensory Cortex Focus



- Physical accessibility
- Best scientific understanding of neural encoding
- Clearly demonstrable utility of scale & precision
- Cortical areas closest to high-precision stimulus
- Complement other DARPA neurotech programs
- Broad industry application beyond initial therapies

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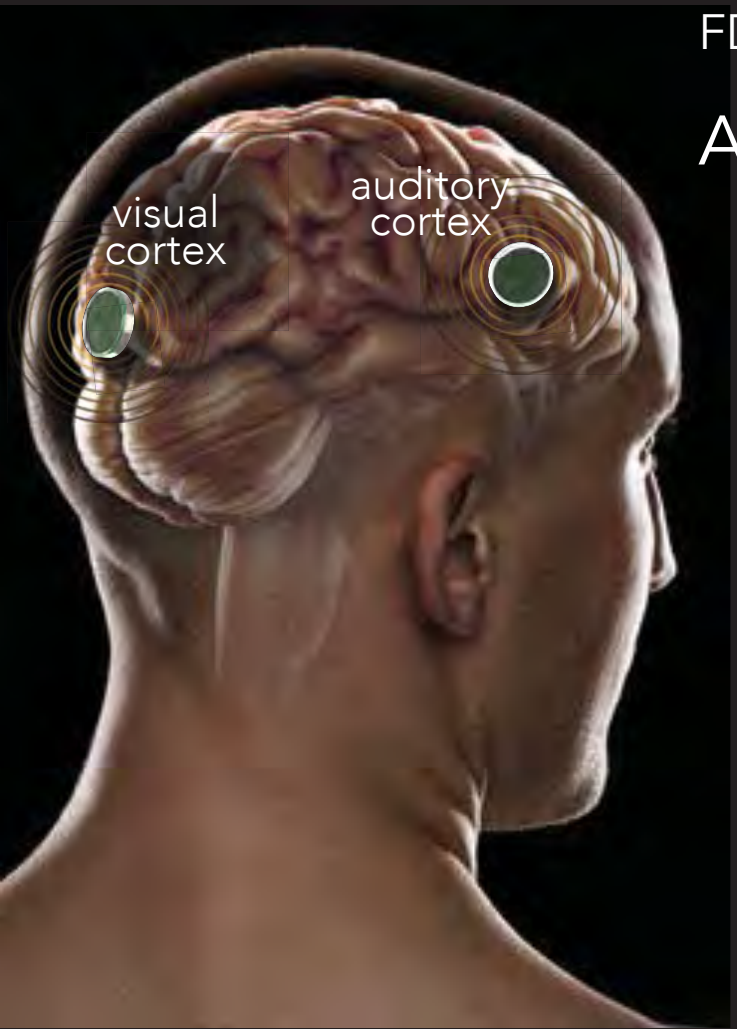
4. Proposer-Defined Therapeutic Application



FDA requirement for human use

Application's potential therapeutic benefit

Proposers must

- Choose a specific initial target therapeutic application.
- Clearly identify the associated area of sensory cortex.
- Use the proposed application to generate appropriate additional system requirements and target metrics.
- Refine the proposed therapy, methodologies, system designs and documentation and engage with the FDA to attain an Investigative Device Exemption [IDE] for use in humans.

BAA 16-09 pages 5 and 6

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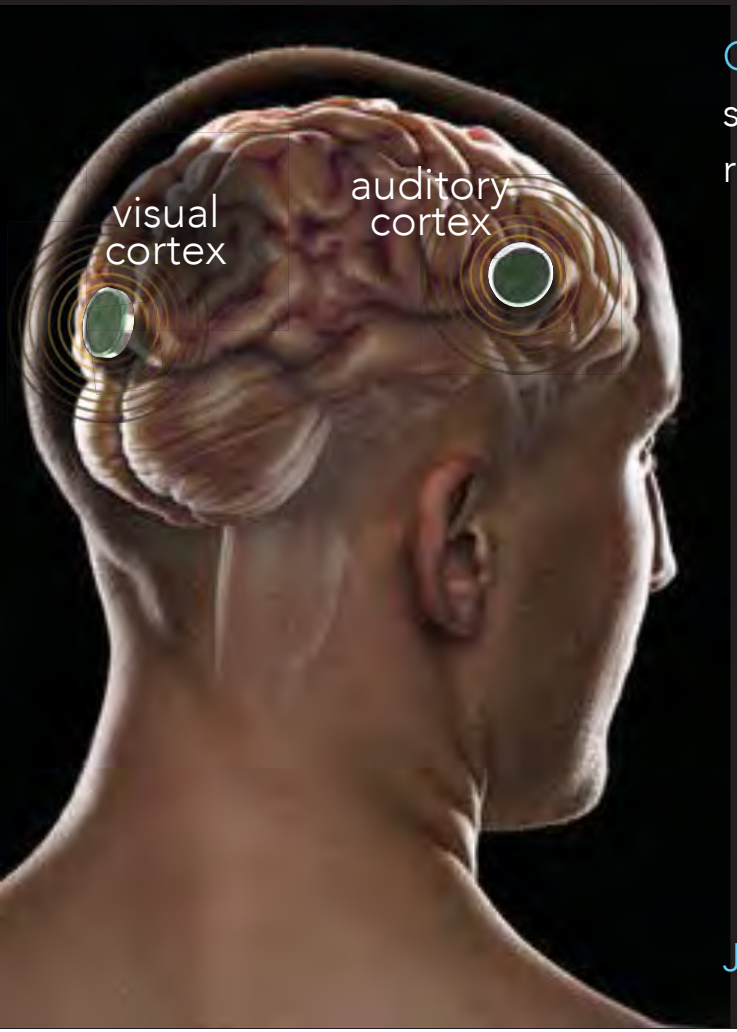
Proposer-Defined Target System Metrics



Once the therapeutic application is selected, its performance requirements should drive and define the NESD architecture and application-specific requirements, and target system evaluation metrics such as:

- Necessary precision
- Cortical layers cortical region of interest
- Cortical area coverage
- Encoding of neural activity
- Computation models
- External and implantable system architecture
- Component performance, size, modularity, materials
- Power and thermal dissipation
- Data representation and transformation algorithms
- Animal model selection and test staging
- Accelerated path to first human experiments
- Validation and clinical testing methods

Justify your decisions

BAA 16-09 page 5 through 6

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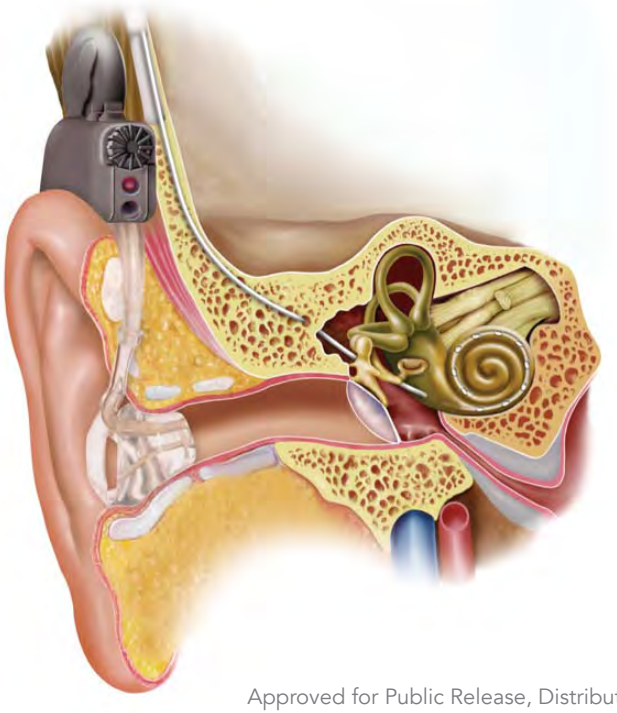
AUDITORY NEURAL INTERFACE

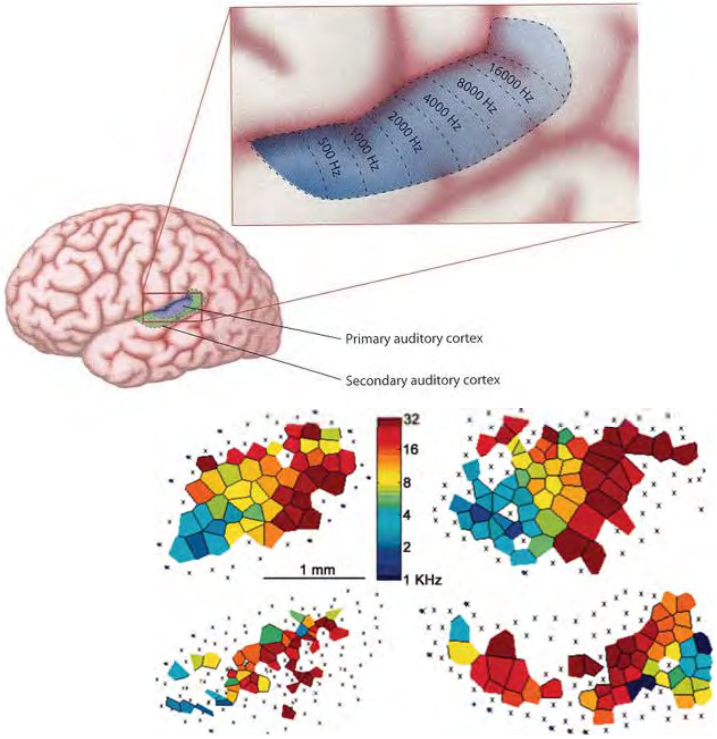
STATE OF THE ART

24 contacts in cochlea, 1985 era technology



NESD CORTICAL INTERFACE

Sensory restoration absent outer ear



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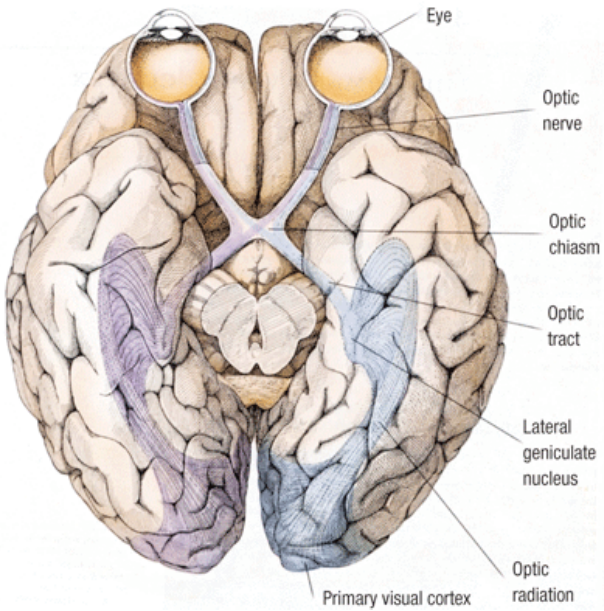
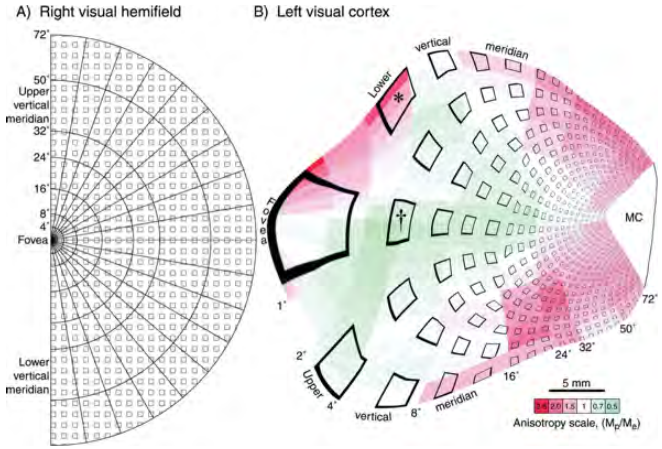
INTERFACE WITH VISUAL CORTEX

Sensory restoration
absent eyes or optic nerves





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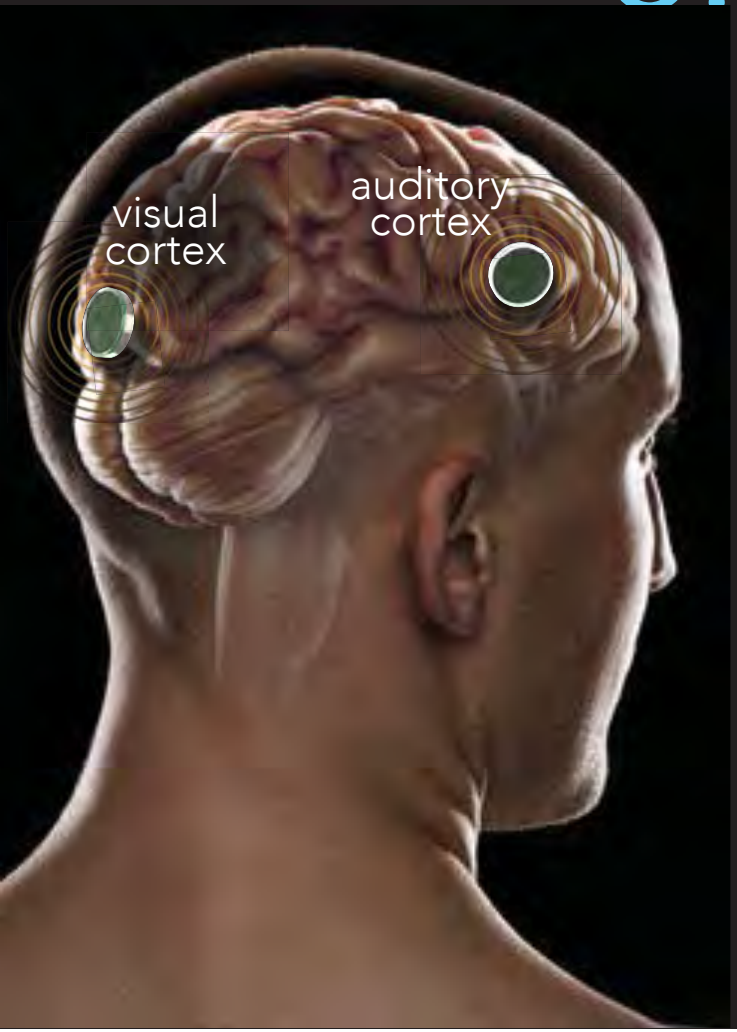
5. Scale & Precision Requirements



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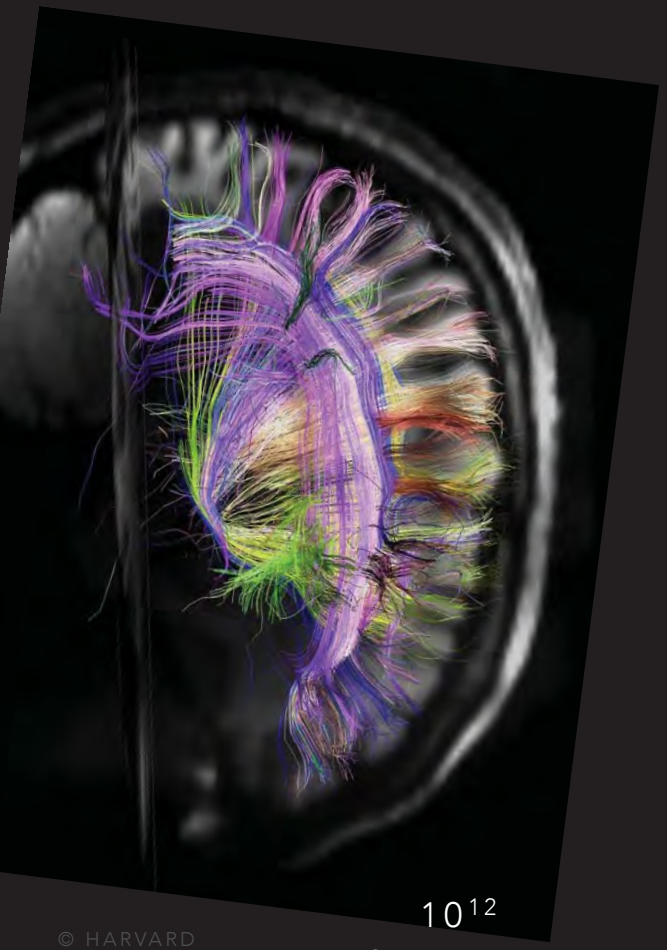
Bridging Micro-biology and Micro-electronics

Neural Modulation & De-Modulation



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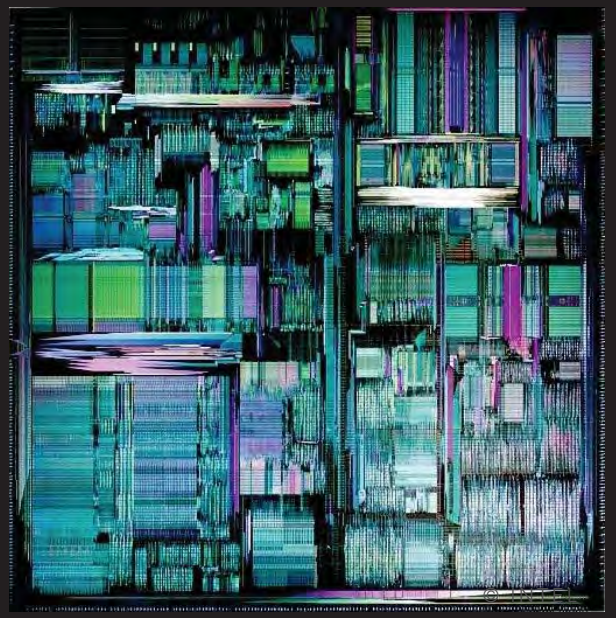
10^{12}
Synapses

Advanced
Neural
Interfaces

Electro-Chemical Impulses
to Digital Bits and Back

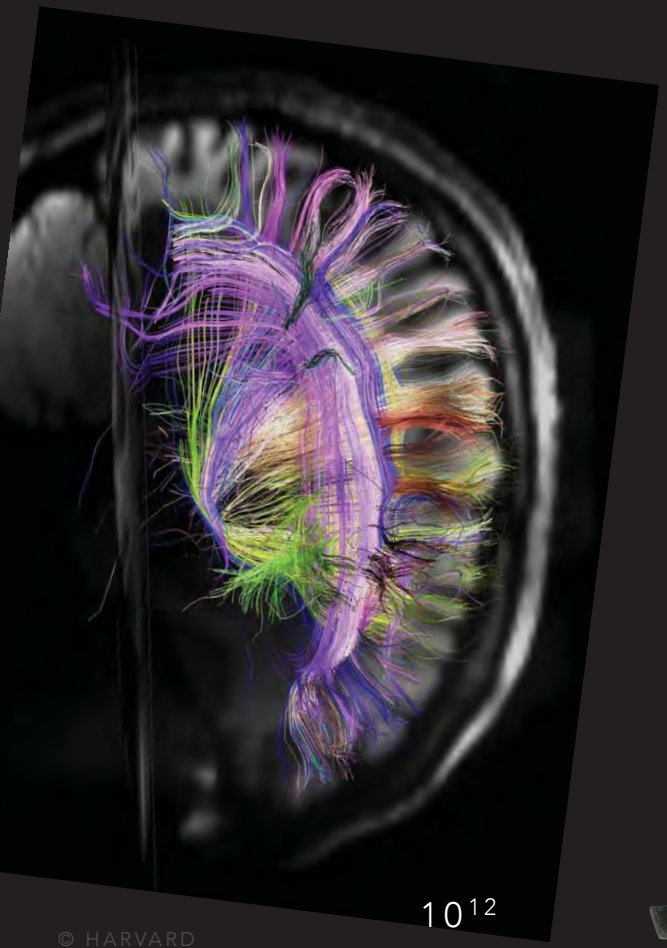


10^{12}
Transistors

DARPA NESD
PROPOSERS DAY

Bridging Micro-biology and Micro-electronics

Neural Modulation & De-Modulation

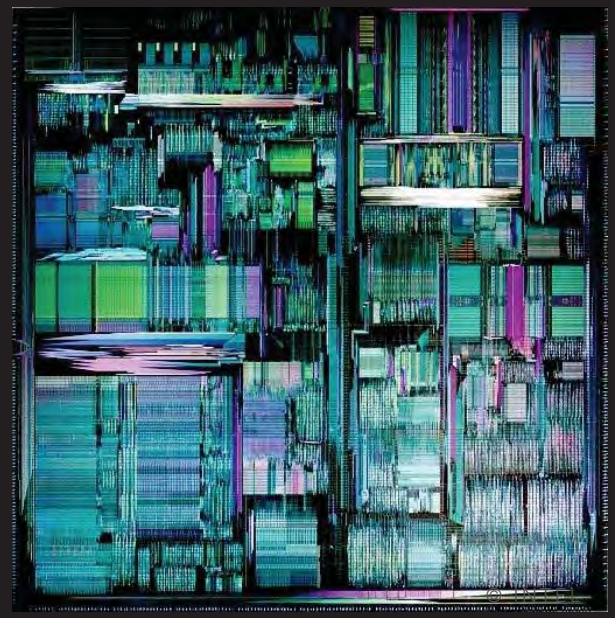


10^{12}
Synapses

Advanced
Neural
Interfaces

Electro-Chemical Impulses
to Digital Bits and Back

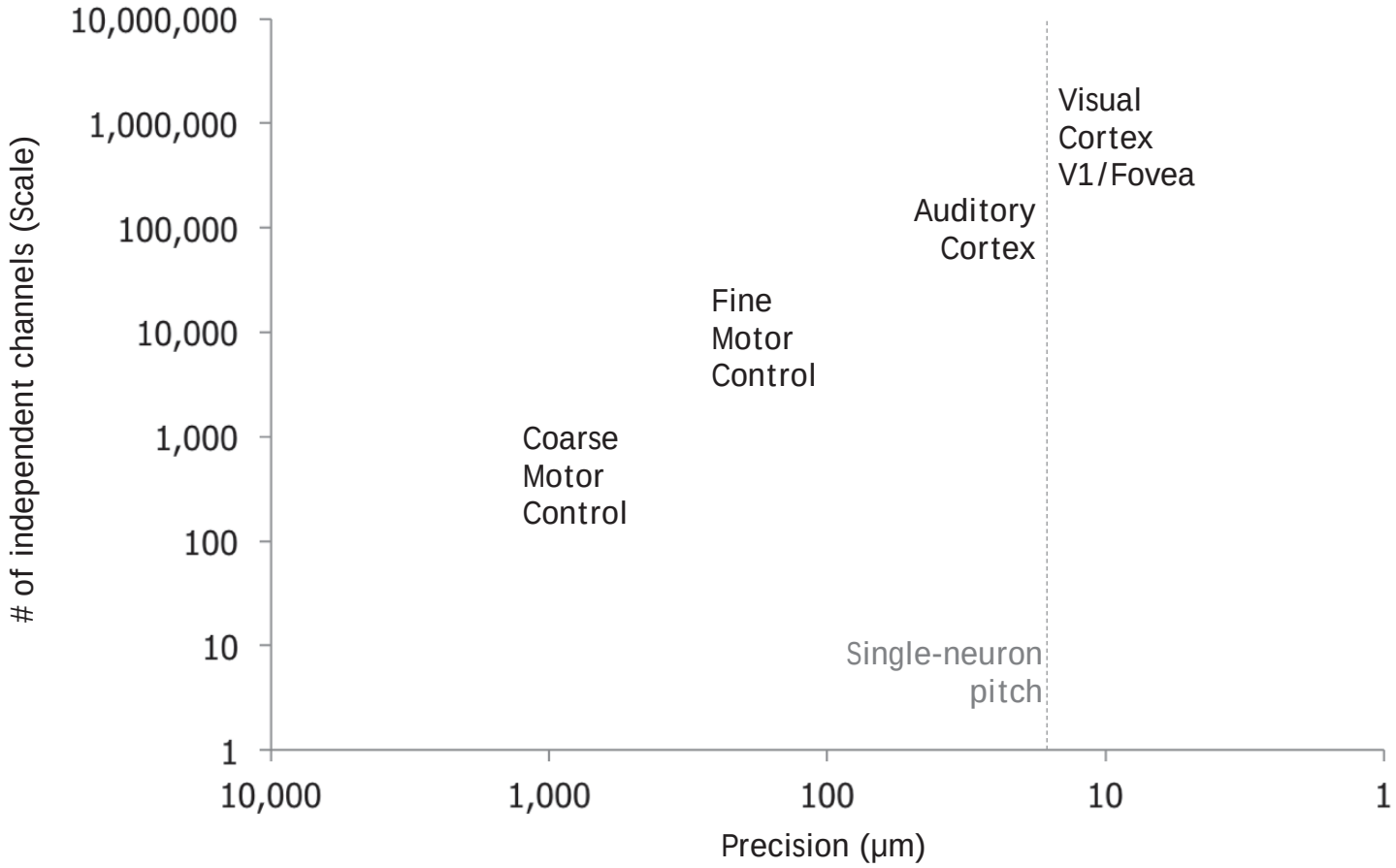
10^{2} Wires



10^{12}
Transistors

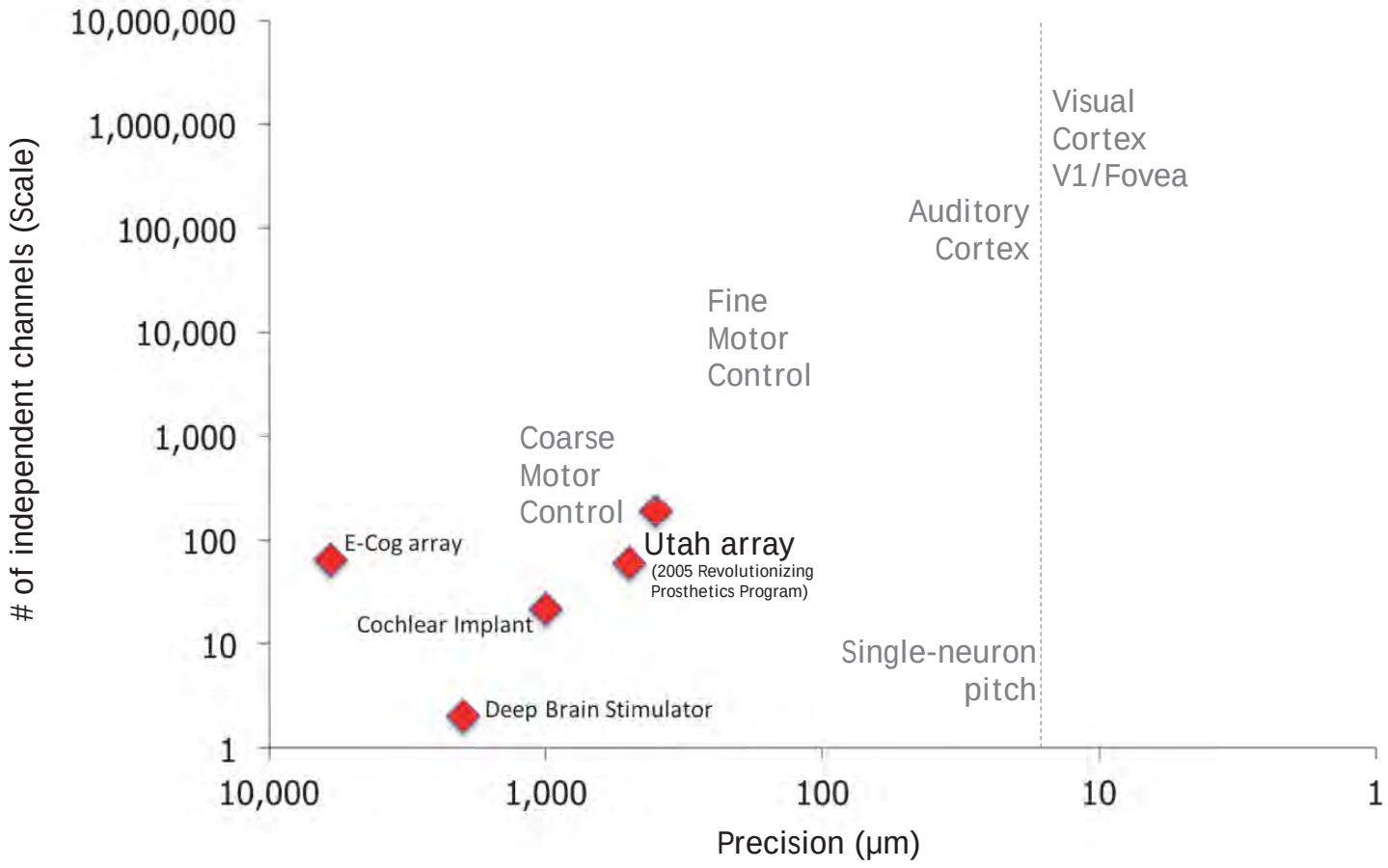
Neural Interface Scale & Precision

Improving scale **and** precision of neural I/O opens new cortical areas for interface.



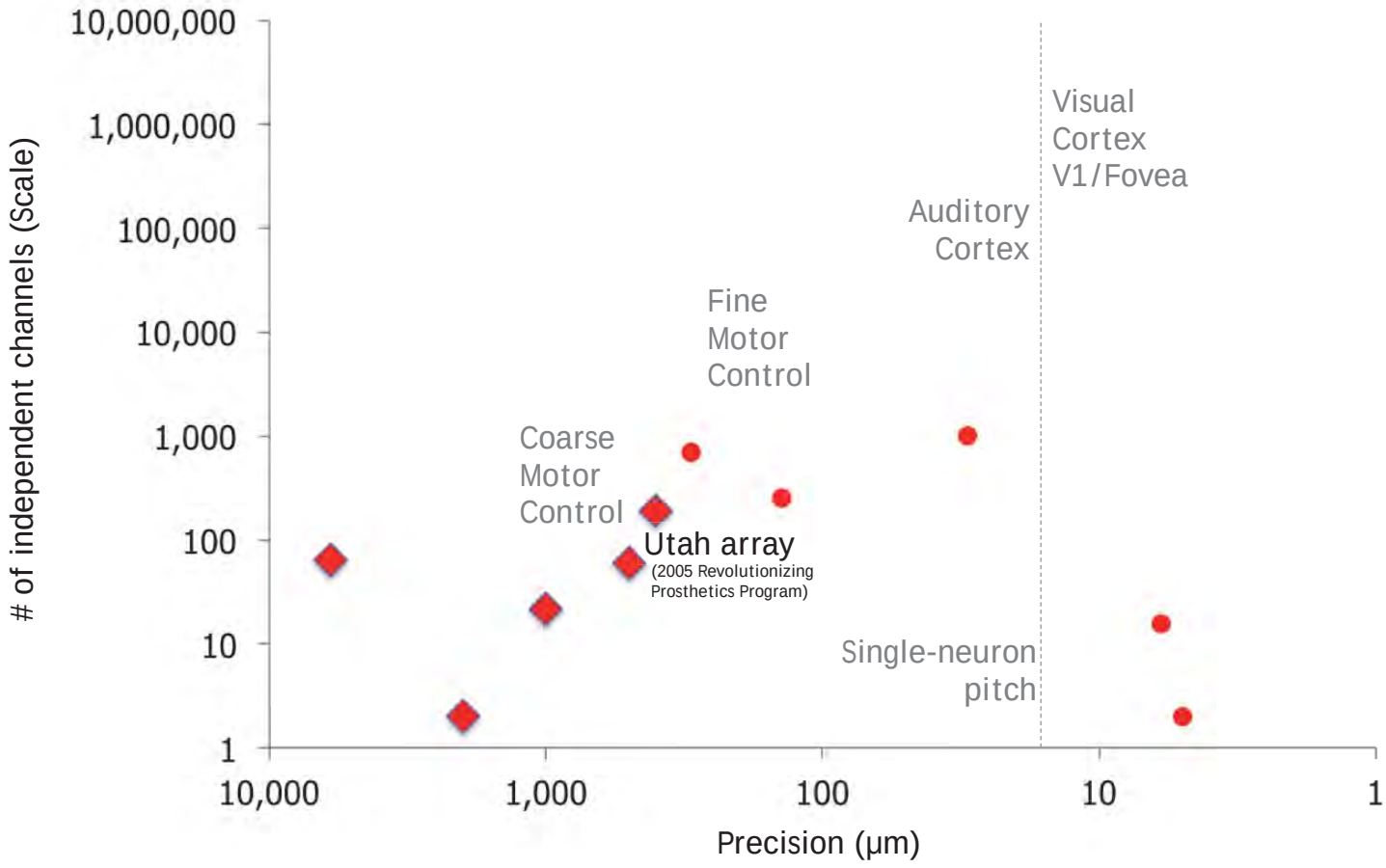
SOA Electronic Probes Cleared for Human Use

No material investments to FDA-qualify new neural I/O tech for human use since 2005



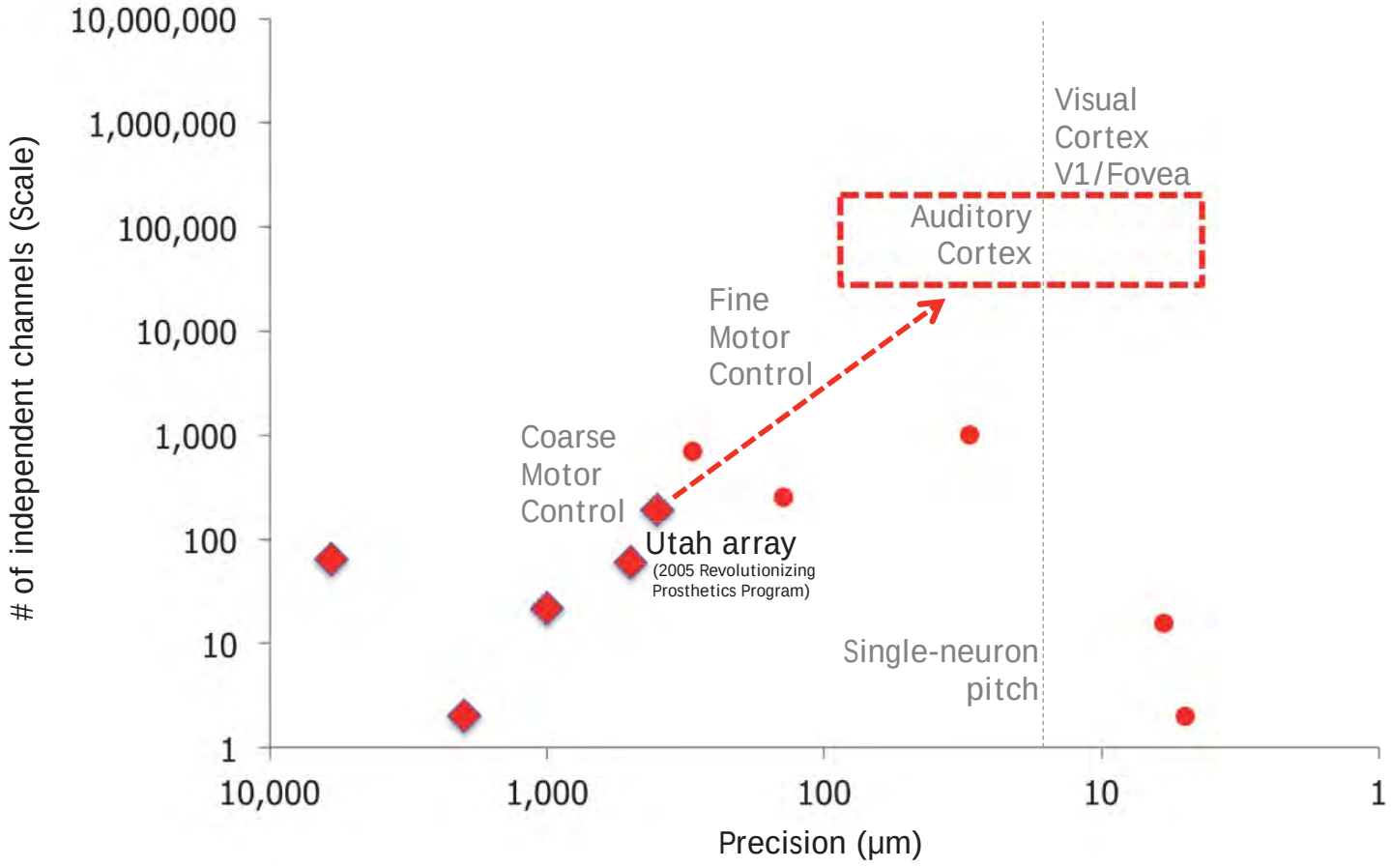
New Electronic Probes Tested in Animals

Significant progress in neuroscience animal experiments, but still lags SOA CMOS Integration



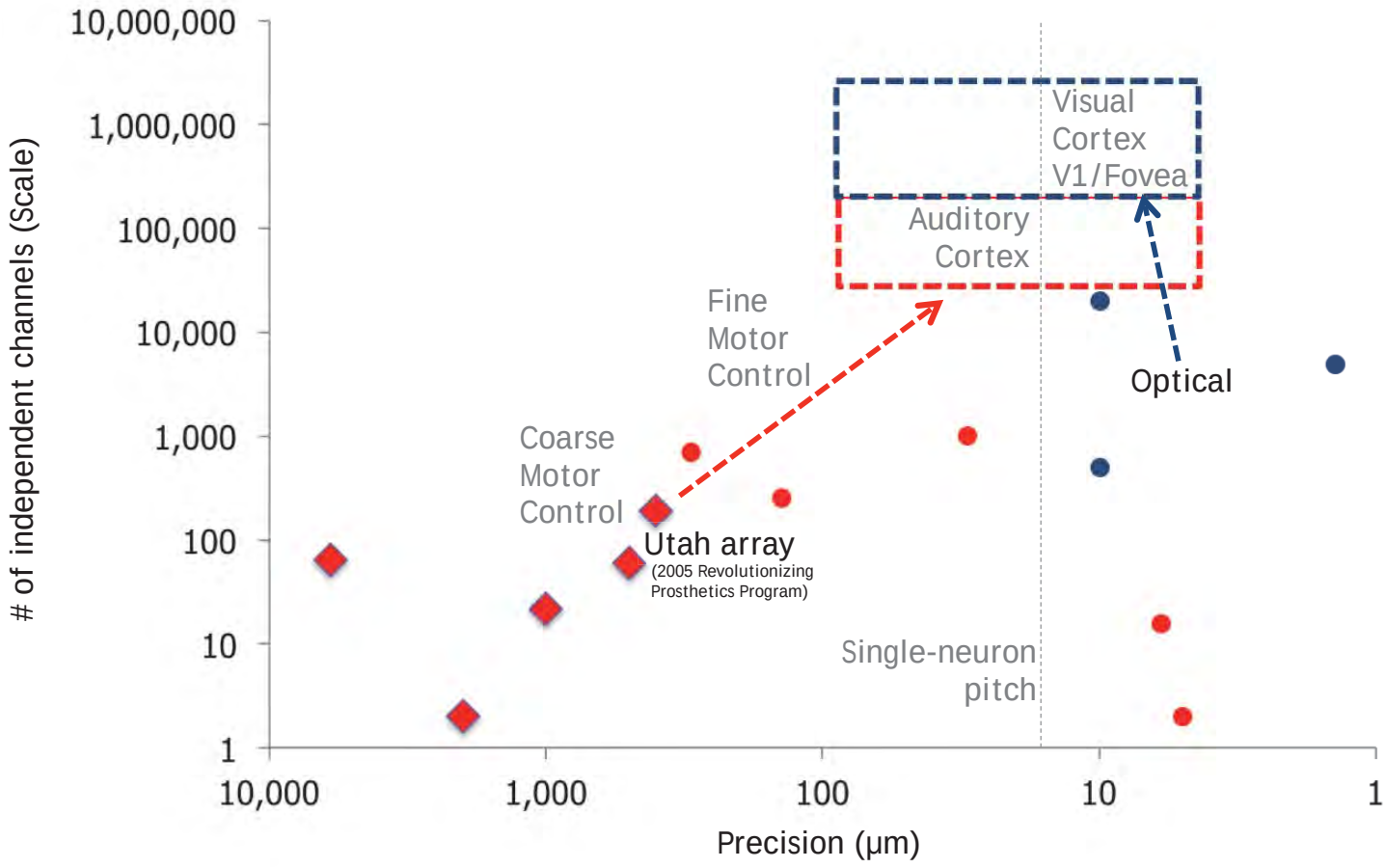
Applying State-of-the-Art Microelectronics

Leverage SOA CMOS & medical device packaging, improve scale of electronic neural I/O in humans x 10^3



How Far Will Optical Interfaces Take us?

Leverage new optogenetic technology demonstrated in animals with SOA photonics to drive additional scale



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PROPOSERS DAY

SCALE REQUIREMENTS

A functional, human-implantable NESD that

- **Reads** at least **10^6** independent channels of individual single-neuron information.
- **Stimulates** at least **10^5** channels of independent neural action potentials in real-time.
- Supports continuous, simultaneous **full-duplex** real-time interaction with at least **10^3** neurons.

DARPA NESD
PROPOSERS DAY

ANY scalable neural transduction method will be considered.

- Electronic
- Micro-Wire
- Optical
- Acoustic
- Hybrid
- Other

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6. Advanced Transformation Algorithms & Protocols

1 **Read & Understand Scalable Neural Codes**
New deterministic single-neuron transcoding

2 **Scalable Write Into Sensory Neurons**
Writing in the new higher-res neural codes

3 **Bi-directional (Reversible) Transcoding**
Infer natural stimuli from neural activity & allow synthesis of perceptually-real stimuli

Demonstrate transformation of complex sensory stimuli between cortical neural activity and the digital domains, adapting over time to variations in stimulus and neural plasticity.

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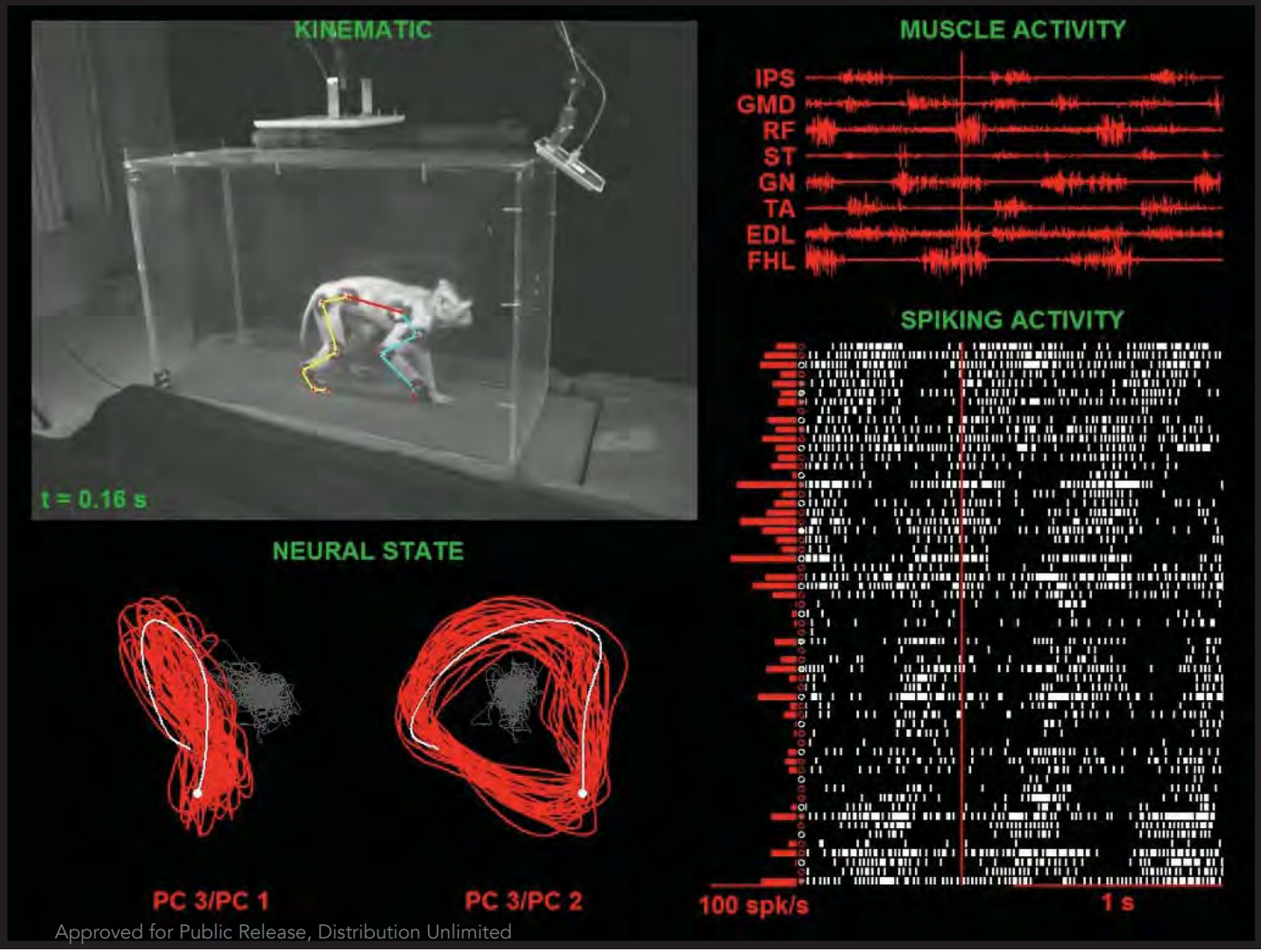
Complex Dynamic Models of Neural State are Critical

Prior Motor Cortex work



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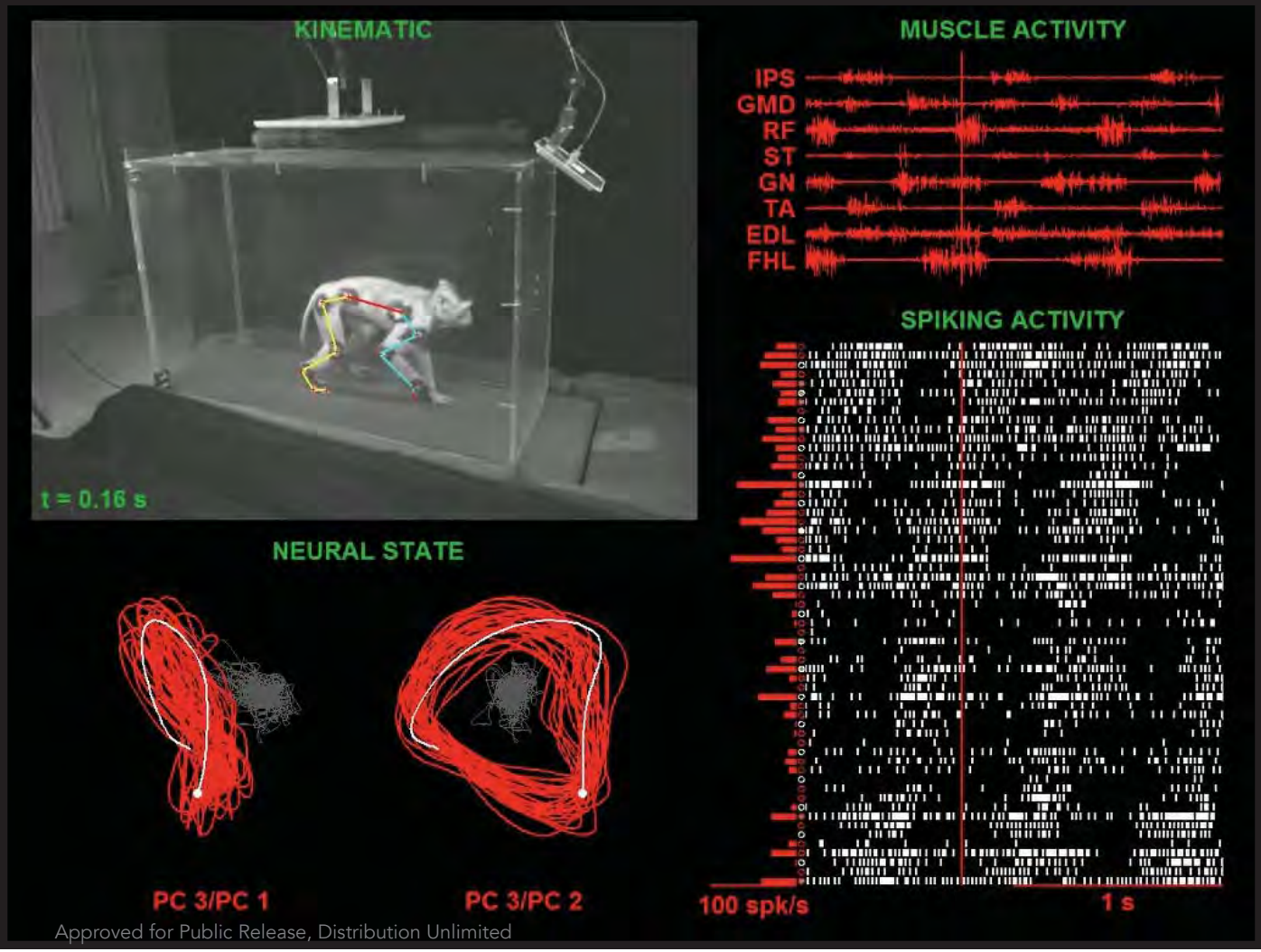

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PROPOSERS DAY

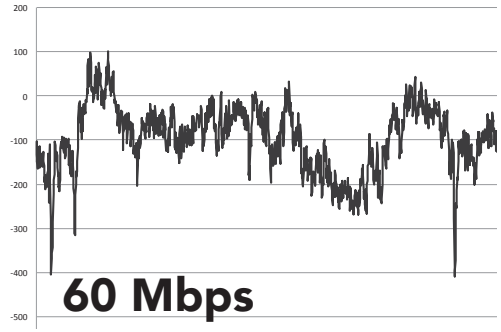
New Neural Data Representations, Compression, Protocols

to manage new megabit-scale neural interface data

State of the art

Aggregate information
Computationally expensive
Low output rate

REVOLUTIONIZING
PROSTHETICS



96 x 16 bit Channels Sampled @ 30,000 Hz

6 degrees of freedom x 4 bits @ 200 Hz

DARPA NESD
PROPOSERS DAY

New Neural Data Representations, Compression, Protocols

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Computationally expensive
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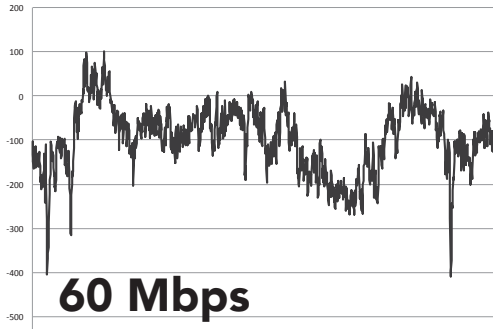


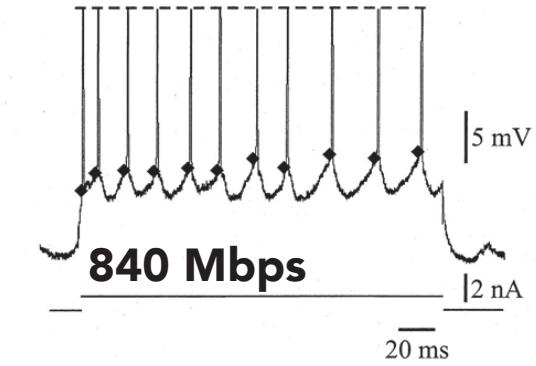
96 x 16 bit Channels Sampled @ 30,000 Hz

6 degrees of freedom x 4 bits @ 200 Hz

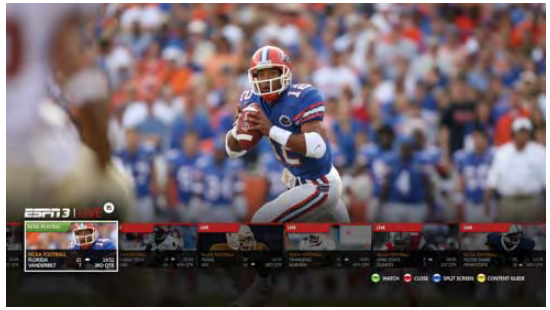
New Opportunities

Precision information
Power-efficient analysis
High compressibility

NESD
INTERFACES



10^6 x 8 bit Channels @ 60 Hz



1.5 Mbps

H.265 Compressed 720P HDTV

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Neural Activity Representation & Protocols

- Minimize data payload necessary to represent & telemeter neural activity at scale.
- Balance power load demands between local processing for signal processing & compression and telemetry
- Tune and Validate representations & protocols to minimize functional loss when compressing neural data.
- Define and publish hardware and software APIs, protocols, and semantics for interoperability between NESD components and systems.
- Example, MPEG encoders use vastly different approaches, but all produce compatible files

BAA 16-09 pages 8 and 10

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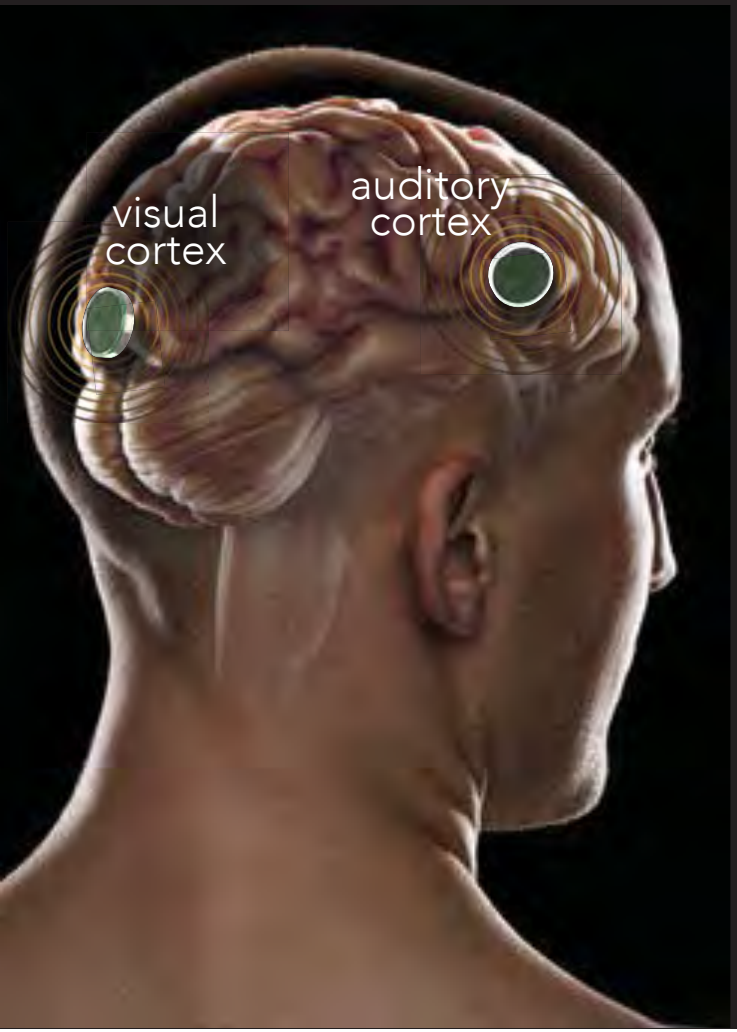
7. System Integration

Packaging, Power & Heat



- Interdisciplinary trade-offs
- Non-toxic materials, hermetic packaging
- Transparent to RF IR, visible spectra
  No tethers or percutaneous connectors for power delivery or communication telemetry.
- Diminutive packaging for implantation
  Desire a single 1 cm^3 device that satisfies all of these capabilities (read, write, and full-duplex), but may be separate 1 cm^3 devices.
- Common package for multiple applications
- Power efficiency for thermal management

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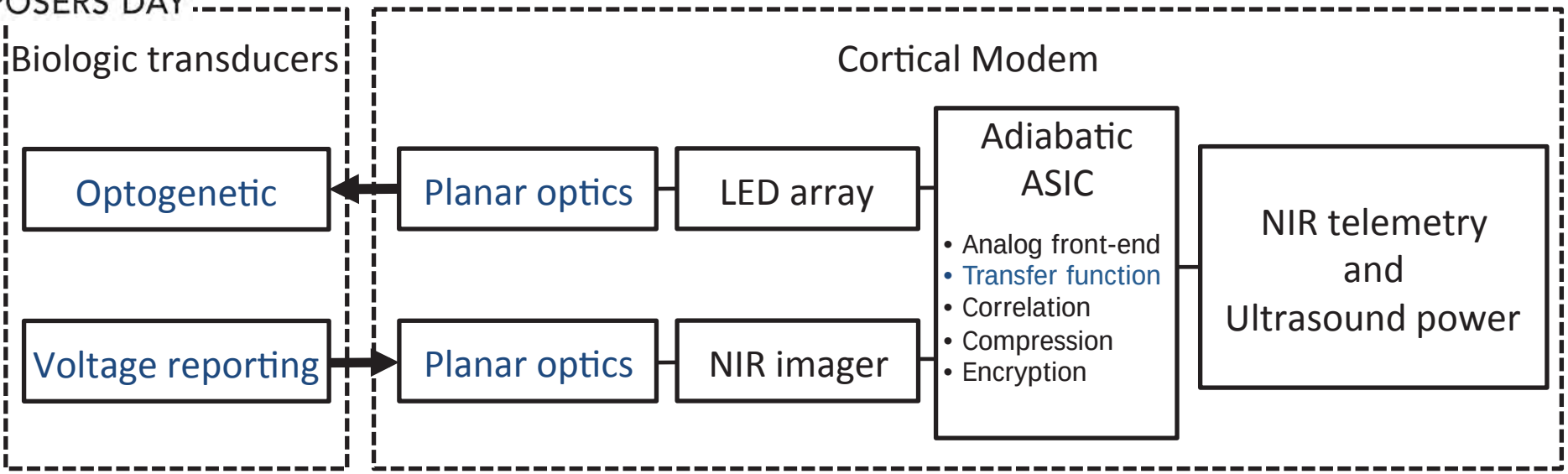
Example System based on Optical Signals



Recent proofs of principle create opportunity for DARPA to demonstrate new capability

Optogenetic transducer: Pre-clinical trials of retinal therapy

Voltage reporting: Fast kinetics; shift to infrared

Planar optics: Point spread function imaging techniques

Neural Transcode: NLP & dynamical-system neural circuit models incorporate physiological, biochemical mechanisms for deterministic models

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One Potential Instantiation

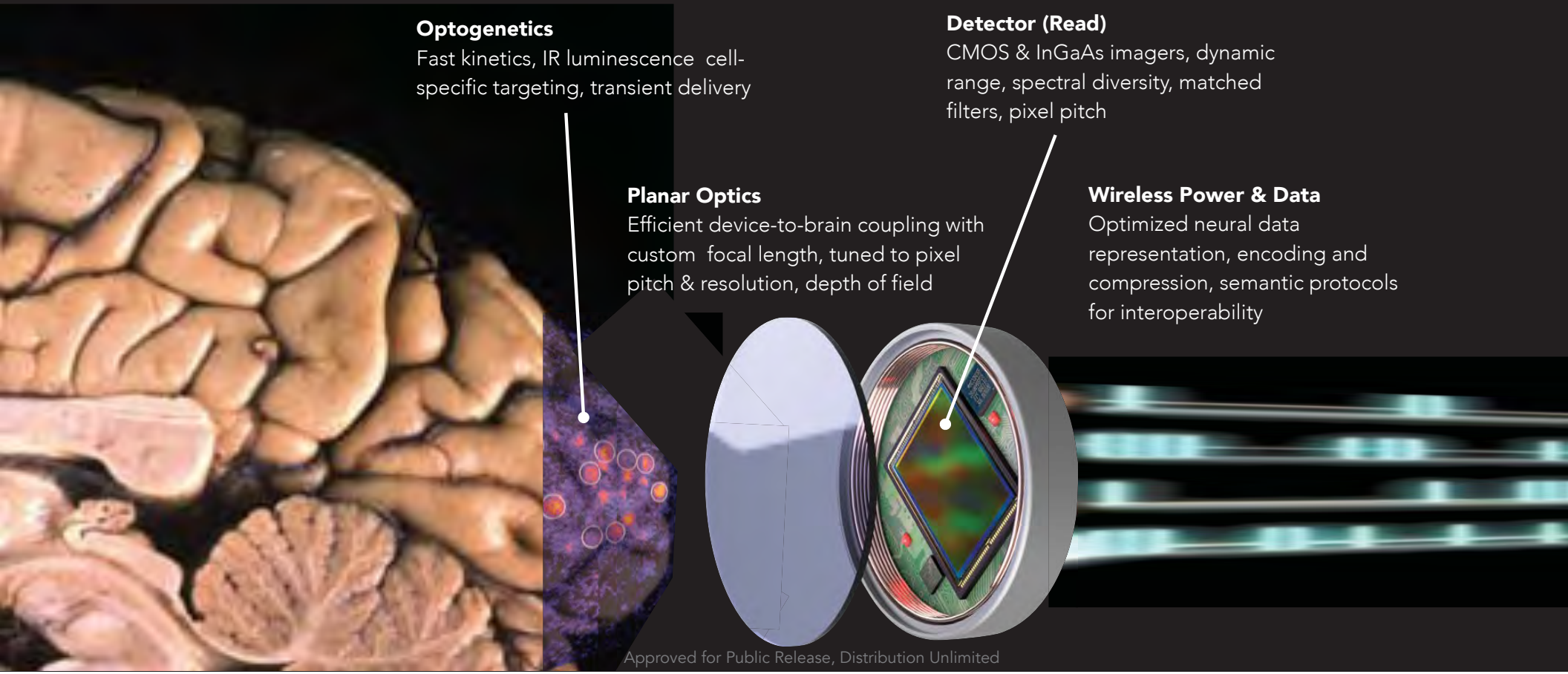
Opto-electronics & Optogenetics

Optogenetics
Fast kinetics, IR luminescence cell-specific targeting, transient delivery

Detector (Read)
CMOS & InGaAs imagers, dynamic range, spectral diversity, matched filters, pixel pitch

Planar Optics
Efficient device-to-brain coupling with custom focal length, tuned to pixel pitch & resolution, depth of field

Wireless Power & Data
Optimized neural data representation, encoding and compression, semantic protocols for interoperability



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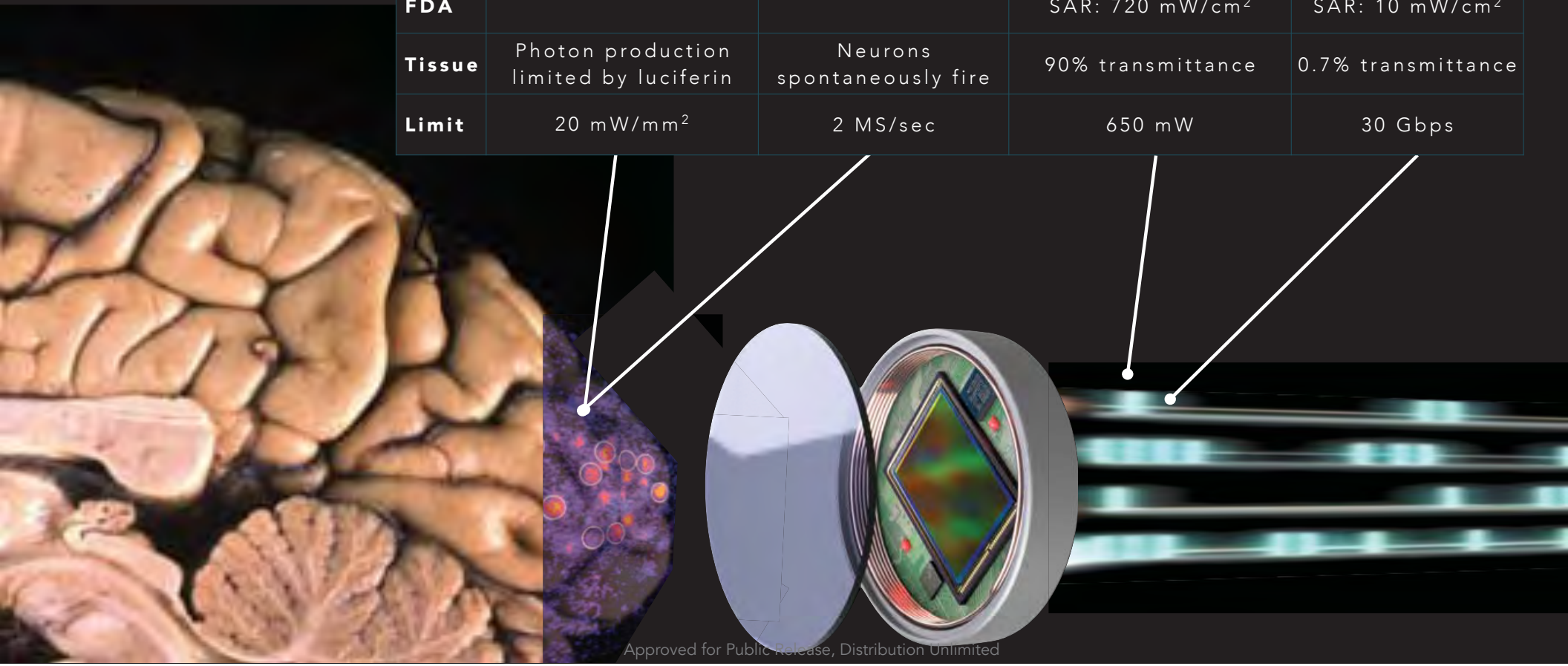
Tissue Energy Limits

	Bioluminescence	Optogenetics	Ultrasound Power	IR Telemetry
FDA			SAR: 720 mW/cm^2	SAR: 10 mW/cm^2
Tissue	Photon production limited by luciferin	Neurons spontaneously fire	90% transmittance	0.7% transmittance
Limit	20 mW/mm^2	2 MS/sec	650 mW	30 Gbps



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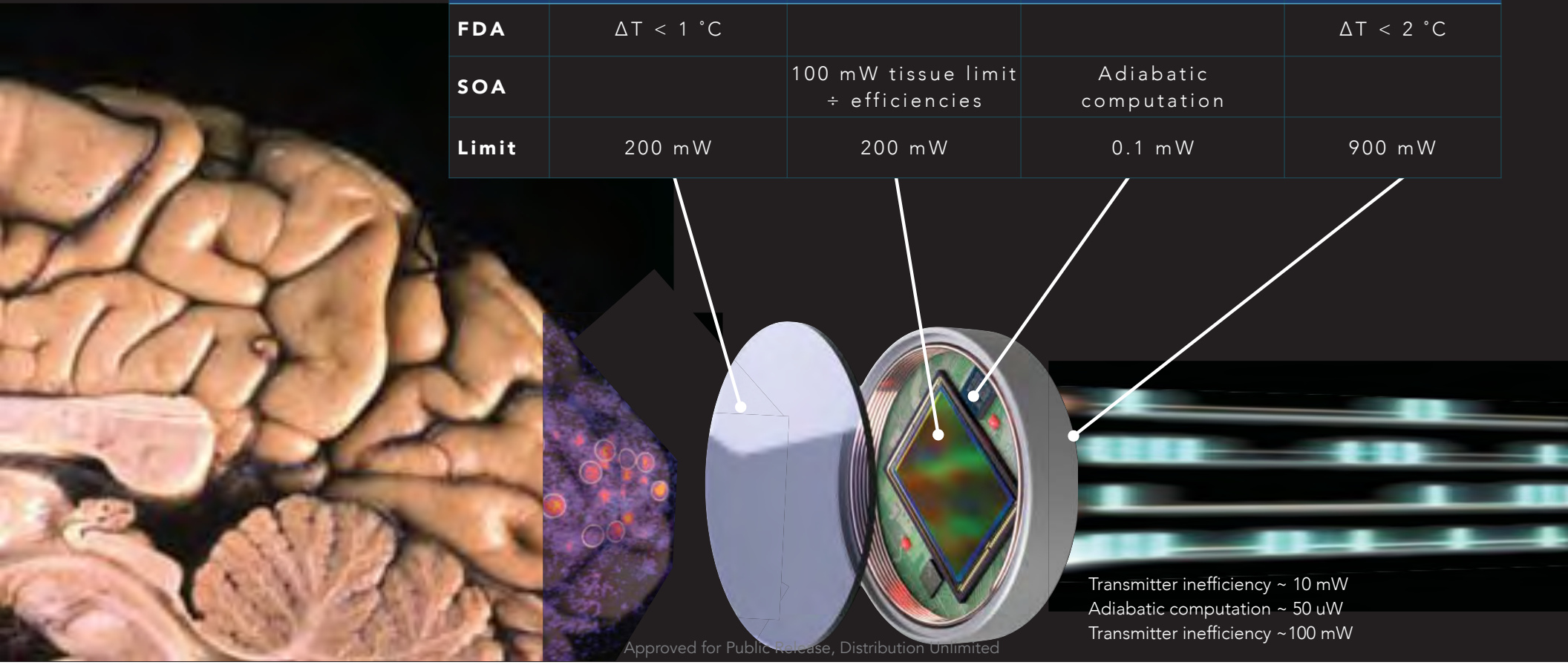
System Energy Limits

	Inside Surface	Transducer	Processing	Outside Surface
FDA	ΔT < 1 °C			ΔT < 2 °C
SOA		100 mW tissue limit ÷ efficiencies	Adiabatic computation	
Limit	200 mW	200 mW	0.1 mW	900 mW



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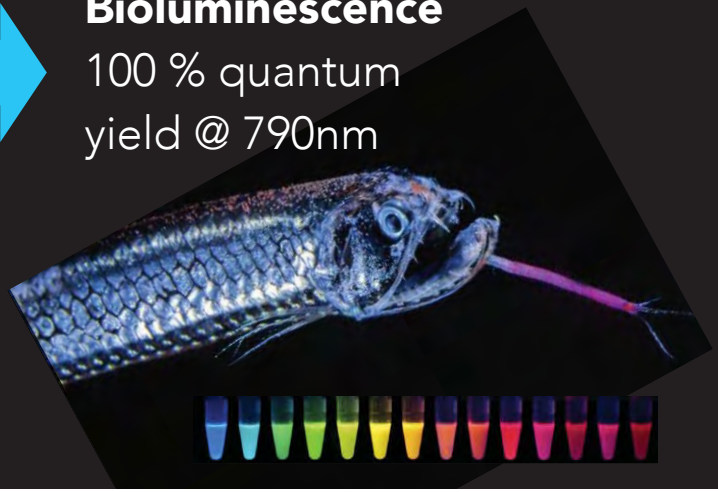
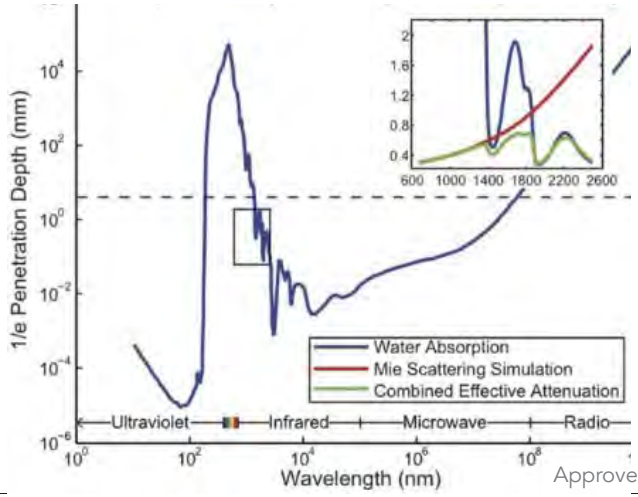
Optical Interface Performance

Fluorescence
77% quantum
yield @ 550nm

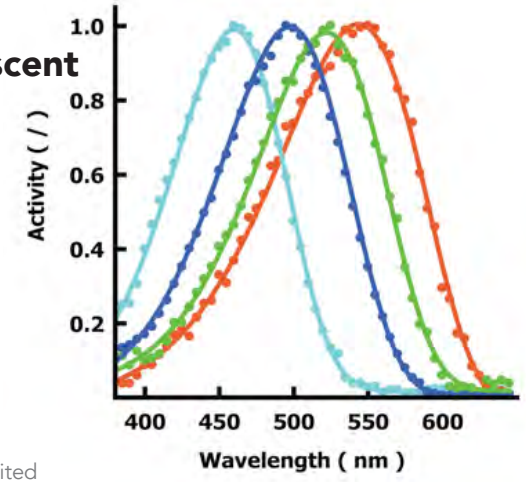
Bioluminescence
100 % quantum
yield @ 790nm





Tissue Transparency

Fluorescent Probes



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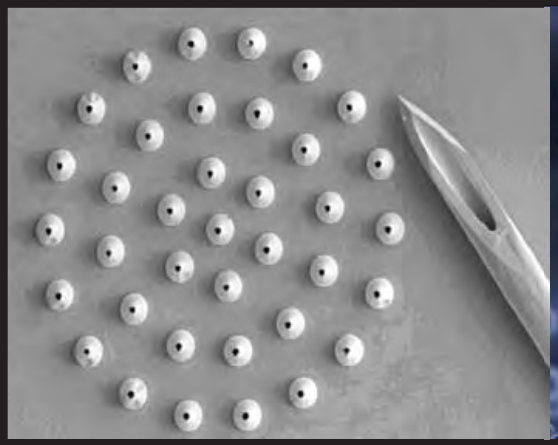
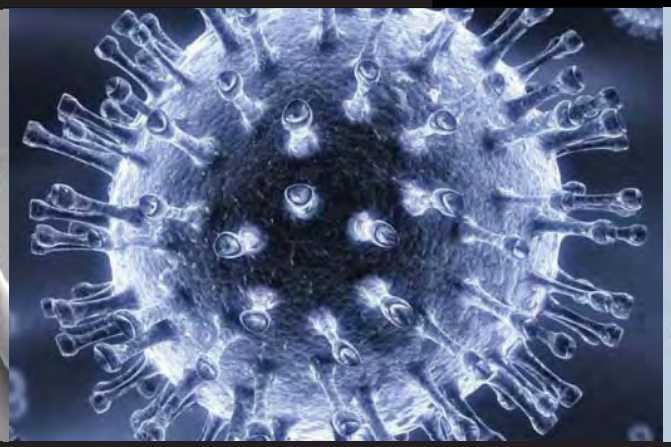
Transgenic Tool Safety

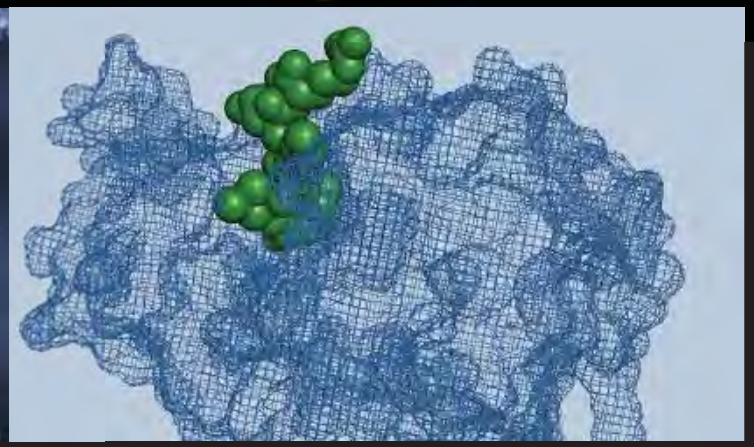
1. Transient Lifetime
mRNA half-life 48 hrs



2. Localization
micro-dosage



3. Delivery Vehicles
nanoparticles



4. Tissue Targeting
peptides & promoters

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8. ETHICAL, LEGAL, & SOCIETAL OBLIGATIONS

1. Follow all Institutional requirements supplied by

- Animal Care and Use Committee (IACUC)
- Institutional Review Board (IRB)
- FDA Investigational Device Exemption (IDE) requirements

2. Approval and continuous monitoring from

- A secondary DoD review board
- DoD Animal Care and Use Review Office (ACURO)

3. Attain an IDE for first human experiments from the FDA

4. Encourage engagement with independent bioethics experts

BAA 16-09 pages 15 through 16

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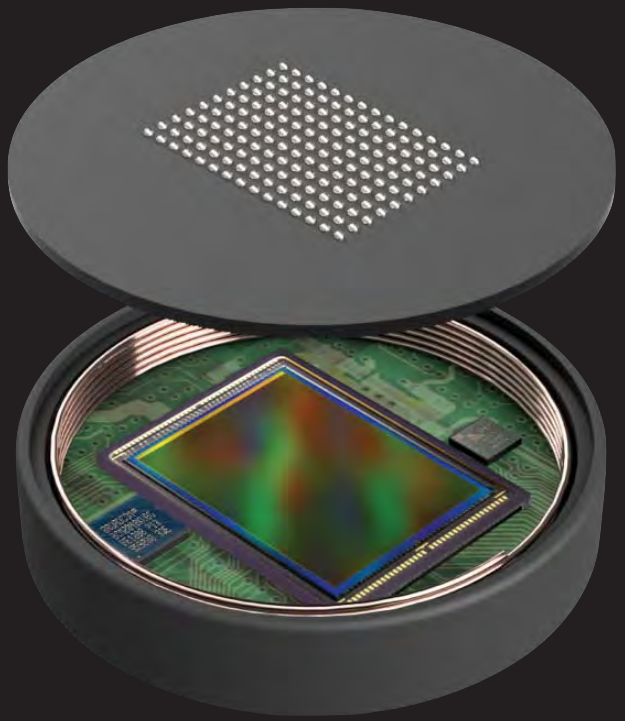
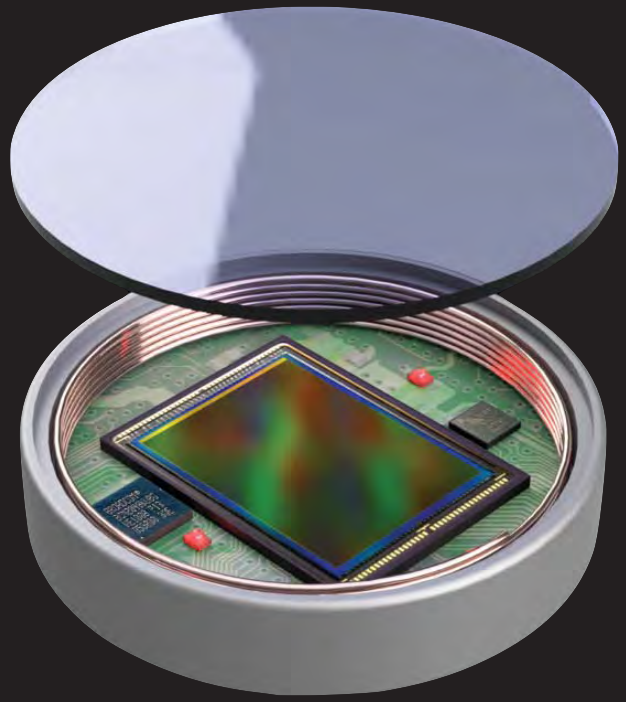
9. LOOKING BEYOND THERAPEUTICS
PLATFORMS FOR FUTURE NEURAL R&D





1 cm

- High-density ceramic vias & electronic feed-through
- Gliosis/scarring mitigation
- Wireless power & data
- Hermitic & non-toxic packages
- Codes, protocols, interoperability
- Integrated photonics
- Transparent bio-materials
- Transgenic neural activation

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10. INDUSTRY GROUP SUPPORT

- Define standards for design for manufacturing [DFM], and overall system design & integration
- Incentivize open IP access for participants to accelerate and promote successful tech transition
- Engage with commercialization, venture, and private equity partners early in program
- Lower barrier to access/license aggregated and well-managed manufacturing IP
- Make SOA design, integration, prototyping and manufacturing assets accessible to participants

SOA Design & Manufacturing

- Application-centric design & packaging
- System in Package (SiP) techniques using optimal technology w/o compromising efficiency
- < 14 nm, low-power electronics, telemetry
- High-precision transducers and photonics
- Medical-grade manufacturing

Cornerstone Technologies

- Micro-electronics
- Photonics
- RF power and data
- Low power, high-performance computing
- Bio materials & medical device packaging
- Clinical support and testing

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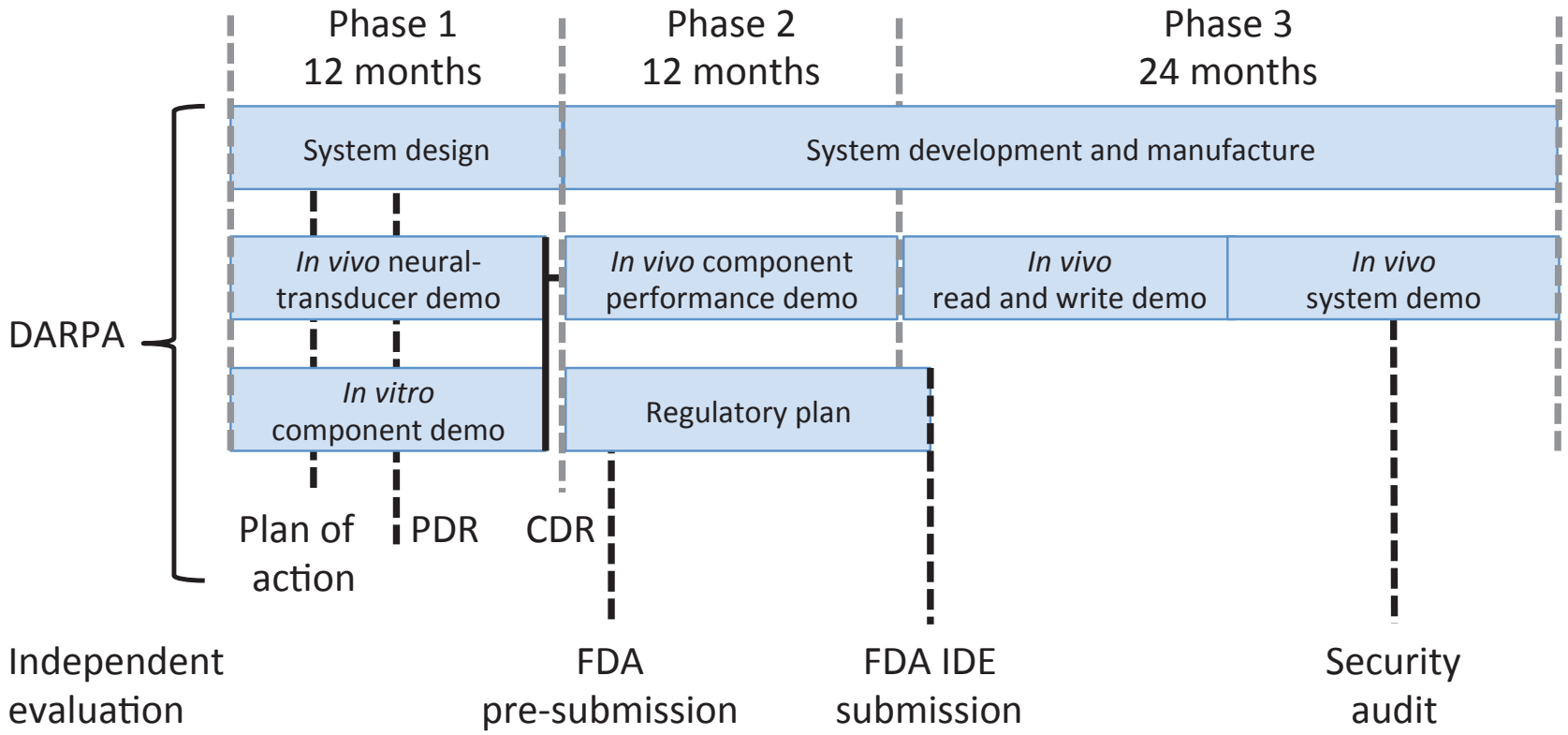
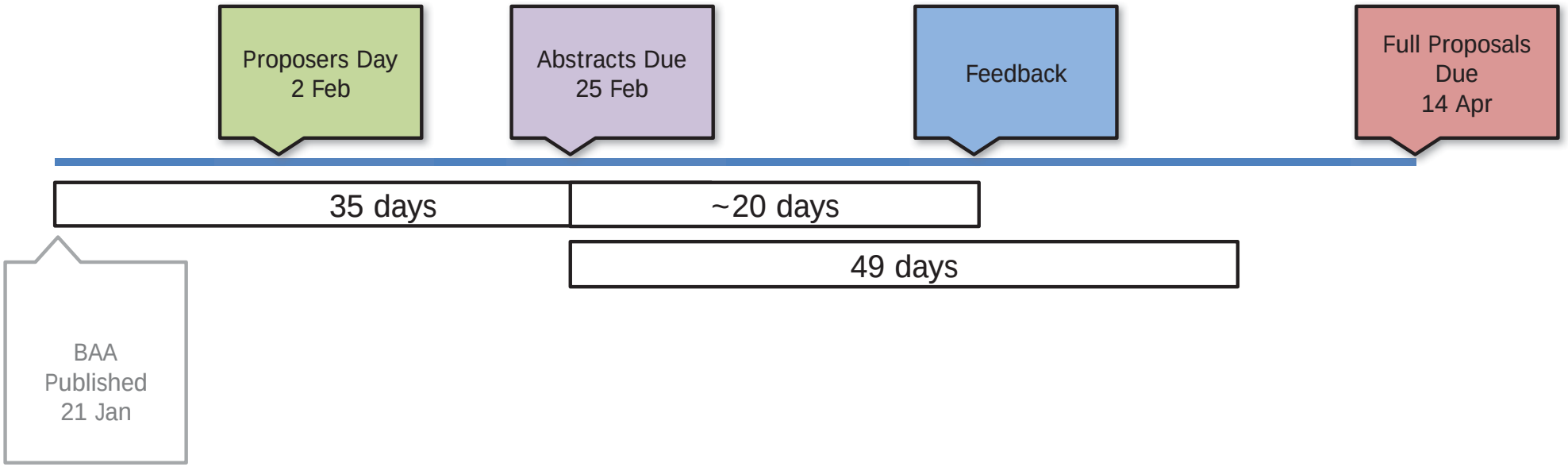
PROGRAM TIMELINE & MILESTONES



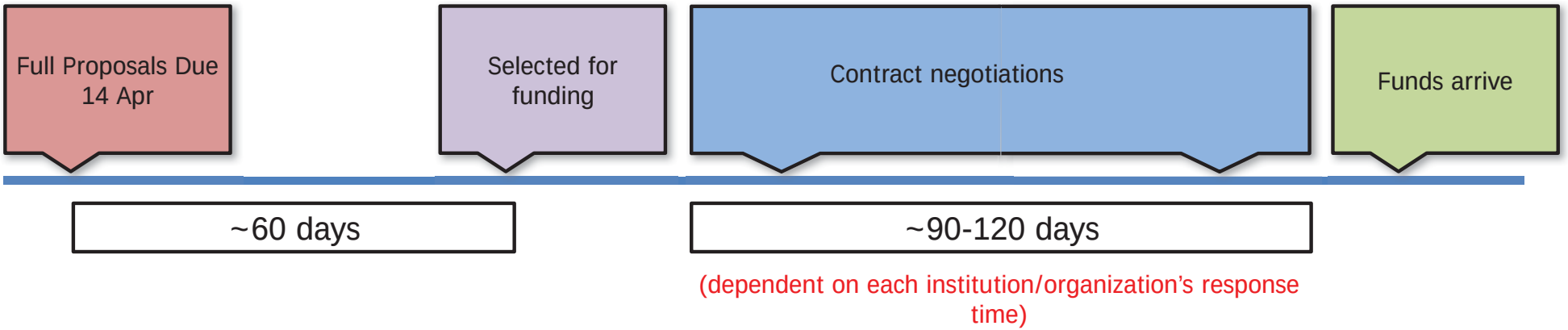
BAA 16-09 Figure 1, page 12

Responding to the BAA

Important Dates

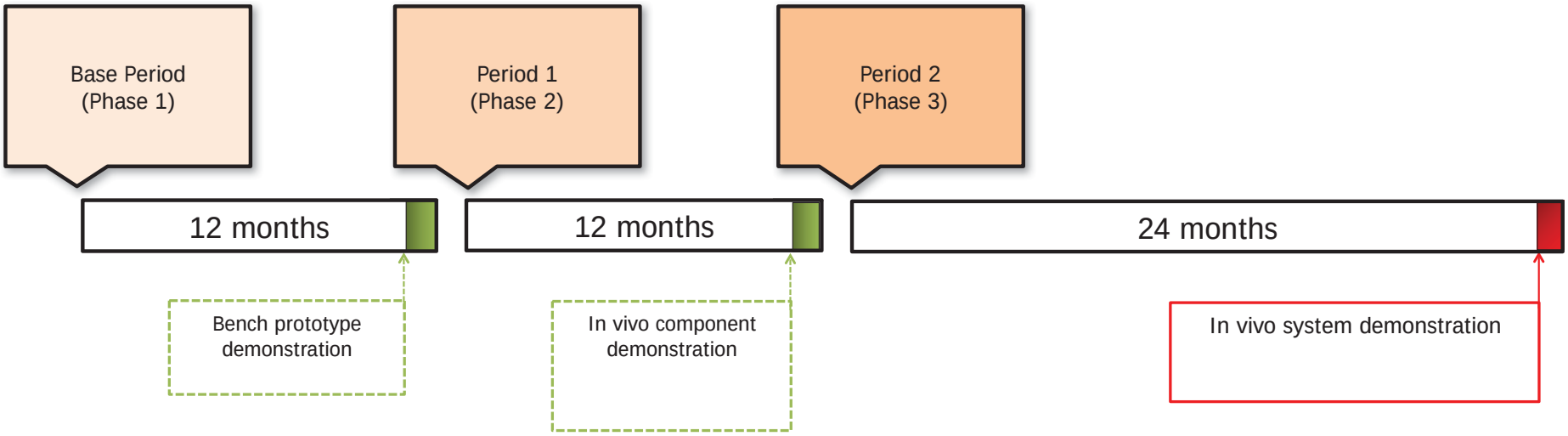


Important, but approximate dates



Period of performance

"The program is scheduled to span four years in three phases with critical milestones and deliverables expected in each phase." BAA pg. 5



Assuming satisfactory progress,

- We anticipate funding multiple performers for all four years.
- Funding for subsequent Periods is contingent on the availability of funds.

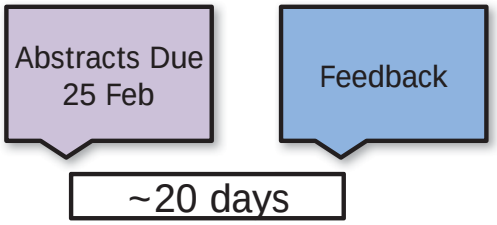
Proposal Abstracts

Abstracts are strongly **encouraged,** but optional.

Abstracts should include:

- Goals and Impact
  - What are you trying to do?
  - What is innovative in your approach?
  - How does it compare to the state of the art?
  - How much will it cost and how long will it take?
- Technical Plan
  - Outline your statement of work
  - Outline the critical risks
  - Provide specific milestones
- Capabilities
  - Team composition
  - Demonstrated translational success

Abstracts limited to 7 pages (excluding cover page).
For more details see BAA pgs. 25-26.

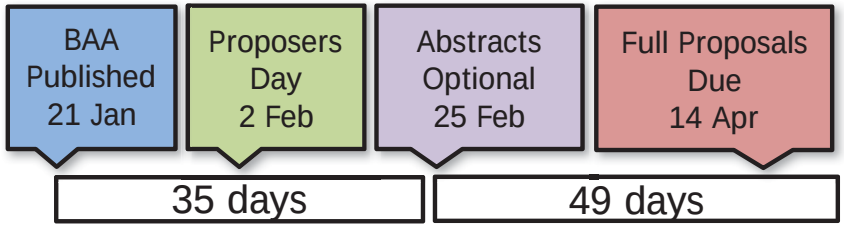


"DARPA will respond to abstracts with a statement as to whether DARPA is interested in receiving a full proposal."

You may submit a full proposal even if you did not submit an Abstract.

Full Proposal – Technical and Management

Nonconforming proposals may be rejected without review.



Volume I – Technical and Management Proposal

A. Executive Summary
B. Goals and Impact
C. Comparison with existing research
D. Technical Plan
E. Statement of Work
F. Schedule and Milestones
G. Program Organization
   Identify the PI, key personnel, and their roles

Attachments:

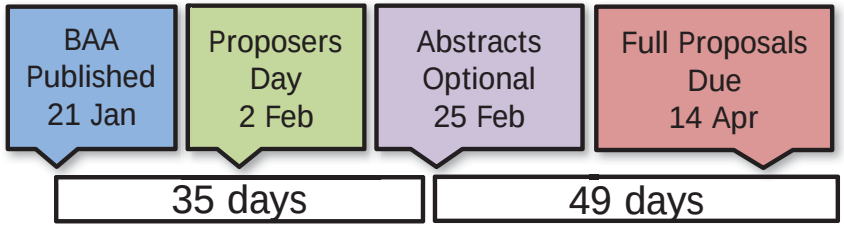
1. Summary Slides (no more than four)
2. Specifications Spreadsheet
3. Statement of Work

Full proposals limited to 30 pages
(plus 1 page each for the cover sheet and official transmittal letter).
For more details see BAA pgs. 26-29

"Proposers are encouraged to expand upon these required milestones (pgs. 12-15) and to add new milestones and deliverables specific to the approaches being proposed."

Full Proposal - Cost

Nonconforming proposals may be rejected without review.



Volume II – Cost Proposal

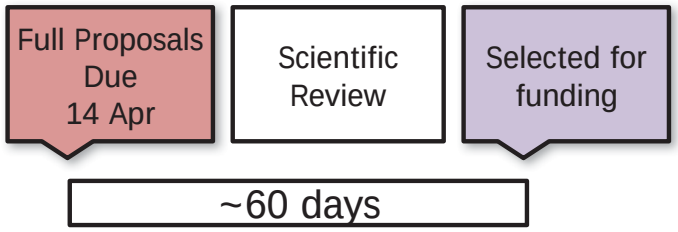
- Detailed cost breakdown by:
  a. major program tasks
  b. government fiscal year
  c. funding Period (phase)
  d. calendar fiscal year
- Summary of total program costs by funding period and task
- Summary of projected funding requirements by month
- Don't forget travel funds for all key personnel to attend the Kickoff Meeting and semi-annual PI Review meetings.
- Subcontractor proposals **must** be prepared at the same level of detail as that required of the prime.

Cost proposal does not have a page limit!
For more details see BAA pgs. 29-32.

More about cost

- DARPA will not provide feedback regarding dollar amounts – you tell us what it will cost to perform the proposed research.
- Additional guidance will be provided after Abstracts are evaluated.
- Evaluators are instructed to consider that "The proposed costs are realistic for the technical and management approach and accurately reflect the technical goals and objectives of the solicitation. The proposed costs are consistent with the proposer's Statement of Work and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach. The costs for the prime proposer and proposed subawardees are substantiated by the details provided in the proposal." (BAA pg. 33)
- "DARPA recognizes that undue emphasis on cost may motivate proposers to offer low-risk ideas with minimum uncertainty and to staff the effort with junior personnel in order to be in a more competitive posture. DARPA discourages such cost strategies." (BAA pg. 33)

The Review Process



- Scientific Review by government personnel from DARPA, NIH, NSF, FDA, and other US Government agencies.
- Proposals are not ranked, but evaluated for strengths and weaknesses with respect to the criteria published in the BAA:
  a) Overall Scientific and Technical Merit
  b) Potential Contribution and Relevance to the DARPA Mission
  c) Cost Realism
- Program Manager recommends proposals for funding.

See BAA pg. 33 for details regarding the evaluation criteria.

Teaming

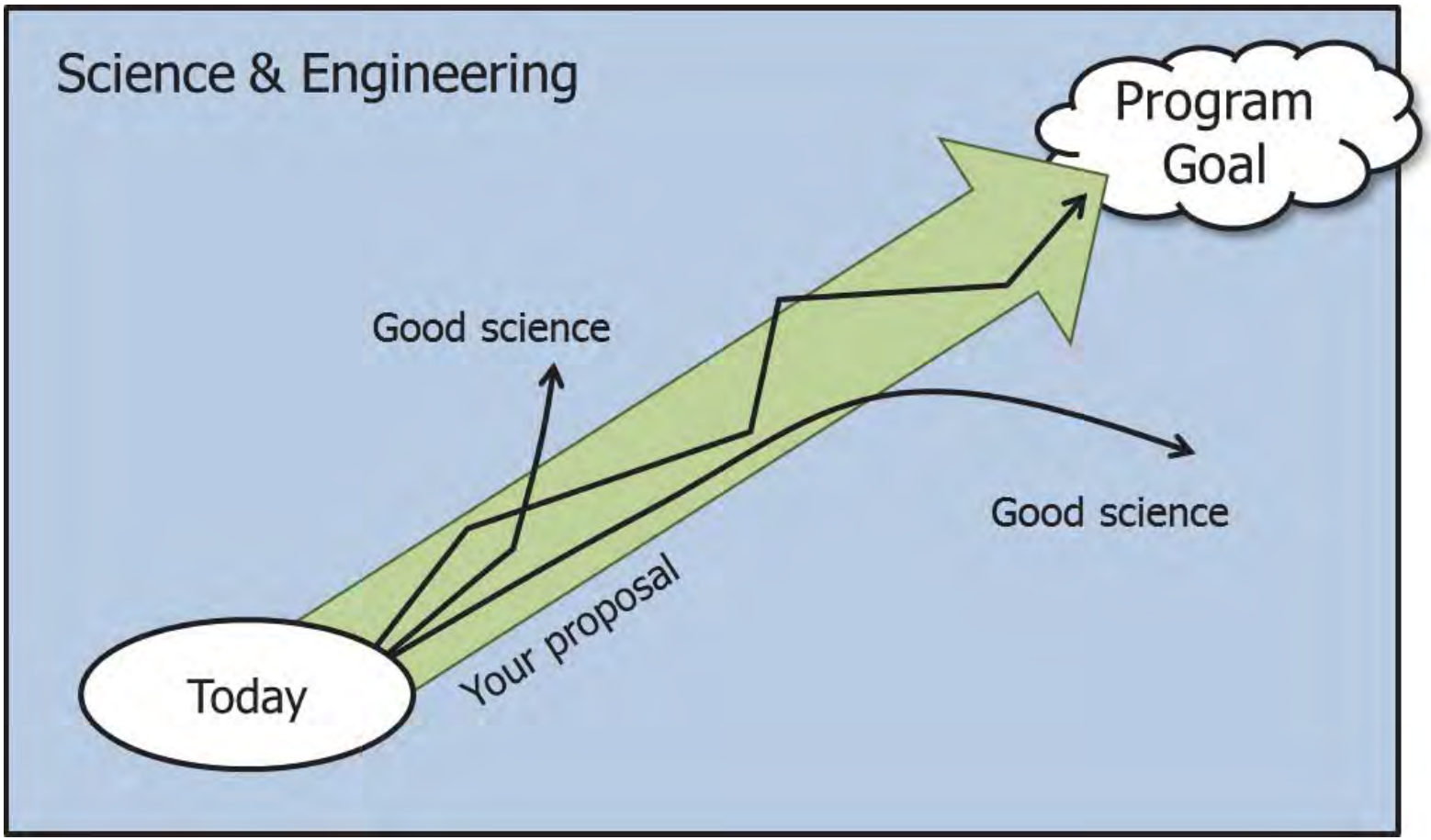
To fully address the BAA you might need to team with other entities.

- You must find your collaborators on your own.
- Your team should submit a unified proposal under a single PI.
- This BAA is open to educational institutions, government labs, and/or private companies.
- Foreign entities may join a team or submit as the PI.
- If you are a member of a team, you may join any number of other teams or form your own and submit a proposal as PI.
- Note that the cost volume for each team member must be at the same level of detail as for the PI.

Final bits of advice

- Read the BAA over and over again and follow all instructions carefully.
- A successful proposal addresses all aspects of the BAA.
  - Pay attention to “must”, “should”, “shall”, and “all” in the BAA.
  - Incomplete proposals will not be evaluated.
- Do not try to shoehorn ongoing, but not applicable, work into the BAA.
- Do not submit a rewritten NIH or NSF proposal.
- Do not propose to do anything that is not directly relevant to the BAA.
- Do not submit an irrelevant or incomplete proposal in the hope we’ll fund it anyway.
- A proposal abstract is highly recommended.

How DARPA thinks about your project



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PROPOSERS DAY

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