DEEP MACHINE LEARNING DETECTION OF PRECLINICAL NEURODEGENERATIVE DISEASES

THIRD WHO GLOBAL FORUM ON MEDICAL DEVICES
ICTS IN HEALTH
MAY 10, 2017, 13:30-14:15
WORKSHOP

AGENDA

• 13:30 OPENING – LUDOVICO CIFERRI / ADVANET CORP. (JAPAN)


• 13:45 THE ARTIFICIAL INTELLIGENCE CHALLENGE – TAMAS MADL / HEARTSHIELD LTD. (AUSTRIA)

• 14:05 THE PLATFORM – ALESSANDRO VERCELLI / UNIVERSITY OF TURIN (ITALY)

• 14:15 THE IMPACTS – GEORG AUMAYR / JOHANNITER (AUSTRIA)

• 14:25 Q&A

• 14:30 CLOSING
OPENING (1/5)

WHY THIS WORKSHOP

• ARTIFICIAL INTELLIGENCE, AN UMBRELLA TERM, AND HEALTHCARE
• TOWARDS DATA DRIVEN HEALTHCARE ORGANIZATIONS
• GLOBAL HEALTHCARE INDUSTRY’S DRIVE TO REDUCE COSTS AND MORE EFFICIENTLY MANAGE RESOURCES WHILE IMPROVING PATIENT CARE
• THE EXPLODING COSTS CAUSED BY AN AGING POPULATION SUFFERING INCREASINGLY FROM PREVENTABLE DISEASES, DRIVES A MORE AND MORE URGENT NEED FOR SCREENING AND PREVENTATIVE HEALTH MEASURES
• MARKET EXPECTED TO GROW TO ALMOST USD 8,0 BILLION BY 2022
60+ STARTUPS USING DEEP LEARNING

CORE AI: COMPUTER VISION
- clarifai
- Tractable
- netra
- HYPERVERSE
- Opticinity
- deepomatic
- sentient
- Sighthound
- TERRALOUE
- imageni
- pilot.ai

CORE AI: OTHER
- TERADEEP
- affectiva
- Learn Computing
- DigitalGenius
- LEAPMIND
- Arya
- twentybn

BI, SALES & CRM
- SKYMNDR
- TalkIQ
- intranetu
- True AI
- KOVID
- MELI
- DEI

E-COMMERCE
- Reflektion
- VISENZE

ACQUIRED
(2014-2016YTD)

ROBOTICS & AUTO
- netredyne
- AdasWorks
- drive.ai
- Rokid
- comma.ai

HEALTHCARE
- imagia
- Mindshare
- BAYLABS
- BUTTERY Network Inc.
- deep genomics
- Atomwise
- zebra
- PATHWAY GENOMICS
- Translating Innovation

SECURITY
- deepinstinct
- umoocv
- Alpaca
- indicio
- SignalSense
- Lunit
- SIGMA
- TUPLE

OTHER
- Alpaca
- indicio
- Iris Automation

istock.com/image

OPENING (3/5)
OPENING (4/5)
THE KEY ISSUE

• DESPITE THE RECENT AI BREAKTHROUGHS AND IMPRESSIVE ACHIEVEMENTS, AND DESPITE THE RECENT UPTAKE OF AI METHODS IN MEDICINE, VERY, VERY FEW MODELS ARE HOWEVER MEANINGFULLY CONTRIBUTING TO CLINICAL PRACTICE

• BEYOND THE NEED FOR ADEQUATE TOOLS (OFF THE SHELF DEEP LEARNING IS INADEQUATE), THE DEVELOPMENT OF PLATFORMS THAT FACILITATE DATA COLLECTION, COLLABORATION BETWEEN MEDICAL AND TECHNICAL RESEARCHERS, AND A TESTING BED FOR NEW, PERSONALIZED, PATIENT-CENTRIC AI MED-TECH WILL BE CRITICAL, AT LEAST AS IMPORTANT AS THE MACHINE LEARNING RESEARCH

• DEEP LEARNING CAN HELP MAKE SENSE OF DATA FROM WEARABLES, SENSORS AND SMARTPHONES, AND EXTRACT PERSONALIZED INSIGHTS VALUABLE FOR SPECIFIC CONDITIONS, SUCH AS CARDIAC MONITORING
THE MEDICAL/SCIENTIFIC CHALLENGE (1/5)

AGING-RELATED NEURODEGENERATIVE DISEASES (E.G. DEMENTIAS)

• CLINICAL DIAGNOSIS (ANTE-MORTEM) = PRESENCE OF HALLMARK CLINICAL SIGNS AND SYMPTOMS
  • TYPICALLY: LOSS OF FUNCTIONAL CAPACITY + CLUSTER OF DEFICITS TO COGNITION, PHYSICAL FUNCTION, SOCIAL ACTIVITY, AND/OR MOOD.

• DEFINITIVE DIAGNOSIS REQUIRES POST-MORTEM ANALYSIS OF THE BRAIN.

• PAST 20 YEARS – EMERGENCE OF BIOMARKERS AND IMAGING TECHNIQUES (MRI, FMRI, CSF, PIB-PET)
  • NONE DISPLAY ADEQUATE SENSITIVITY OR SPECIFICITY FOR CLINICAL DIAGNOSIS OF AD

• STILL UNKNOWN: CAUSAL AGENT FOR MOST AGE-RELATED NEURODEGENERATIVE DISEASES

• TREATMENT: NO TREATMENT (CURE), ONLY TREATMENT FOR SYMPTOMS
THE MEDICAL/SCIENTIFIC CHALLENGE (2/5)

DEMENTIA

- ABSENCE OF SIGNS OR SYMPTOMS
- MILD “SUBCLINICAL” SIGNS OR SYMPTOMS SUGGESTIVE OF DISEASE
- BEYOND WHAT IS CONSIDERED NORMAL AGING
- LESS SEVERE THAN CLINICALLY RECOGNISED SIGNS/SYMPTOMS
- PRESENCE OF RECOGNISED CLINICAL SIGNS OR SYMPTOMS OF DISEASE
- ABSENCE OF OTHER EXPLANATORY DIAGNOSIS
- NO KNOWN CAUSAL AGENT – NO BIOMARKER TO DETECT DISEASE
THE MEDICAL/SCIENTIFIC CHALLENGE (3/5)

ASSUMPTIONS
- Common causal agent → Preclinical disease → Clinical disease

FOR DEMENTIA
- ? Unknown → Mild cognitive impairment → Alzheimer’s dementia

BUT WHAT IF ASSUMPTION IS TOO SIMPLISTIC?
- Causal agent 1 → Preclinical disease 1 → AD type 1
- Causal agent 2 → Preclinical disease 2 → AD type 2
- Causal agent 3 → Preclinical disease 3 → AD type 3

Common signs and symptoms
THE MEDICAL/SCIENTIFIC CHALLENGE (4/5)

AI AS A POSSIBLE WAY FORWARD IN DETECTION AND DIAGNOSIS OF PRECLINICAL DISEASE STATES (THE CURRENT USE)

- **Goal:** To identify individuals within a population who display markers of disease
- Can be used to screen brain imaging or other imaging (e.g. MRI, mammograms) to detect abnormal scans
- May enhance detection accuracy compared with human screening (e.g. radiologist)
- But cannot lead to detection of preclinical disease for diseases where the causal agent is unknown
AI AS A POSSIBLE WAY FORWARD IN DETECTION AND DIAGNOSIS OF PRECLINICAL DISEASE STATES (A NEW WAY FORWARD?)

• GOAL: TO DETECT CHANGE IN FUNCTION WITHIN AN INDIVIDUAL OVER TIME
• AI LEARNS USES PATTERN RECOGNITION TO DETECT INSIDIOUS DECLINE IN FUNCTION/PERFORMANCE WITHIN THE INDIVIDUAL
• THEREFORE – CAN DETECT PRECLINICAL DISEASE STATES AT THE LEVEL OF THE INDIVIDUAL
• USING DATA FROM MULTIPLE INDIVIDUALIZED AI SYSTEMS MAY LEAD TO DIAGNOSTIC CRITERIA FOR PRECLINICAL DISEASE
• POTENTIAL FOR INDIVIDUALIZED HEALTH MONITORING AND INTERVENTION
Modern AI methods ("deep learning") can **match or even exceed** human classification accuracy

- Lung cancer from tissue samples (Yu et al., 2016)
- Alzheimer’s disease from fMRI (Sarraf et al., 2016)
- Skin cancer from photos (Esteva et al., 2017)
  - Works for everyday monitoring e.g. on smartphones

...BUT need **huge volumes of training data**
- E.g. 129,450 clinician-annotated images for skin cancer

→ **Challenge 1:** learning with little supervision ...within an individual
Adequate, concise representation crucial to learn without thousands of clinically reliable diagnoses
THE AI CHALLENGE (3/16)

- **Deep autoencoders**: inspired by the visual cortex
  - What are the smallest number of “neurons” (features) reconstructing the input signals?

- **Require no “labels” / ground truth.** Learn without feedback

\[
E(x, s, D) = \|x - Ds\| + \lambda f(s)
\]

Optimize $\|\text{error}\|$ & sparsity (e.g. unsupervised deep learning such as stacked sparse autoencoders)
AI as a possible way forward in detection and diagnosis of preclinical disease states

→ Challenge 1: learning with little supervision
→ Challenge 2: combining data-driven machine learning with expert input and physiological knowledge

**THE AI CHALLENGE** (4/16)
AI as a possible way forward in detection and diagnosis of preclinical disease states

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THE AI CHALLENGE (5/16)
AI as a possible way forward in detection and diagnosis of preclinical disease states

→ Challenge 1: learning with little supervision

→ Challenge 2: combining data-driven machine learning with expert input and **physiological knowledge**

**Spiking neuron models account for heart activity**

**Physiological Models**
Challenge 3: Recognize decline without a clear, formal definition

- Distinguish significant preclinical decline from normal aging
- Notice abnormal markers and events
  - E.g. frequent falls, cardiac arrhythmias
• Distinguish **significant preclinical decline** from **normal aging**

• Notice abnormal markers and events
  • E.g. frequent falls, cardiac arrhythmias
THE AI CHALLENGE (9/16)

- Time series in learned representation
- Low-dimensional representation
  - Captures most of relevant variance
  - Discrimination of pathological states
- Individual with symptoms of preclinical decline
- Separating hyperplane
- Low-dimensional representation space
- Healthy aging

- Anomaly detection
- Trend detection
THE AI CHALLENGE

Anomaly detection

Trend detection

Low-dimensional representation

- Captures most of relevant variance
- Discrimination of pathological states

Human Expert

Low-dimensional representation space

Individual with symptoms of preclinical decline

Healthy aging

Separating hyperplane
AI as a possible way forward in detection and diagnosis of preclinical disease states

→ Challenge 1: learning with little supervision

→ Challenge 2: combining data-driven machine learning with expert input and physiological knowledge

→ Challenge 3: **automatically** detecting ill-defined trends and anomalies, with little supervision
THE AI CHALLENGE (12/16)

Outline of a possible AI architecture

Single person
Multiple sensors
Continuous data sampling

Physiological models
Personalized deep learning
Anomaly & trend detection

Detect relevant outliers
Detect preclinical decline

Expert input (mechanisms)
Expert input (very few labels)
THE AI CHALLENGE (13/16)

Previous work

**Representation learning** with little supervision

- Learn concise representations of participant’s spatial memory
- Model could predict >250 participant’s memory structure (Madl et al., 2016a)
- Model allowed a humanoid robot to learn spatial memories with comparable accuracy to humans (Madl et al., 2016b)

**Combining machine learning** with physiological models

- Spiking neuron model of cardiac pacemaker
- Model could detect stable coronary artery disease from inter-beat intervals (Madl et al., 2016c)
Previous work

Combining machine learning with physiological models

Spiking neuron model of cardiac pacemaker

Model could detect stable coronary artery disease from inter-beat intervals (Madl et al., 2016c)

Outperforms lipid profile based screening & ECG analysis

Works on any smartphone  www.heartshield.net

Can work on wearables or smart watches
THE AI CHALLENGE  (15/16)

Combining machine learning with physiological models
Outperforms lipid profile based screening & ECG analysis
Works on any smartphone  www.heartshield.net

- Heart beat intervals from “pulse oximetry” using camera+flashlight
- Analysis with biologically inspired deep learning

WHO study, n=79 039 (Roth et al., 2010): **majority of risk factors either undiagnosed or uncontrolled**

31 % die of cardiovascular disease, and 80% would be preventable (WHO, 2012)

Population-wide, **ubiquitous screening with smartphones** could tackle CVD burden

Can be **extended to screening for neurodegenerative diseases on smartphones**
THE AI CHALLENGE (16/16)

*AI as a possible way forward in detection and diagnosis of preclinical disease states*

→ Challenge 1: learning with little supervision
→ Challenge 2: combining data-driven machine learning with expert input and physiological knowledge
→ Challenge 3: automatically detecting ill-defined trends and anomalies, with little supervision

Off the shelf AI not applicable

BUT recent breakthroughs place individual monitoring and detection and diagnosis of preclinical disease states within arm’s reach
THE PLATFORM (1/5)

PHC-21-2015: ADVANCING ACTIVE AND HEALTHY AGEING WITH ICT: EARLY RISK DETECTION AND INTERVENTION (CONTRACT # 689592)

• TO IMPROVE EARLY DETECTION AND MINIMIZATION OF RISKS ASSOCIATED WITH AGEING, INCLUDING COGNITIVE IMPAIRMENT, FRAILTY, DEPRESSION AND FALLS.

• NEW ICT-BASED INTERVENTIONS TAILORED TO THE NEEDS OF OLDER ADULTS IN ORDER TO PREVENT PHYSICAL, COGNITIVE, PSYCHOLOGICAL AND SOCIAL DECLINE.

• ICT TOOLS THAT ARE ABLE TO CONTINUOUSLY SUPPORT CHANGES IN BEHAVIOR OF OLDER ADULTS IN DAILY LIFE, IN ORDER TO TACKLE AGEING AND FRAILTY.

• AN INTERNATIONAL MULTICENTRE RCT INVOLVING PARTICIPANTS FROM EUROPE, ASIA AND AUSTRALIA (300 TREATED VS 300 CONTROLS).
THE PLATFORM (2/5)
THE PLATFORM (3/5)

TECHNOLOGY IN USE

- Mobile applications for health monitoring
- Wearable devices for continuous health monitoring
- Remote medical consultations
- Personalized health advice and tips

Devices:
- Blood pressure monitor
- Pulse oximeter
- Thermometer
THE PLATFORM (4/5)

LIFELONG - SCALING UP FROM MY-AHA

• AI PLATFORM THAT USES DEEP LEARNING PARADIGMS TO DETECT AND RECOGNISE UNIQUE PRECLINICAL SIGNS AND SYMPTOMS OF AGE-RELATED DISEASES

• ABLE TO DEPLOY INDIVIDUALLY TAILORED RESPONSES TO THE PERSON’S NEEDS (THE VIRTUAL COACH), WITH THE RESPONSES BEING CONTINUALLY MODIFIED AND UPDATED ACCORDING TO CHANGES IN THE INDIVIDUALS LEVEL OF FUNCTION OVER TIME

• IMPLEMENTING INTERVENTION BEFORE DISEASE BECOMES EVIDENT
THE PLATFORM
(5/5)
THE IMPACT (1/4)

SAVING TIME

Diagnostic support AI Output ➔ Diagnosis ➔ Therapy ➔ Care ➔ Personalization

DT - X
THE IMPACT (2/4)

SAVING TIME

hDATA Cycle

- Symptoms
- Basic Vital parameters
- Monitoring
- Processing data
- Interpretation
- Diagnosis
- Understanding of patient and disease interaction
- Therapy design

THE IMPACT (3/4)

BEHAVIOUR MONITORING

Data input by sensors → AI Analysis → Behavior Identification → Semi Automated Documentation
                         → Early detection of diseases/monitoring of diseases
                         → Case management support

CARE AND THERAPY IMPROVEMENT
# THE IMPACT (4/4)

## TECHNOLOGY’S OUTCOMES

<table>
<thead>
<tr>
<th>Mobile Care</th>
<th>Ambulatory Care</th>
<th>Case management</th>
<th>Diagnostics</th>
<th>substitute of highly expensive equipment</th>
<th>Therapy control</th>
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<tbody>
<tr>
<td>Sensors help monitoring</td>
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<tr>
<td>AI is helping in analysing.</td>
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<tr>
<td>DL is helping in understanding.</td>
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<td>NN is helping in interpreting.</td>
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RESEARCH TEAM
SPEAKERS TO THE WS*

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THANK YOU

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