IEEE SPMB 2020

Artificial Intelligence for Clinical Trial Design

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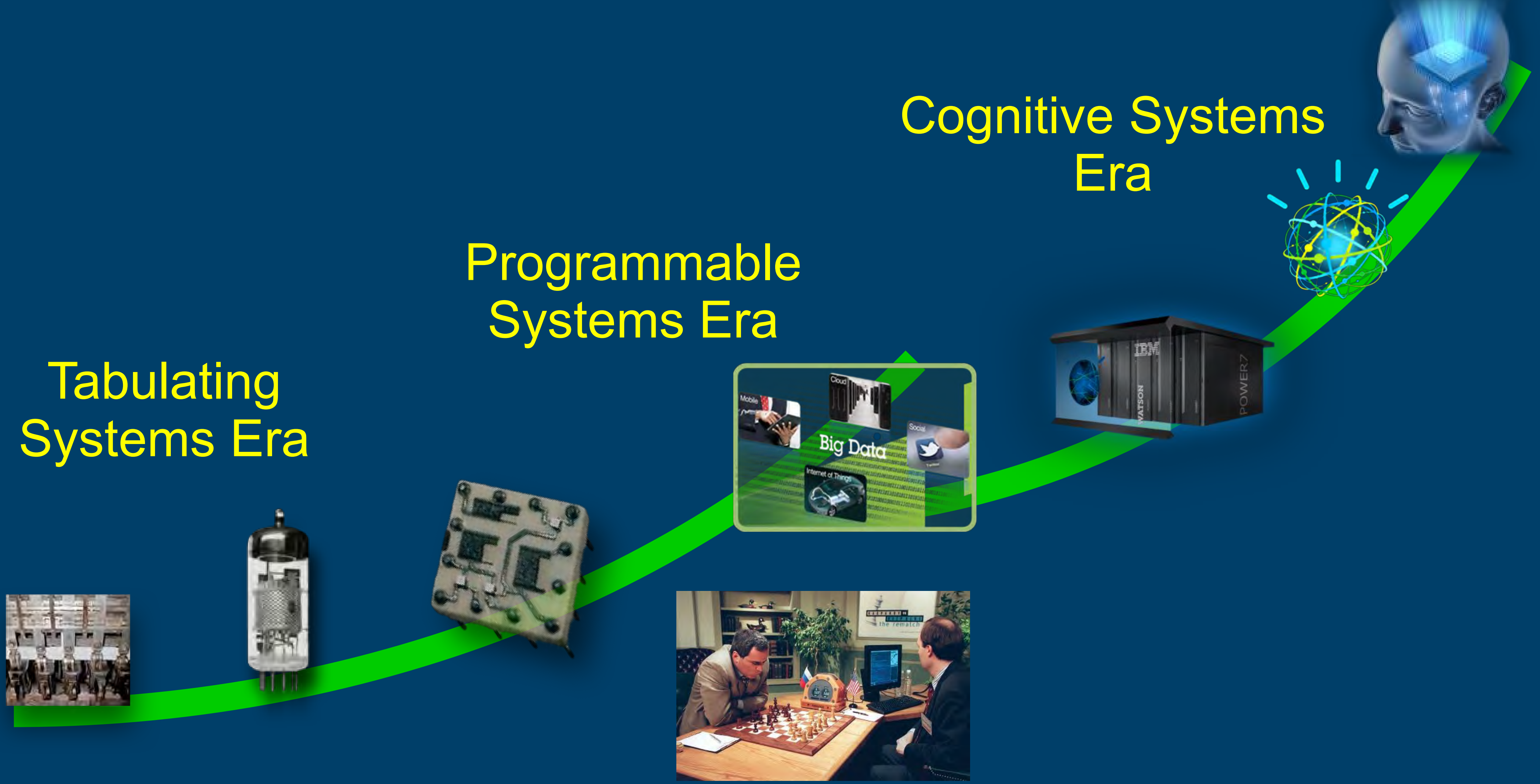
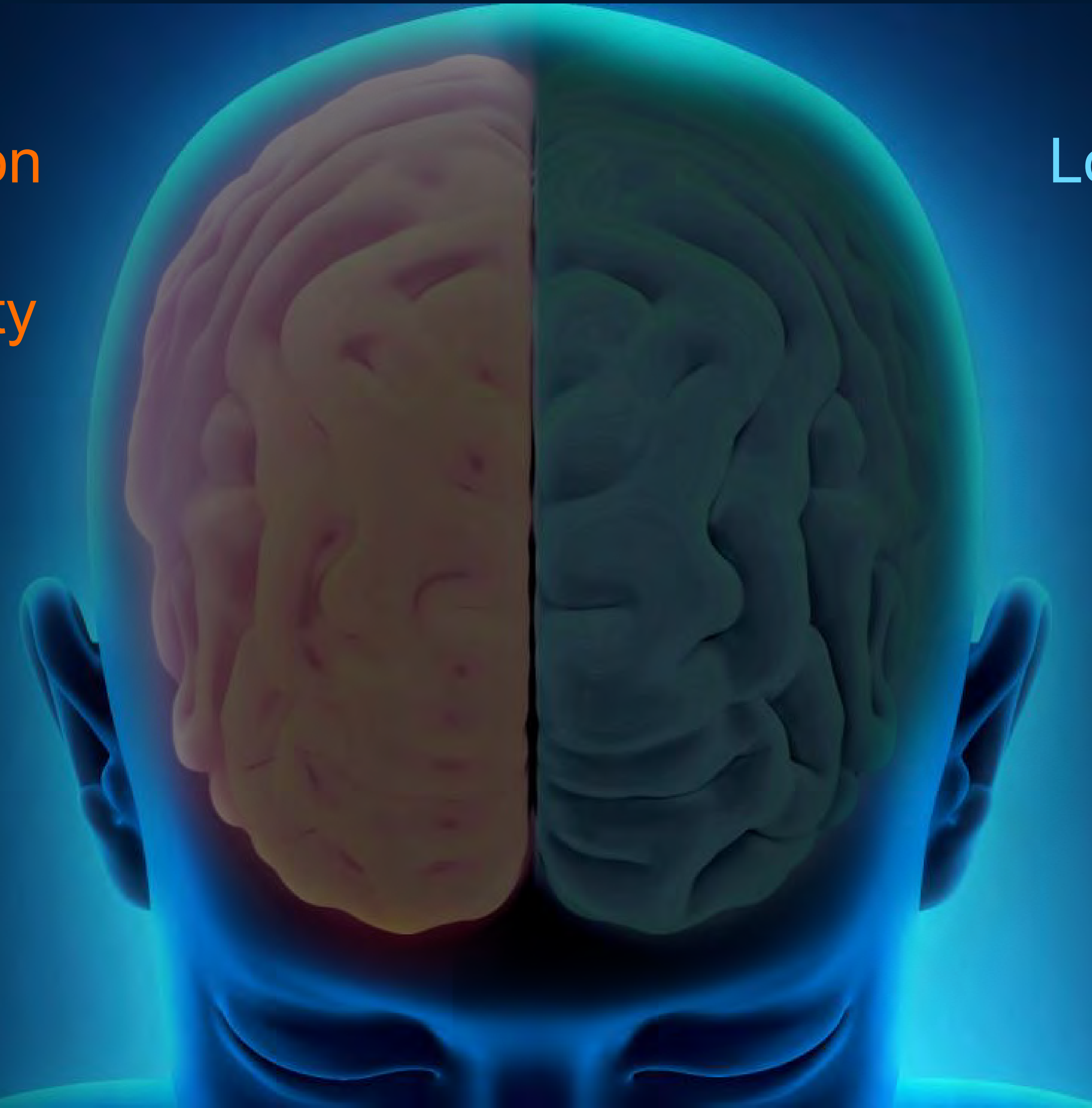
IBM Research

December 5, 2020

A (very) short history of AI





Emotion

Artistic ability

Imagination

Creativity

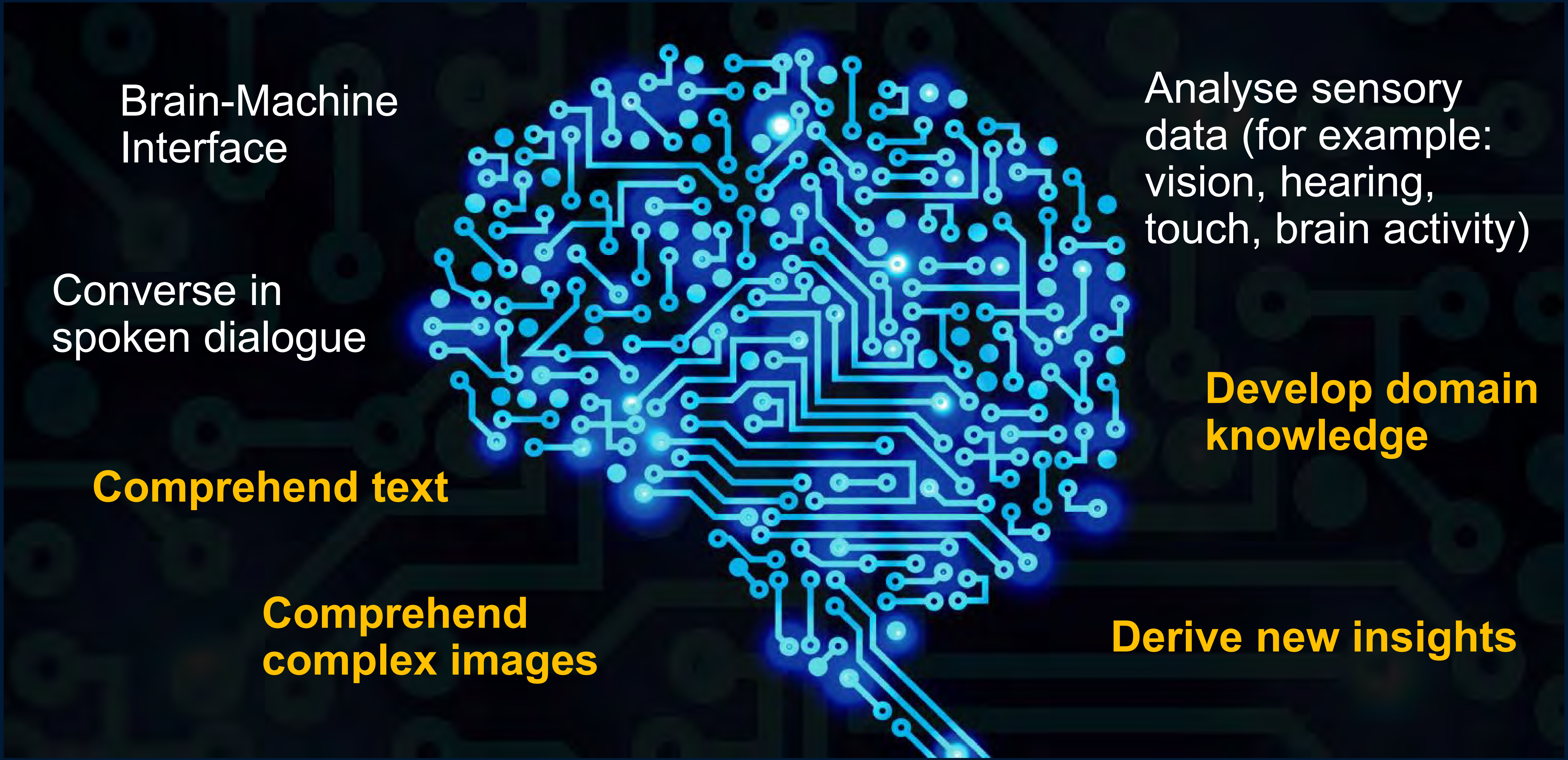
Logic

Analytical thought

Language

Objectivity

AI = Augmented (human) Intelligence



Data is the new natural resource

Social
- Twitter
- Facebook
- Instagram
- Non traditional social platforms

Genomics
- Family history
- Single Nucleotide Polymorphisms
- Copy Number Variation

Lifestyle
- Wearables
  - Fitbits
  - Monitors
- Apps
  - Phones
  - Watches
- Socioeconomics

Survey
- Cognitive test
- Questionnaires
  - Directed
  - Bureau of Statistics
  - Commission for Mental Health

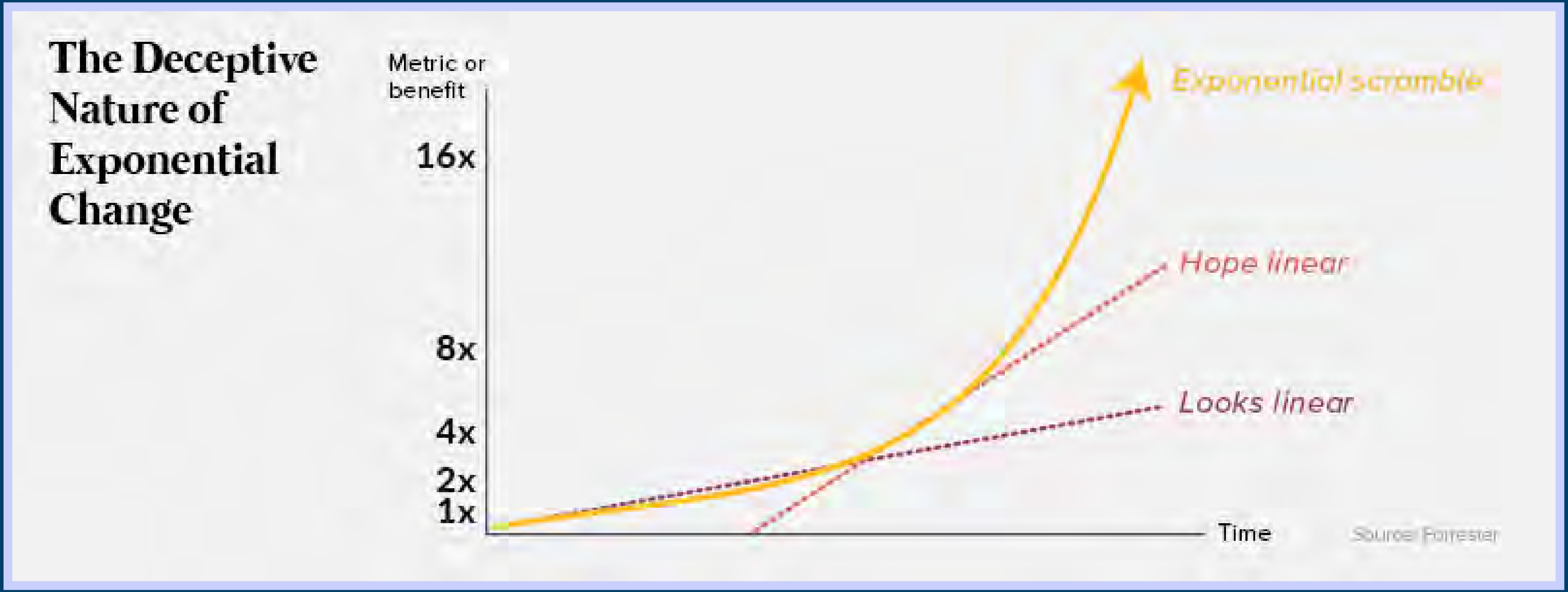
Response
- Times to apps
- To images

Clinical data
- Clinical GP notes
- Exit notes from hospitals
- Pathology laboratory

Imaging
- Eye
  - Retina
  - Movement & tracking
- CCTV
  - Behaviour
  - Movement

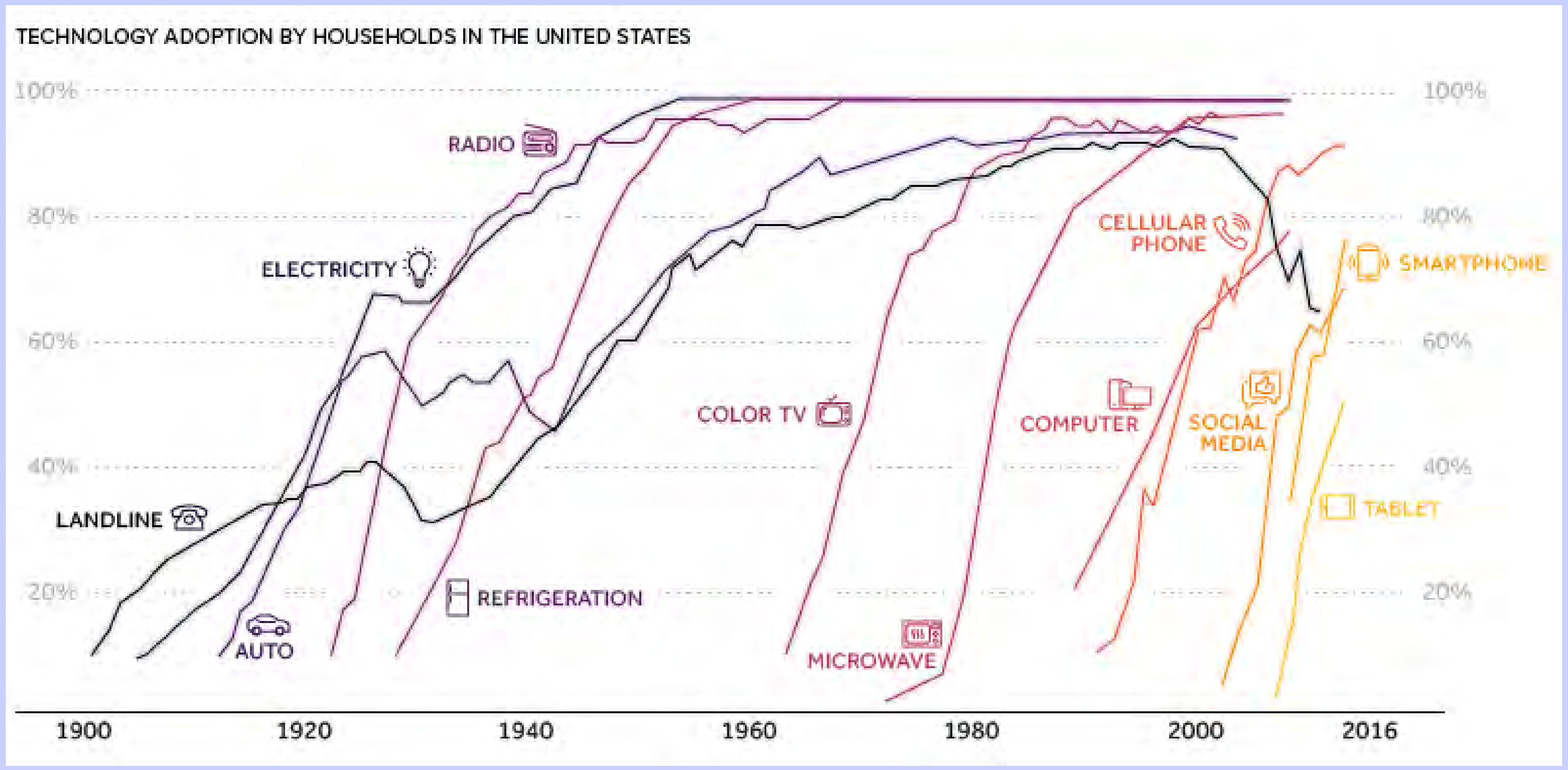
Speech
- What was spoken
- How it was said
  - Tone, volume, etc.

The pace of technological progress – a human misconception



http://www.visualcapitalist.com/the-8-major-forces-shaping-the-future-of-the-global-economy/

The future comes earlier these days than it used to…

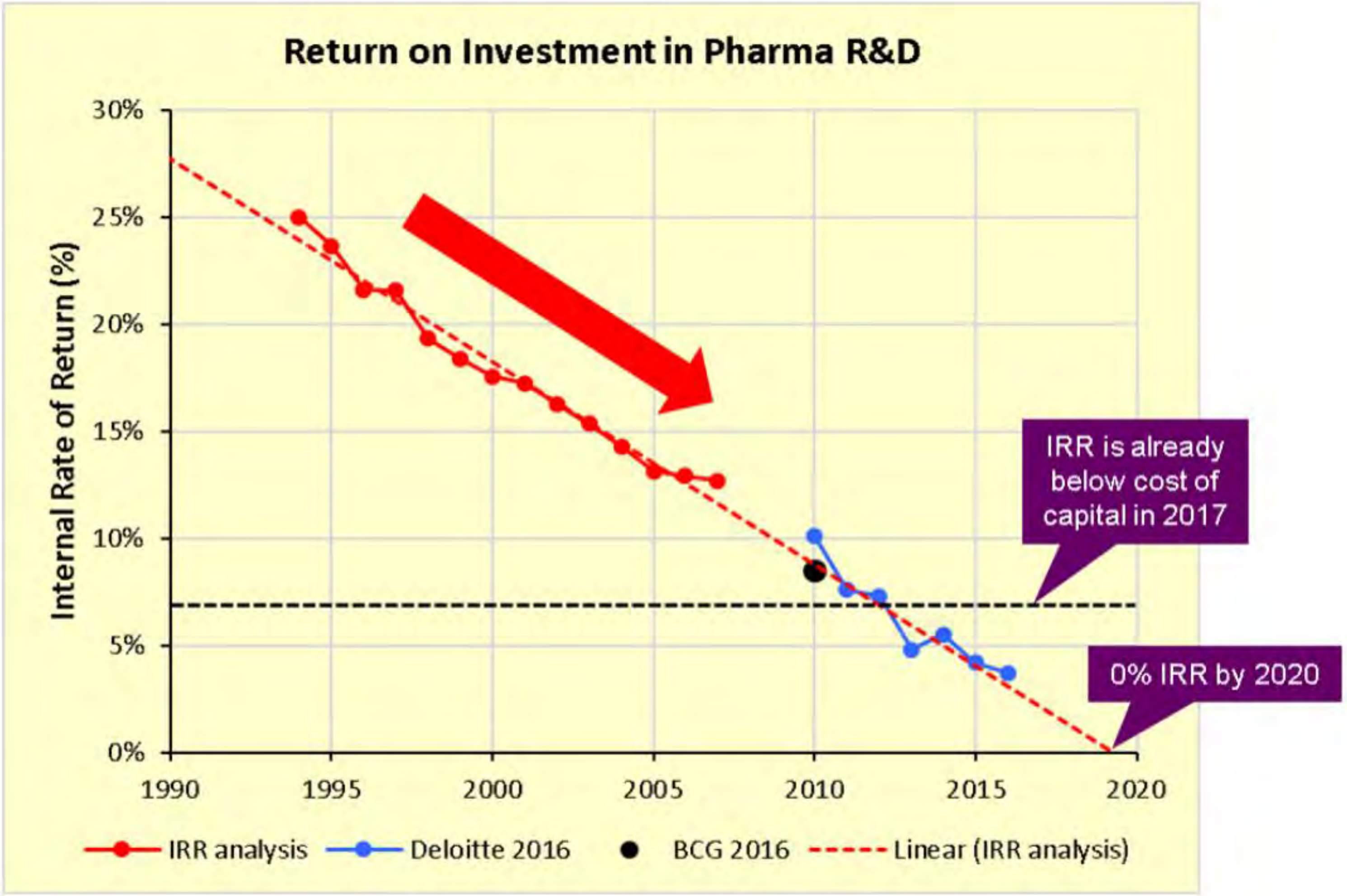


http://www.visualcapitalist.com/the-8-major-forces-shaping-the-future-of-the-global-economy/

AI must be used to assist the human decision maker

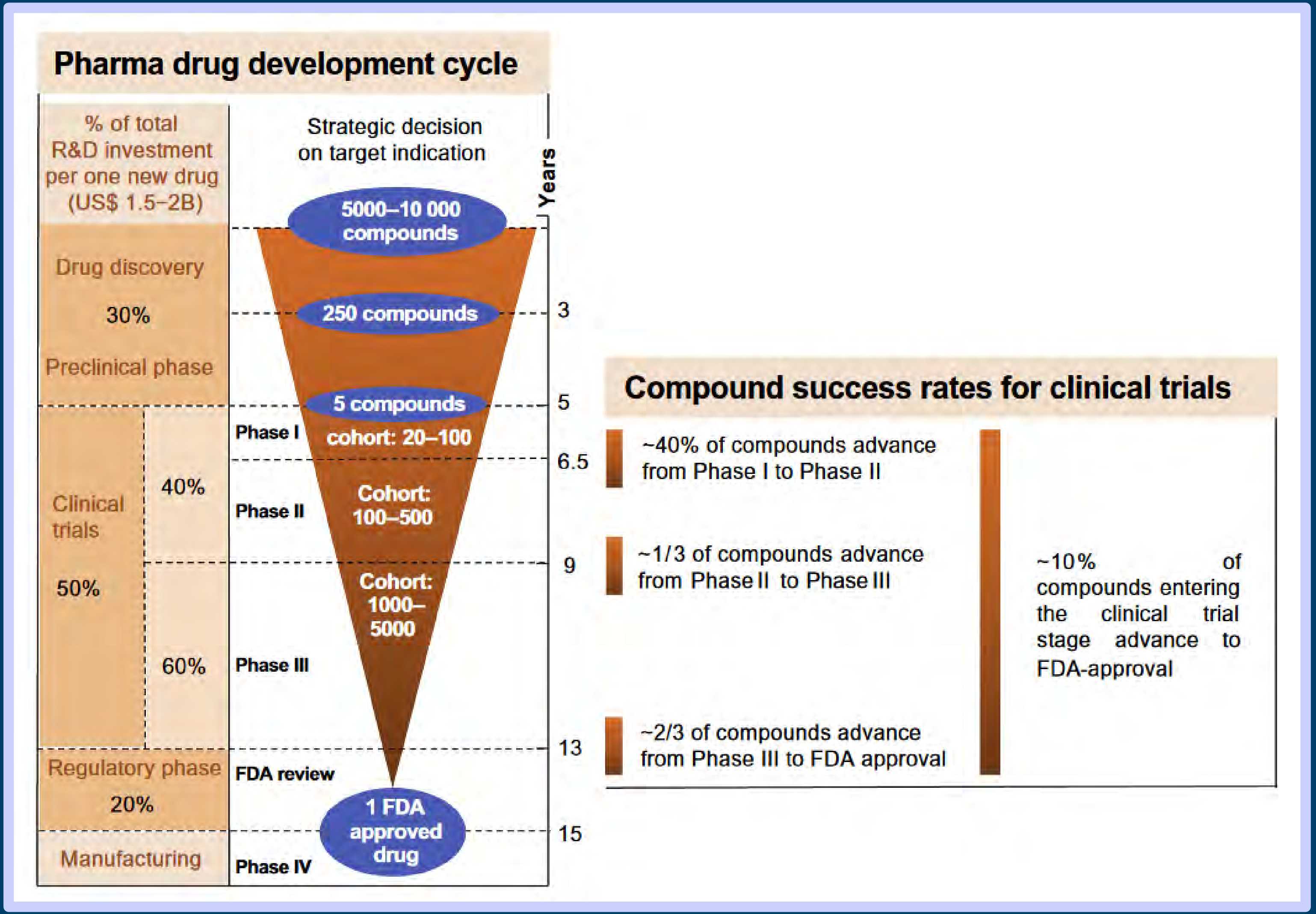
- Learn
- Extract Know-ledge
- Query & Retrieve
- Reason & Plan
- Decide

The ‘Pharma Dilemma’

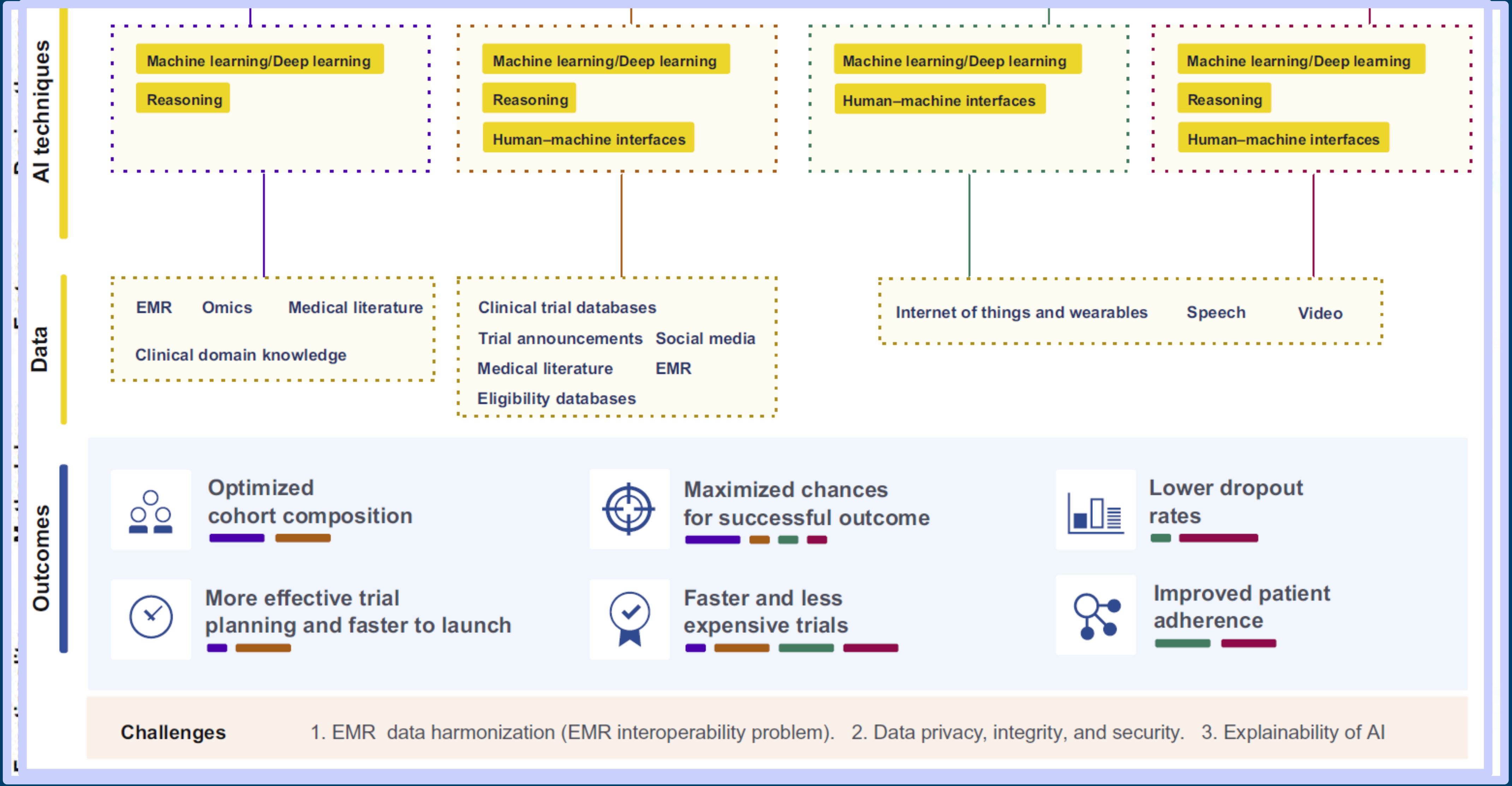


Source: EvaluatePharma, IRR analysis

The Drug Development Cycle



AI for clinical trial design: from themes to functionality…



Neurological diseases: burden on healthcare system

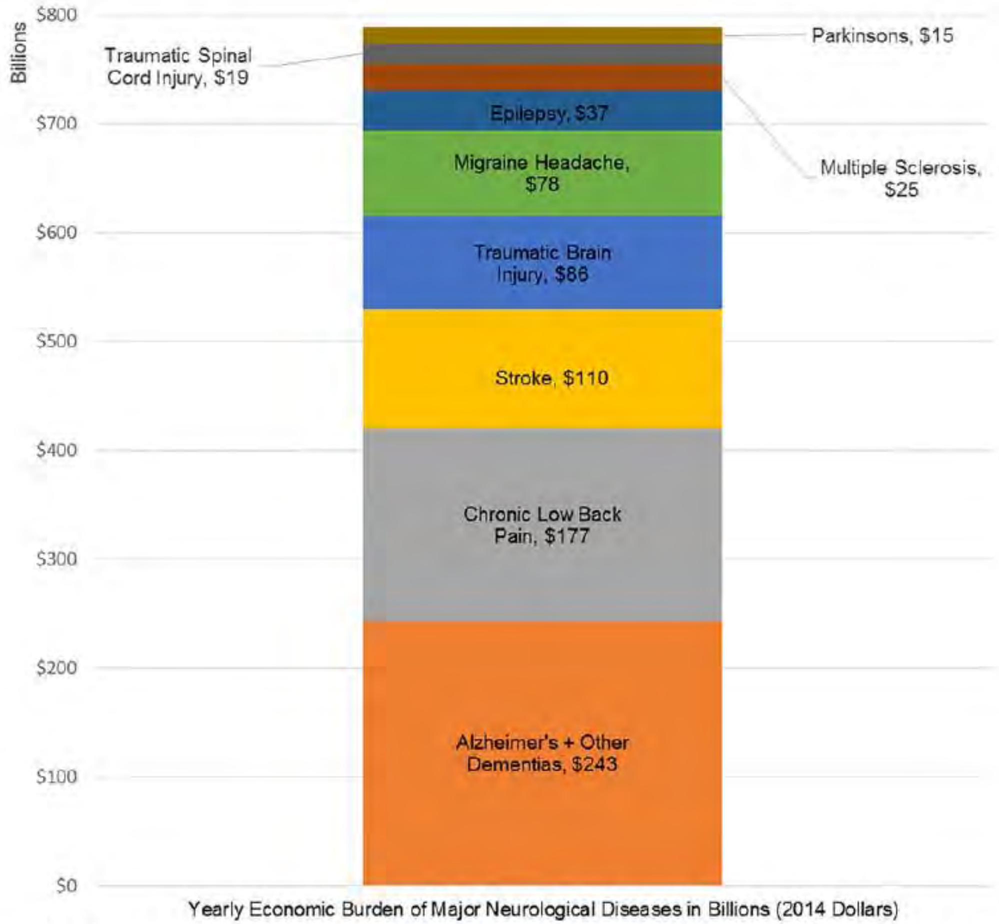


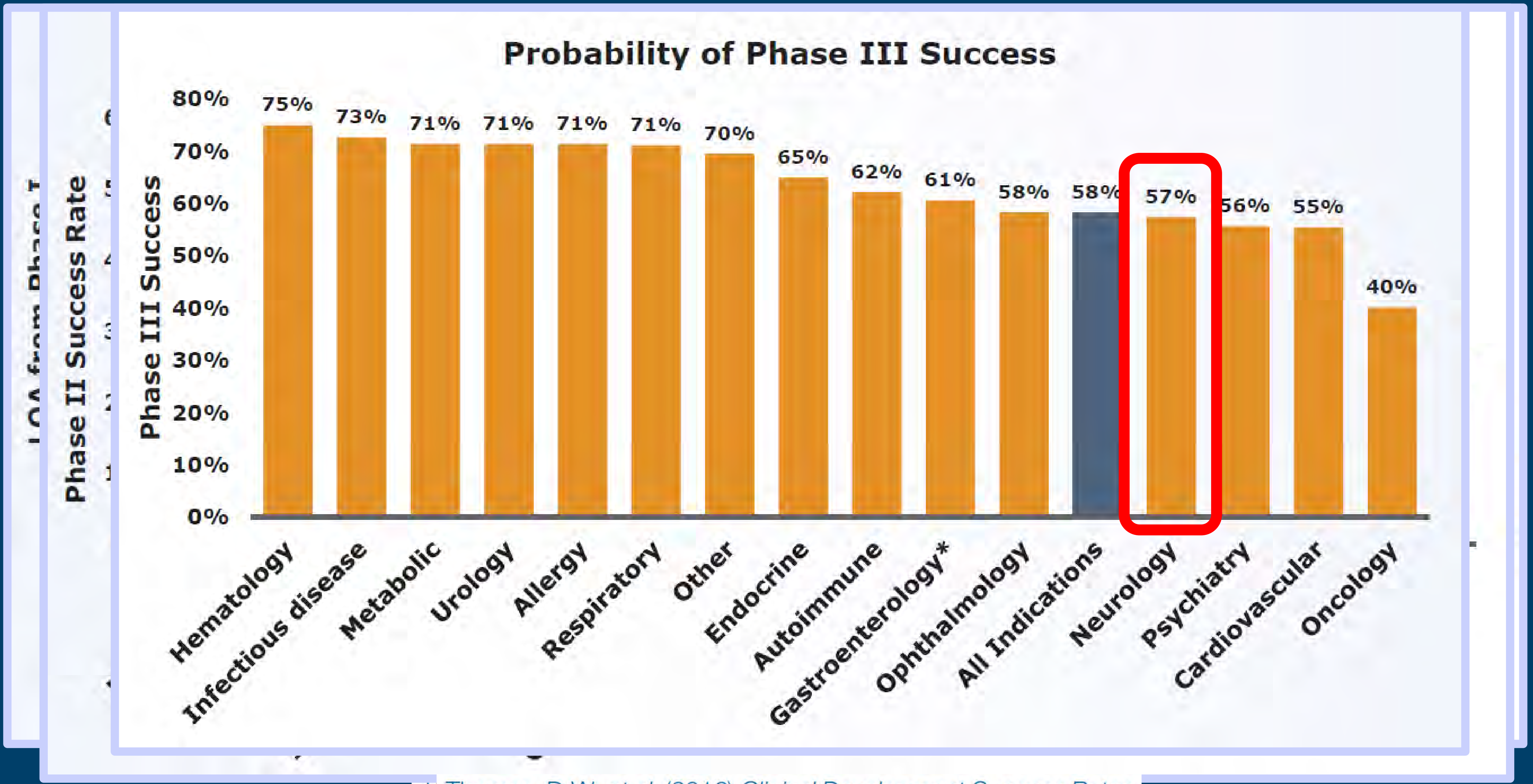
FIGURE: Annual costs of major neurological diseases. Costs of Alzheimer disease and other dementias, chronic low back pain, stroke, traumatic brain injury, migraine headache, epilepsy, multiple sclerosis, spinal cord injury, and Parkinson disease. Dollar figures were converted into 2014 values using the all items consumer price index for nonmedical (indirect) costs. Direct costs were converted using the medical price index.

Annals of NEUROLOGY — An Official Journal of the American Neurological Association and the Child Neurology Society

Invited Editorial

The burden of neurological disease in the United States: A summary report and call to action

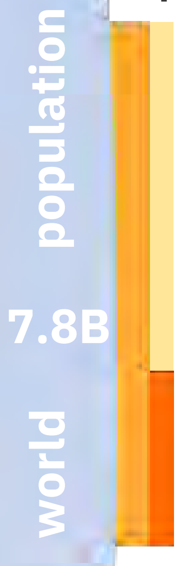
Clifton L. Gooch MD, Etienne Pracht PhD, Amy R. Borenstein PhD



Thomas, D.W. *et al.* (2016) *Clinical Development Success Rates 2006–2015,* BIO, Biomedtracker, and Amplion

Epilepsy: Patient Monitoring Using AI

Epileptic seizures are electro-chemical signalling disturbances in the brain.



~1% 65M **chronic epilepsy**

65% **treated with varying degrees of success**

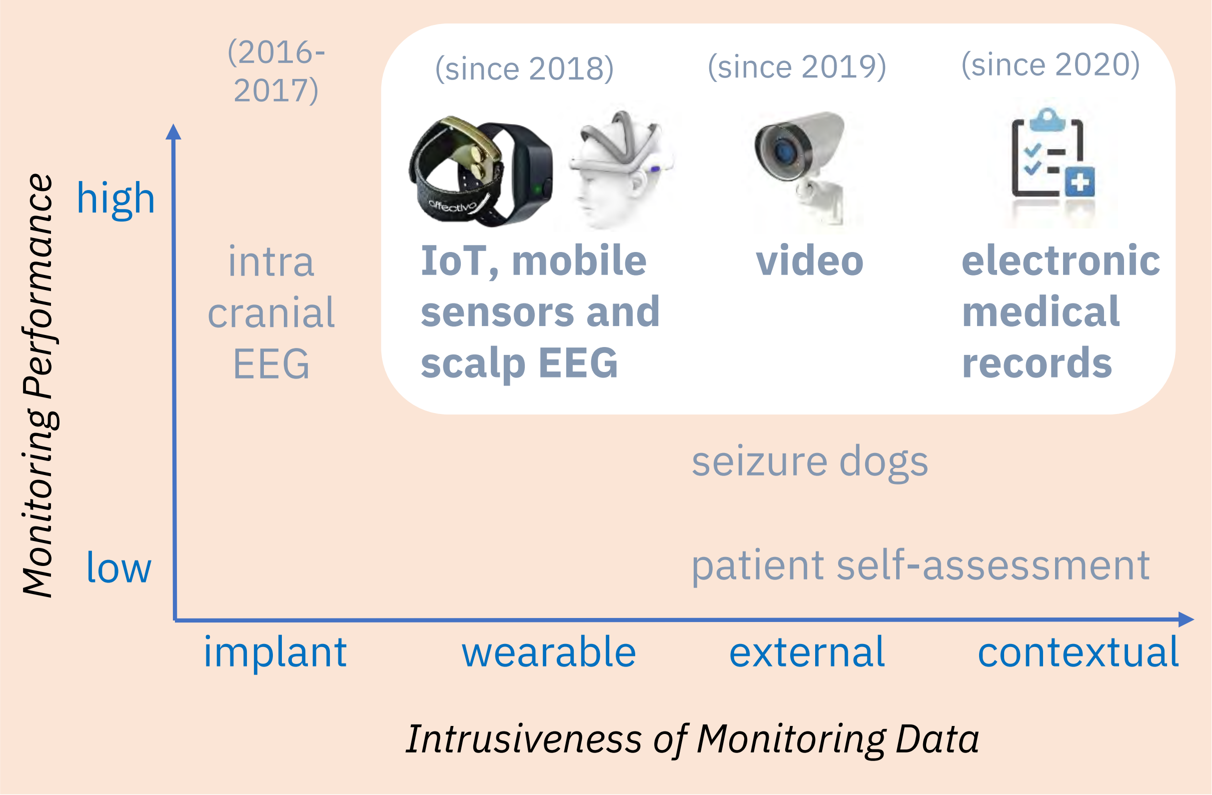
35% **drug resistant**

Disease burdens in the US and Europe are $15B and €20B p.a.

Automatically Detecting and Classifying Seizures

- Patients are often unaware of their seizures.
- Patients keep **diaries** but these are vastly inaccurate.
- Drugs are tested against diaries.
- Accurate seizure counts allow better treatment evaluation.

Digital Seizure Diaries: Automatic Seizure Tracking



We combine **deep learning**, **mobile sensors** and **video** data to monitor epilepsy patients for automatic real-time detection and classification of epileptic seizures. Integrating these logs with **Electronic Health Records** in **Digital Seizure Diaries** allows to design more efficient clinical trials and enables improved personalized diagnosis, treatment and disease management.

Selected Publications

- ***Trends in Pharmacological Sciences*** *(Cell Press)* 2019; 40(8), pp. 577-591.
- ***EBioMedicine*** *(The Lancet)* 2018; 27, pp. 103-111.
- ***MICCAI*** *(MLCN)* 2020; "SeizureNet: Multi-spectral deep feature learning for seizure type classification".

Partners

- *Harvard Medical School, Boston Children's Hospital, Royal Melbourne Hospital, The Alfred, St. Vincent's Hospital Melbourne, Temple University*

Personalized epileptic seizure prediction using electroencephalography (EEG) data measured by implanted electrode sensors

From Wearables to THINKables

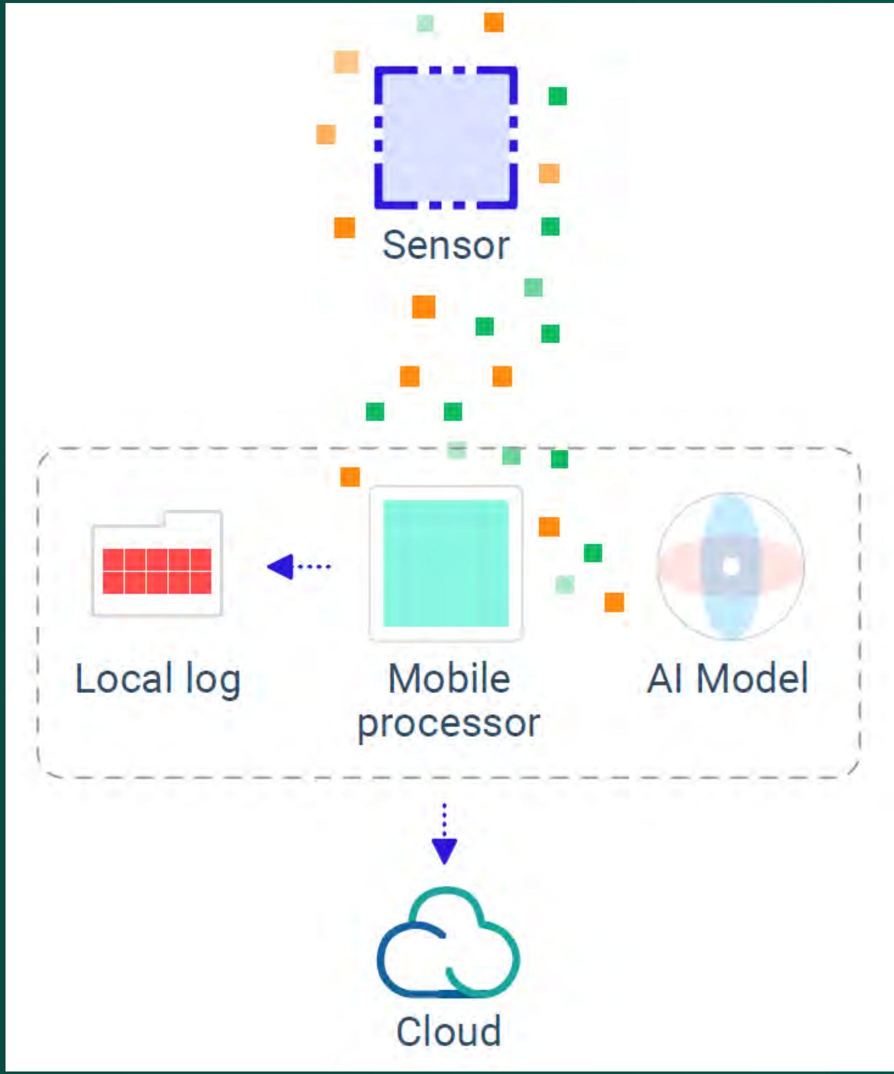


Table 1 Possible Candidates for Incorporation into Cognitive Sensors

Type of sensor	Components [a]	Application
Neural implants	Retinal stimulation electrodes	Bionic Eye
	EEG and ECoG electrodes	Brain activity monitoring, deep brain-stimulation, controlling prostheses with thought
	Artificial skin sensors	Tactile prostheses
	Electroceuticals	Nerve- and brain- stimulation
Tattoo sensors	Smart contact lenses	Biomarker detection
	Electrochemical tattoo batteries	Multimodal data measurement
	Always-on EEG electrode tattoos	
	Low-cost integrated circuit patches	
Molecular sensors	Nano- and Microfluidic sensors, portable DNA sequencers	DNA sequencing
	Smart pills, nanobiosensors, functionalized nanoparticles	Biomarker detection

a Abbreviations: ECoG, electrocorticography; EEG, electroencephalography.

Predicting epileptic seizures

Motivation

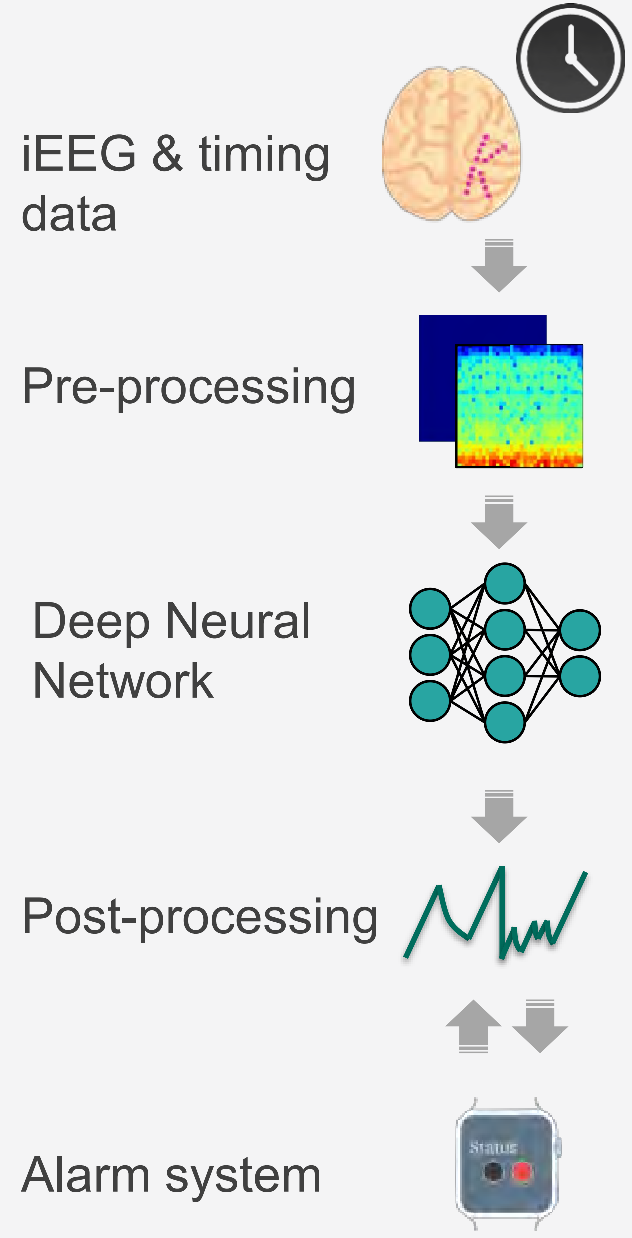
Build algorithms that allow a patient to manage their condition, alerting them to impending seizures

Data

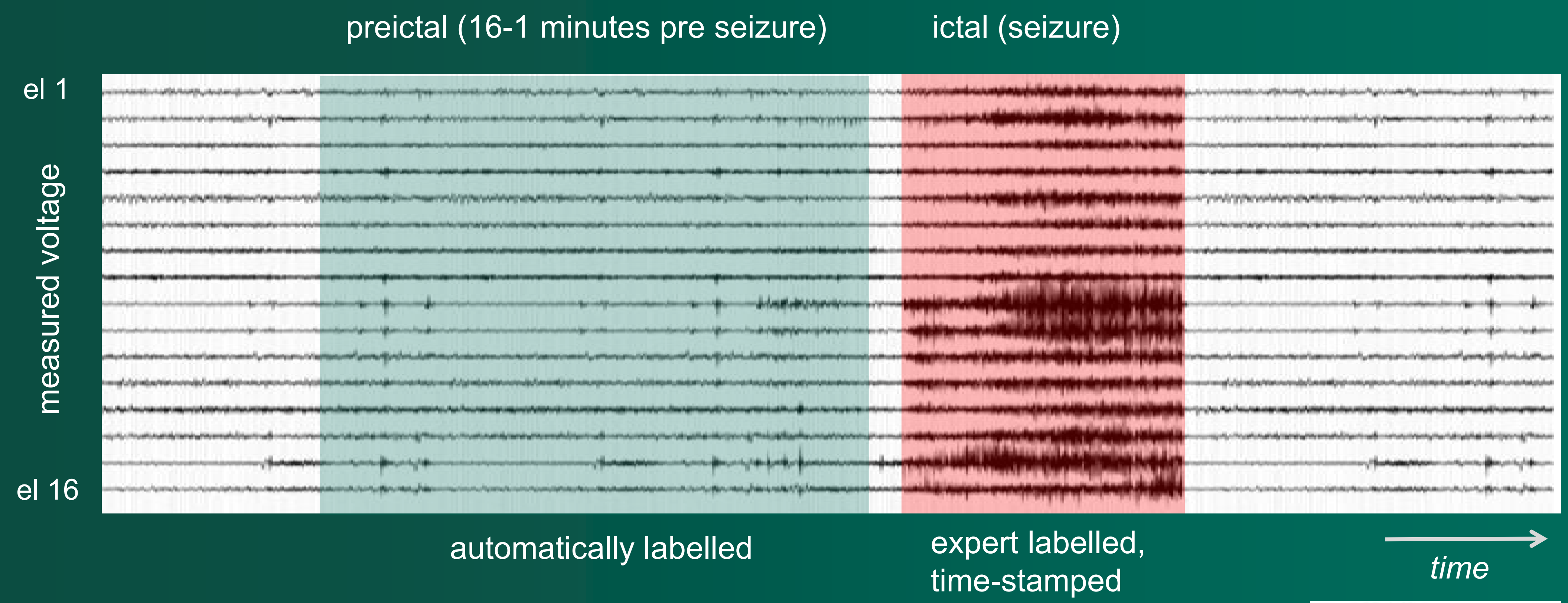
Long-term **intracranial** Electroencephalography (EEG) recordings from 15 patients provided by **Melbourne St. Vincent's Hospital** and **The University of Melbourne**, labelled by expert neurologists

Approach

- Train **deep neural network** to recognise patient-specific patterns emerging *before* a seizure
- Design a system that allows for **real-time** alarms
- Allow for tuning based on **patient's needs**

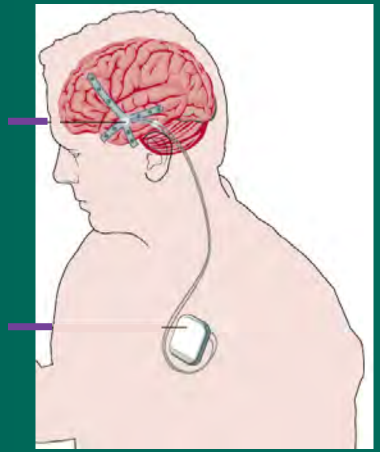


Data selection



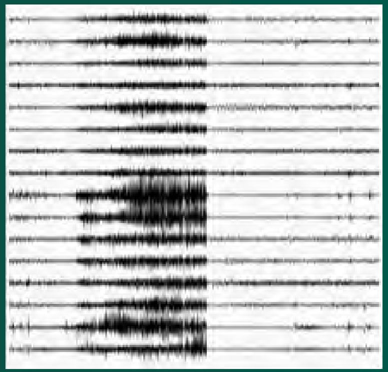
Seizure Prediction Task

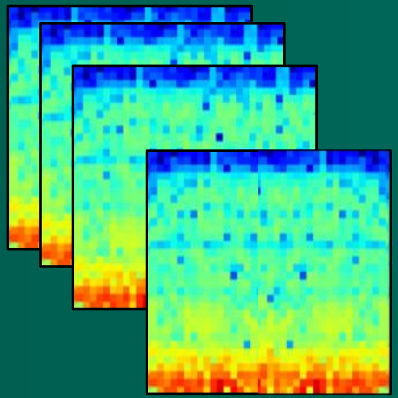
Train algorithm to distinguish between preictal and interictal (normal) brain signal
Interictal: at least 5 hours away from seizure



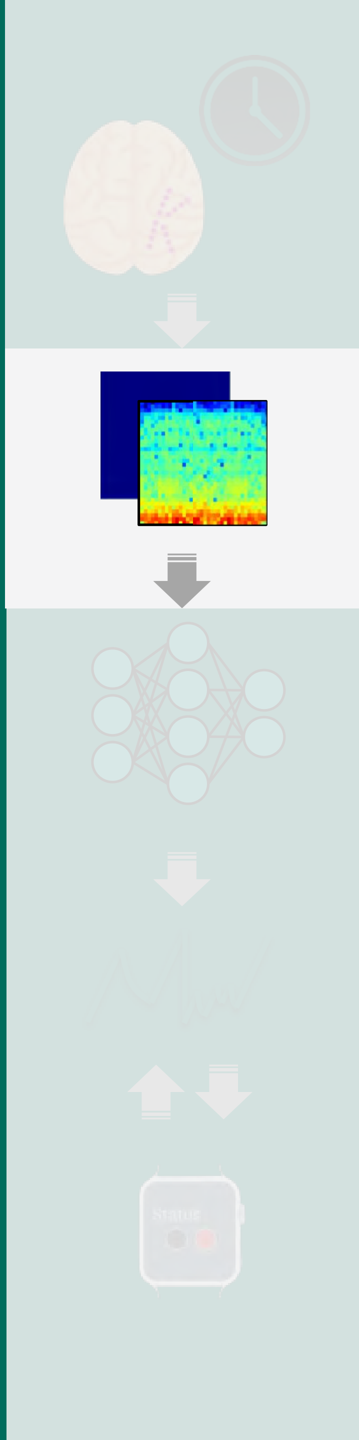
Data pre-processing

16 channel iEEG signal



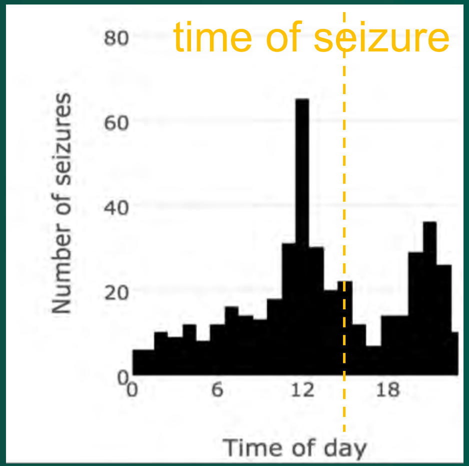


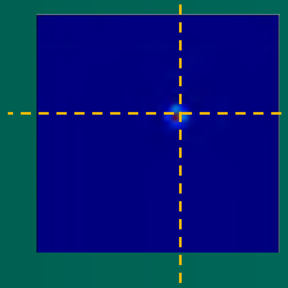
16 32x32 pixels spectrograms every 30 seconds



Spectral Information

Epileptic seizures correlate with neuronal synchronisation, which can be visualised using spectrograms.

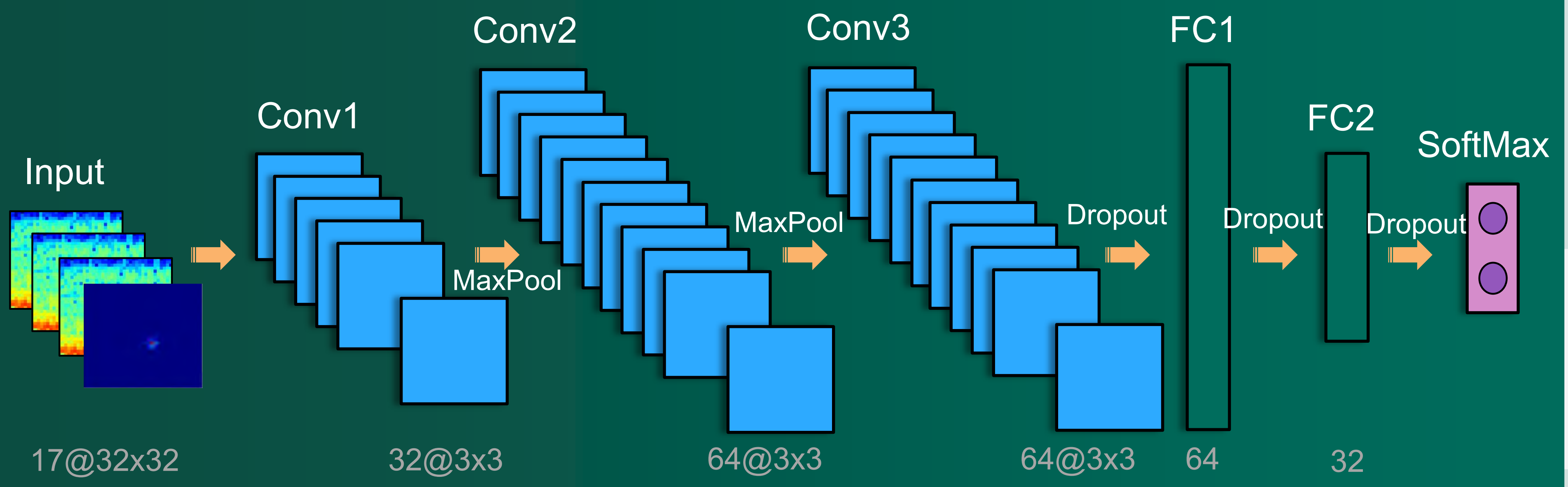


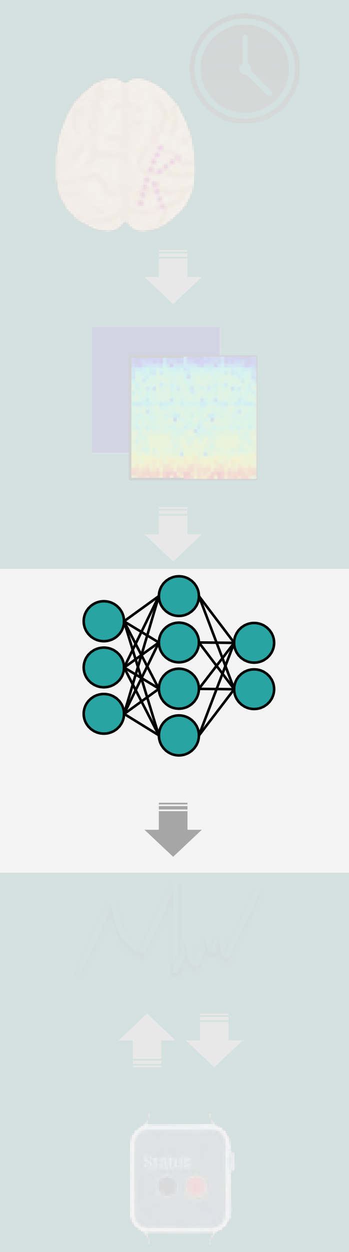


32x32 pixels timing image

Timing information: Seizures have been shown to follow different circadian rhythms in different patients.

Neural network architecture

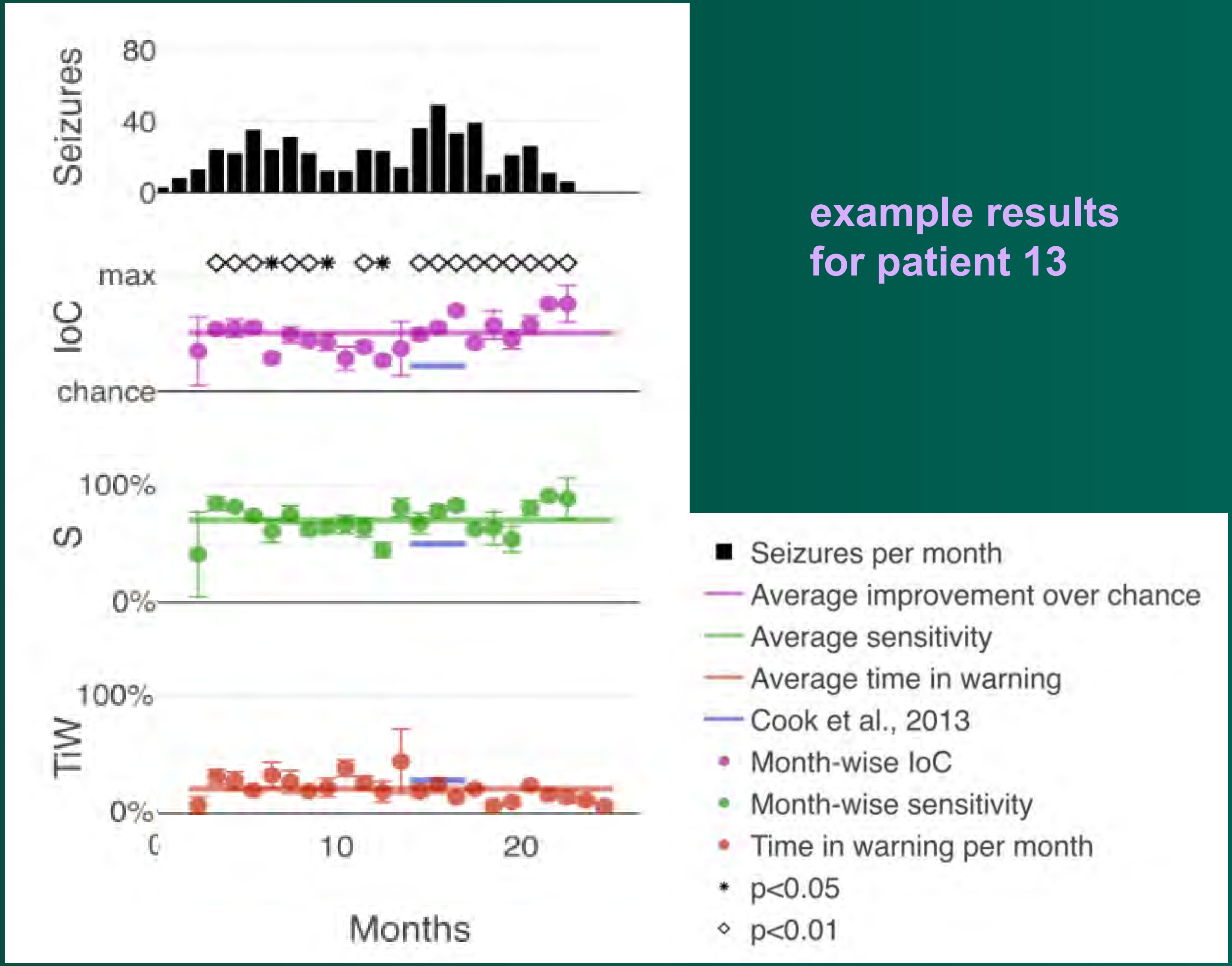




Real-Time Classifications

- Network classifies each sample of 30 seconds
- Without post-processing, this would result in one prediction every 30 seconds
- Exploiting the sequential structure of the data, temporal averaging should improve classification accuracy

Epileptic seizure prediction – study results



example results for patient 13

Study strategy:

- Pseudo-prospective
- Spectrograms + time information
- Post-processing (integrate and fire)
- Network retrained once a month
- **Tunable** by patients (max sensitive vs. least intrusive)

Results across all patients for entire duration of study:

- Mean sensitivity of **69%**
- Mean time in warning of **27%**
- Mean improvement over chance **42%**

Ultra-low power consumption mobile processor implementation for mobile deployment

Precursor: Predicting Epileptic Seizures - Published in EBioMedicine (2018)

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This AI can spot epilepsy seizures before they happen

WIRED — Elon Musk Isn't the Only One Trying to Computerize Your Brain

Elon Musk Isn't the Only One Trying to Computerize Your Brain

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WIRED — IBM Wants to Implant Fake Brains in Real Brains to Prevent Seizures

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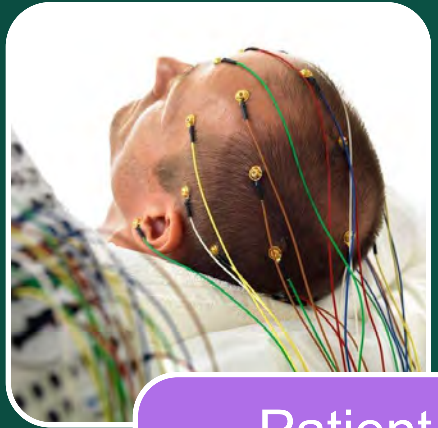
EMERGING TECH

From drones to bionic arms, here are 8 examples of amazing mind-reading tech

Mind-reading tech is here to help, not put you away for thoughtcrime

Epileptic seizure detection: re-inventing the epilepsy monitoring unit

Manual interpretation of scalp EEG – process pipeline

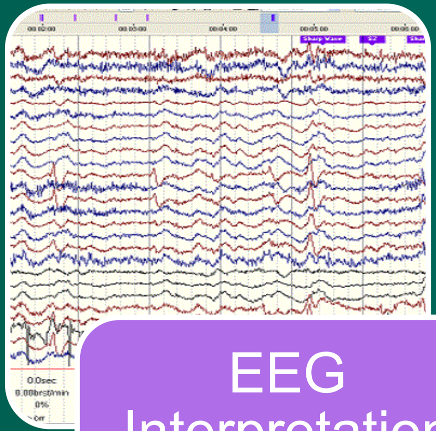


Patient Preparation

- Patients are prepared for the test.

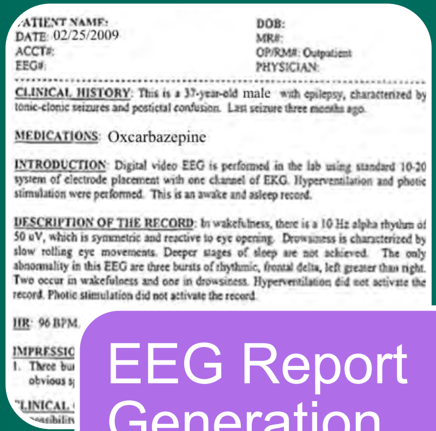
EEG Recording

- EEG ranging from 22 minutes to several days is recorded.



EEG Interpretation

- Certified physicians interpret EEG.



PATIENT NAME: DOB:
DATE: 02/25/2009 MR#:
ACCT#: OP/RM#: Outpatient
EEG#: PHYSICIAN:

CLINICAL HISTORY: This is a 37-year-old male with epilepsy, characterized by tonic-clonic seizures and postictal confusion. Last seizure three months ago.

MEDICATIONS: Oxcarbazepine

INTRODUCTION: Digital video EEG is performed in the lab using standard 10-20 system of electrode placement with one channel of EKG. Hyperventilation and photic stimulation were performed. This is an awake and asleep record.

DESCRIPTION OF THE RECORD: In wakefulness, there is a 10 Hz alpha rhythm of 50 uV, which is symmetric and reactive to eye opening. Drowsiness is characterized by slow rolling eye movements. Deeper stages of sleep are not achieved. The only abnormality in this EEG are three bursts of rhythmic, frontal delta, left greater than right. Two occur in wakefulness and one in drowsiness. Hyperventilation did not activate the record. Photic stimulation did not activate the record.

HR: 96 BPM.

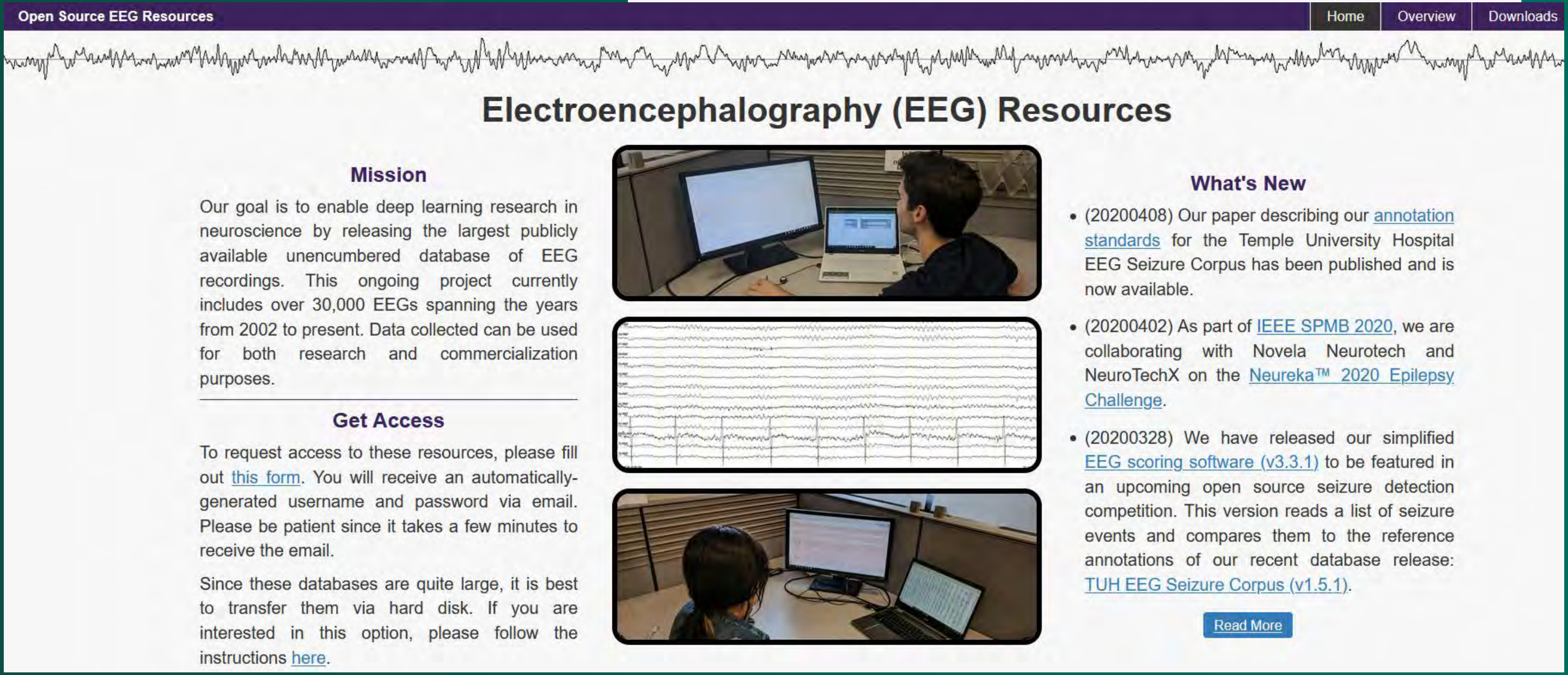
EEG Report Generation

- A report of findings (e.g. abnormality) is prepared.

Normal or abnormal EEG? → **Is there an epileptic seizure? Can we timestamp it?** → **Which type of seizure is it?**

Automatic interpretation of scalp EEG – data

Seizure type Label, Type, [Superclass]	Available train and test data		
	Patients	Files	Seconds


Open Source EEG Resources

Home | Overview | Downloads

Electroencephalography (EEG) Resources

Mission

Our goal is to enable deep learning research in neuroscience by releasing the largest publicly available unencumbered database of EEG recordings. This ongoing project currently includes over 30,000 EEGs spanning the years from 2002 to present. Data collected can be used for both research and commercialization purposes.

Get Access

To request access to these resources, please fill out this form. You will receive an automatically-generated username and password via email. Please be patient since it takes a few minutes to receive the email.

Since these databases are quite large, it is best to transfer them via hard disk. If you are interested in this option, please follow the instructions here.

What's New

- (20200408) Our paper describing our annotation standards for the Temple University Hospital EEG Seizure Corpus has been published and is now available.
- (20200402) As part of IEEE SPMB 2020, we are collaborating with Novela Neurotech and NeuroTechX on the Neureka™ 2020 Epilepsy Challenge.
- (20200328) We have released our simplified EEG scoring software (v3.3.1) to be featured in an upcoming open source seizure detection competition. This version reads a list of seizure events and compares them to the reference annotations of our recent database release: TUH EEG Seizure Corpus (v1.5.1).

Read More

Identifying epileptic seizure types

Motivation:

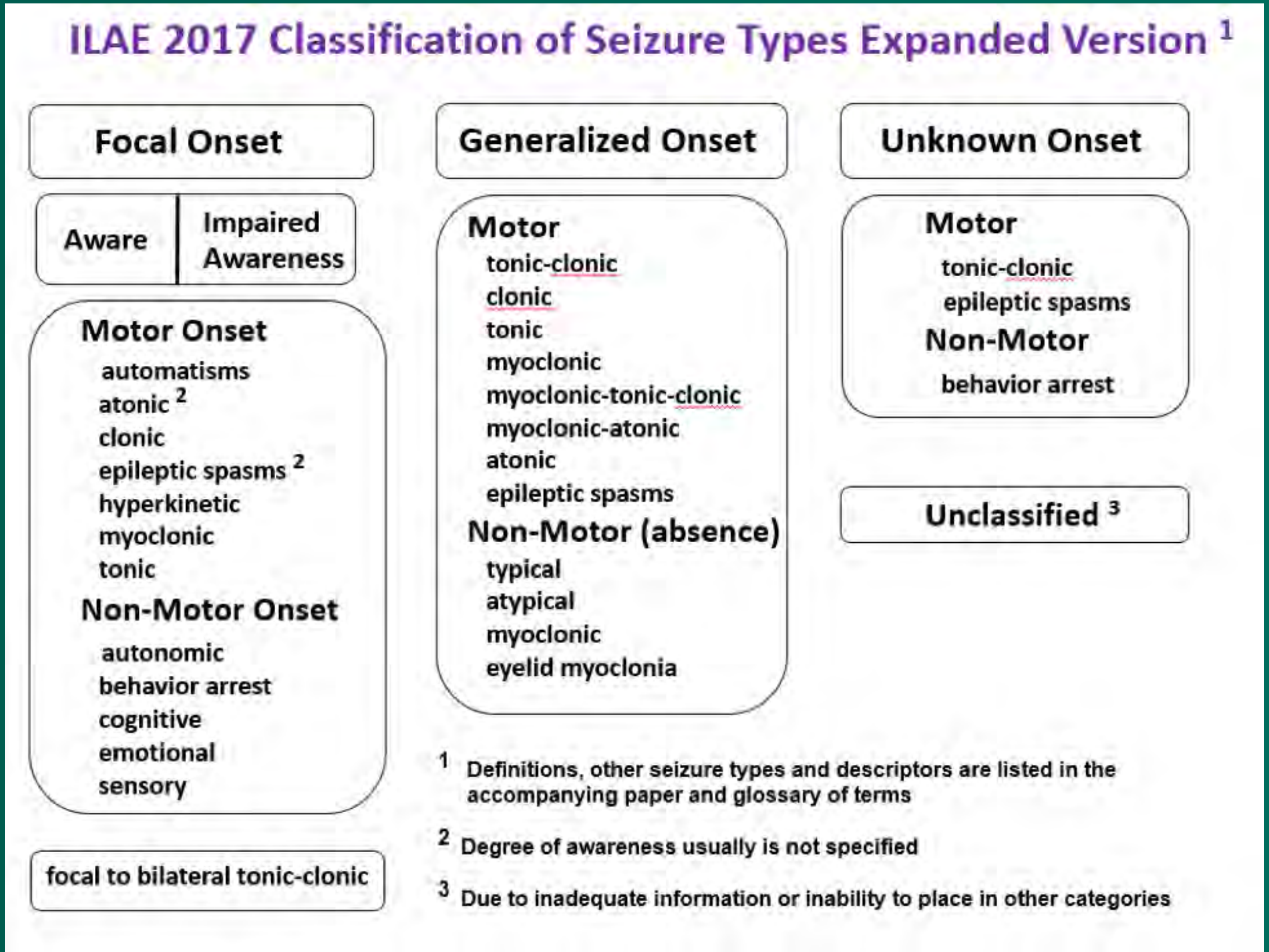
- Patients may have more than one type of seizure
- The type of seizure may inform therapy/medication
- Tracking types and each type’s rate may further inform medication adjustments
- Type information may help in diagnosis and to make clinical trials more nuanced

Implementation:

- Convolutional neural networks for binary classifiers
- Focus on preserving spatial electrode information

Seizure classes investigated:

- Focal/General, Motor/Non-motor, Tonic/Tonic-clonic, Complex-partial/Simple-partial



What type of epileptic seizure is it?

MLCN 2020

MACHINE LEARNING IN CLINICAL NEUROIMAGING, IN CONJUNCTION WITH MICCAI, 4 OCTOBER 2020, LIMA – PERU

SeizureNet: Multi-Spectral Deep Feature Learning for Seizure Type Classification

Umar Asif (IBM Research)*; Subhrajit Roy (IBM Research); Jianbin Tang (IBM Research); Stefan Harrer (IBM Research)

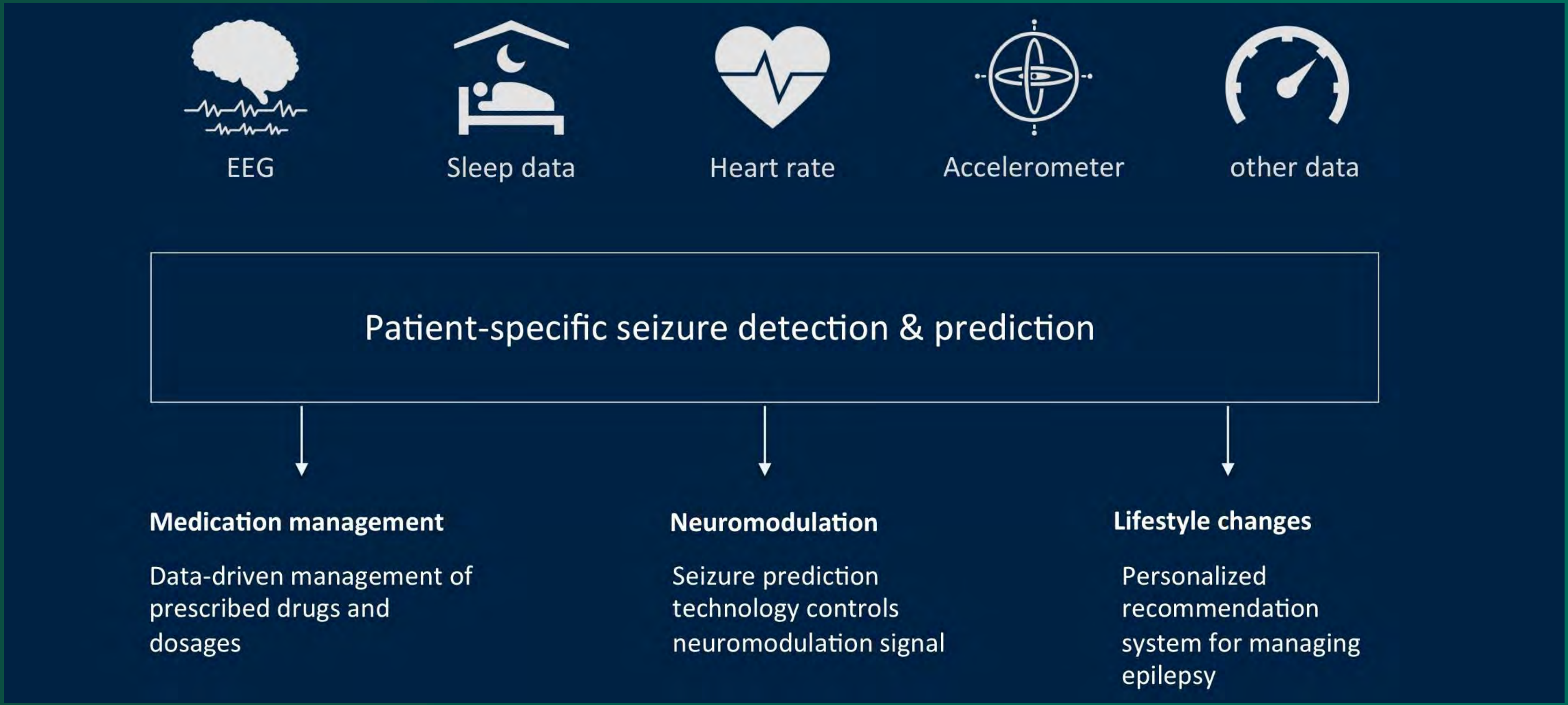
VB The Machine GamesBeat Jobs Special Issue

The Machine
Making sense of AI

IBM's AI classifies seizures with 98.4% accuracy using EEG data

Towards a fully automated digital seizure diary

Current work: multimodal data classification



Data modalities include:

intracranial EEG, **scalp EEG**, **ECG**, **body temperature**, blood pressure, movement patterns, sleep data, **heart rate**, **video**, audio, **electronic health records**, electrodermal activity, photoplethysmogram

Find out more…

Trends in Pharmacological Sciences

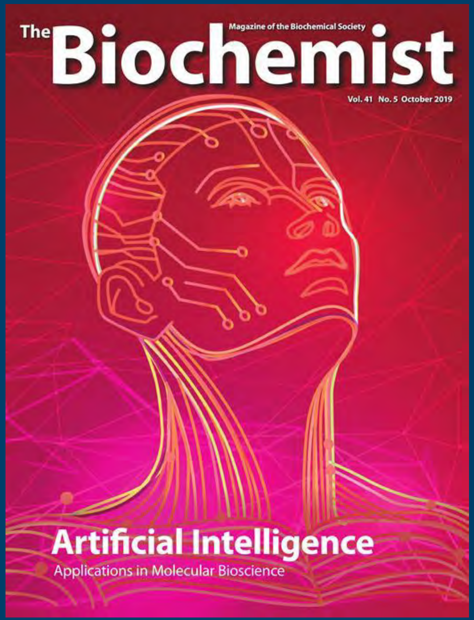
CellPress REVIEWS

Special Issue: Rise of Machines in Medicine

Review

Artificial Intelligence for Clinical Trial Design

Stefan Harrer,[1,*] Pratik Shah,[2] Bhavna Antony,[1] and Jianying Hu[3]



Artificial Intelligence

A new promising way for tackling the 'Pharma Dilemma': artificial intelligence for clinical trials

Stefan Harrer, Bhavna Antony, Akram Bayat and **Jianying Hu** (IBM Research, Australia, MIT Media Lab, USA and IBM T. J. Watson Research Center, USA)

Artificial intelligence (AI) is certainly not a panacea for solving the 'Pharma Dilemma', in which the cost of producing new drugs continues to spiral. However, AI can be used to fundamentally change the way we perform essential steps in clinical trial design and execution, from cohort selection to patient monitoring. Merging AI and clinical expertise across engineering and medical disciplines to explore the impact of these changes on trial performance and success rates is one of the most promising leads we have for restoring efficiency and sustainability to the drug development cycle.

…and read this book:

M. Mirmomeni, T. Fazio, S. v. Cavallar, and S. Harrer “**From Wearables to THINKables: AI-enabled sensors for health monitoring**”, in *Wearable Sensors – Fundamentals, Implementation and Applications – 2nd Edition*, ISBN 9780128192467, **Academic Press,** November 2020.

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