DIRECTOR'S VISION

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Over the course of evolution, humans have gained a special status in relation to other species. Notably, we have produced a far more complex and flexible society and tools for driving our own destiny. What is the essence of human intelligence (HI), which is the source of civilization, science, and technology? From a socio-biological perspective, HI can be considered a consequence of superior brain function, despite the fact that our physical capabilities are far less advanced than those of many other animal species. These mental functions enable social cooperation, long-term planning, and the accumulation and transmission of knowledge through spoken and written language.

With tremendous technological advances, however, modern society is also facing significant challenges in mental health. For example, autism spectrum disorder (ASD), schizophrenia, and other psychiatric conditions are imposing costly burdens on society. Such disorders reflect maladjustment to the social environment created by HI, underscoring the need for innovative solutions.

Artificial intelligence (AI), created only by the human brain, is strikingly outpacing HI in many areas. Through deep learning and other machine learning, AI is increasingly having a significant social impact. Efforts to elucidate how HI emerges, and to link HI and AI within the same framework, are sorely needed. Together, they allow us to explore the essential underpinnings of humanity and culture. **Uncovering principles of the brain basis for HI is the most challenging and urgent scientific frontier.**

To this end, we aim to establish a new WPI center that pioneers the innovative interdisciplinary study of **'Neurointelligence'** – a novel concept in neuroscience made possible only through a synergistic, multi-disciplinary collaboration with world-class researchers. Never before in human history have the experimental and computational tools for understanding how biological circuits underlie behavior and the potential to emulate their complex dynamics in machines been so perfectly aligned. Building on complementary resources and expertise at the University of Tokyo (UTokyo) and specific research institutes overseas, it is now timely to establish an International Research Center for Neurointelligence (IRCN). The team members assembled herein are already recognized world leaders in their individual disciplines, who now jointly seek an integration that promises unprecedented understanding of HI.

Together, we will tackle 3 aims:

1. **Establish bottom-up principles of neural circuit development.**
2. **Unravel mechanisms of neurodevelopmental disorders.**
3. **Innovate AI technologies based on these brain-based principles.**

By uniquely integrating biological, medical, cognitive, mathematical, and information sciences, this WPI will tackle the greatest challenge to mankind: **can the human brain understand itself?** The center's strategy will herald a new scientific paradigm of Neurointelligence**,** leading the way toward revealing core mechanisms of HI, correcting its disorders, and eventually shaping AI technologies to positively impact our future society. This new WPI center is characterized as follows:

1. Internationally Recognized Research Network

As Professor at Harvard University, Hensch leads the Boston Children's Hospital satellite of IRCN. Rapid, synergistic progress with global impact is further achieved by our extensive network of international partners across Europe, North America and Asia. Active student exchange programs amongst this network, supported by in-kind matching and the Director's Globalization Award (DGA), offer unparalleled training opportunities for scholars worldwide.

2. Integration of Neuroscience with Information Sciences and Clinical Research

The concept of Neurointelligence, the trademark of our WPI center, is based on a uniquely deep integration of neuroscience and AI research. For example, Kenichi Ohki, Kazuyuki Aihara, Mingbo Cai, Takamitsu Watanabe and Yukie Nagai actively incorporate computational approaches to neurobiology, clinical data and assistive robotics. Notably, IRCN includes large clinical centers in Tokyo and Boston for active translational research across ages, which cannot be achieved by other brain science institutes without clinical branches.

3. Research Goals with Major and Visible Social Impact

Building on the novel concept of Neurointelligence, IRCN addresses the global scientific challenge of identifying neural mechanisms underlying HI, how it emerges in development, and to better inform medical efforts for overcoming psychiatric and mental health problems. Ultimately, the center will give rise to new AI technologies, their social application and greater social impact.

IRCN takes a **Team Science** approach to research fusion combining 16 world-class principal

investigators (PIs) selected from renowned scientists among UTokyo and overseas research institutions. Team science will engage PIs across four research domains in close cooperation and coordination with each other, and the synergy among them will facilitate breakthrough insights. Specifically, the PIs of IRCN will have a common interest in the structural and functional development of neural circuits as the basis of Neurointelligence.

First, the area of **Neurodevelopment** includes Yukiko Gotoh, Masanobu Kano, Kazuo Emoto, Kenichi Ohki, and Yoko Yazaki-Sugiyama. They are engaged in biological research on the process of neural circuit development, modification and maturation from late fetal to postnatal periods. Second, **Human/clinical** research includes Sho Tsuji, Zenas Chao, Kiyoto Kasai and Hensch. Understanding how infants acquire language and the etiology of creativity or psychiatric pathology arising during critical periods of brain development will further deepen our knowledge of HI. Hensch focuses on early developmental disorders like autism in preclinical models and infants, while Kiyoto Kasai examines neurotypical adolescents and patients with schizophrenia by conducting MRI-based structural / functional analyses. Third, a strong **Computational** domain will be led by Kazuyuki Aihara, and includes Mingbo Cai, Takamitsu Watanabe and Yukie Nagai. Their work will give rise to new predictive modeling, neuromorphic hardware, robotics and AI technologies. Finally, **Technology** innovations will come from Haruo Kasai, Yasushi Okada and Shoji Takeuchi. They will develop cutting-edge approaches for assessing neural circuit plasticity, such as ultra-high resolution microscopy, functional analysis and manipulation of single synapses, or biohybrid sensors.

Together, these four domains now seed concerted bottom-up efforts to achieve the center's overall goals. Currently 13 Team Science projects are running in areas as diverse as Social Learning, Critical Period Timing, Prediction, Reinforcement, Intrinsic Activity, Multiscale imaging, Autism or Psychosis risk. These are also magnets for sustainable funding in the second half of our WPI term. Further, our Center stimulates joint projects with Harvard, including Boston Children's Hospital for translational research, as well as our vast network of complementary international partner institutions, to establish tools and broaden its global footprint and global outreach for training the next generation of Japanese and foreign scientists.

4. Recommendations of interim review

1) How will principles of brain development inspire next-generation AI?

Genes and environment dynamically shape the neural networks in the brain. Current AI is only loosely based on their final, feed-forward layered structure. We will, therefore, incorporate concepts of neuronal dynamics, synapse proliferation and pruning, excitatory-inhibitory circuit balance, sequential critical periods of plasticity, neuromodulation, reinforcement, prediction, top-down feedback, intrinsic activity, attention and collective behavior for a more wholistic approach to neuro-inspired computation. Such fusion Team Science reflects areas of strength amongst our stellar international faculty. The ultimate goal is to create next-generation AI that mimics HI more accurately and can succumb to mental illness insightfully. By doing so, we seek to understand the hallmark homeodynamic nature of HI to leverage the explore (plasticity) / exploit (stability) tradeoff and malleable 'moods' of the developing brain toward a more flexible and generalizable neuromorphic AI. Toward this undertaking, we note that the global pandemic has firmly established remote work as an efficient new normal. While also leading the Boston satellite, the Director will alternate stays in Japan once the quarantine restrictions are fully lifted.

2) Establishing IRCN graduate (PhD) program.

While the WPI mission does not support a teaching mission *per se*, all IRCN PIs are fundamentally involved in the training of multidisciplinary next-generation scientists through co-mentorship in Team Science and participation in WINGS and FoPM graduate training programs. Obstacles to teaching and formally mentoring PhD students will be discussed with the UTokyo IRCN Taskforce.

3) Continued improvement of gender balance

IRCN has already surpassed the gender disparity at our host UTokyo medical school by recruiting four female PIs. This ratio has been further improved to 25% by the recent pruning of male PIs who are no longer able to commit adequate time to the center. We will continue to target exceptional female PIs for recruitment as well as nurture them amongst our trainees.

4) Sustainability plan and UTokyo Commitment

Continuous support from the University remains critical to maintain and expand IRCN. In its draft *Fourth Mid-Term Goals and Plans*, the University of Tokyo (UTokyo) is committed to "facilitate the activities by research hubs such as IRCN and … will be transformed into permanent institutions," including plans for a new building on the current site. IRCN has already successfully acquired large-scale government funding, leading Gakujyutu Henkaku A ("iPlasticity") and Moonshot ("disease prediction") projects under DDs Kano and Aihara, respectively. The "Sustainability Office" will continue to seek domestic and foreign funding, as well as Social Collaboration Partnerships with companies (eg. Daikin, Softbank) and venture capital entrepreneurs. Philanthropic funds will be sought to sustain further trainee globalization activities.