Artificial Intelligence
in healthcare

October 27-28, 2020

Digital Event

molit.eu/AInHealth20

OVERVIEW

OVERVIEW

THE ORGANIZERS

Lars Steinmetz
Director Life Science Alliance & Senior Scientist EMBL

Professor of Genetics Stanford University and Co-director Stanford Genome Technology

Life Science ALLIANCE

The EMBL | Stanford Life Science Alliance is a joint research initiative dedicated to the advancement of biomedical research. By bringing together leading researchers from the European Molecular Biology Laboratory (EMBL) and Stanford University, we are cultivating new ideas, sharing best practices, and facilitating access to technology and resources. We enable transatlantic cooperation with programs for joint research fellows, exchanges and outreach.

Christian Fegeler
Co-founder MOLIT institute for personalized medicine, Heilbronn

Uwe Martens
Co-founder MOLIT institute for personalized medicine, Heilbronn

MOLIT
Institute for personalized medicine

The MOLIT Institute for personalized medicine joins EMBL as Co-Organizer. MOLIT is a non-profit research institute for personalized medicine located in Heilbronn, Germany. Its focus is the development of customized therapies for cancer diseases and their translation into general medical care. It is adopting an integrated approach of medicine and IT by joining and mathematically modelling complex data of different molecular analytical methods as well as clinical and patient reported outcome.

PRECISION MEDICINE PARTNERSHIP UNIT (PMPU)

Artificial Intelligence has the potential to increase effectivity and efficiency in medicine manyfold, while making better use of existing resources. Already today there are AI systems which outperform experienced clinicians in some specific areas, like pathology. However, good data quality and availability are essential for research that support artificial intelligence and pattern recognition approaches extending beyond the already conquered disciplines of medicines. This undertaking requires interdisciplinary alliances of stakeholders together with a strong emphasis on information technology, structured data exchange and semantic interopability.

The PMPU is a strategic alliance of the European Molecular Biology Laboratory (EMBL), the MOLIT research institute for personalized medicine and the SLK Clinics Heilbronn. It aims towards a clinical translation of basic in-vitro research into the in-vivo bedside decision-making process. Aspects of molecular biology could thereby complement clinical diagnostics in order to provide more efficient patient care in oncology. PMPU consists of three key missions from bench to bedside to healthcare system: I) running a translational research program, II) bringing liquid biopsy into routine practice and III) establishing a learning knowledge platform, making sure the acquired knowledge can be incorporated in the clinical practice. In the sense of open-science, data and information additionally is made accessible to approved clinical trials acting as an incubator for new research.

OCTOBER 27 Day 01

13:00 - 13:15
Opening Remarks

Session 1:
Big Data in Healthcare

13:15 - 13:35
Markus List
Technical University of Munich, Germany
Big Data in Systems Medicine

13:35 - 13:55
Isidro Cortés-Ciriano
EMBL-EBI Hinxton, UK
What is realistic and what are illusions in Artificial Intelligence in drug discovery? A discussion on ways to impact, and why we are not there yet

13:55 - 14:15
Alexandra Reichenbach
Heilbronn University, Germany
Leveraging longitudinal phenotypic data for subtyping neurodegenerative disease

14:15 - 14:35
Hagai Rossman
Weizmann Institute of Science, Israel
Rapid deployment of a nationwide symptoms survey during the outbreak and spread of COVID-19 - framework and applications

14:35 - 15:00
Open discussion with all speakers from Session 1

15:00 - 15:10
Selected Short Talk
Florian Huber
EMBL Heidelberg, Germany
Combining chemical genetics with machine learning to study antibacterial drug mode of action

15:10 - 15:20
Selected Short Talk
Theodore Alexandrov
EMBL Heidelberg, Germany
Spatial and single-cell metabolomics in the age of AI

15:20 - 15:45
Coffee break and meet the speakers

OCTOBER 27 Day 01

Session 2:
Smart Healthcare Systems

15:45 - 16:05
Christof von Kalle
Berlin Institute of Health
& Charité Universitätsmedizin Berlin, Germany
First principle thinking in translational data research

16:05 - 16:25
Patrick Werner
MOLIT Institute for personalized medicine, Germany
Structured data first – Implementing interoperability in clinical processes

16:25 - 16:45
Saila Rinne
European Commission, DG CNECT,
eHealth Unit, Belgium
Data and AI for healthcare – EU policy and research initiatives

16:45 - 17:05
Wendelin Schramm
GECKO Research Institute, Germany
Generic Health-Economic Disease Models - Intermediary Between Personalized Data and Societal Value

17:05 - 17:25
Open discussion with all speakers from Session 2

17:25 - 17:35
Selected Short Talk
André Ferreira
Instituto Superior Técnico
– Universidade de Lisboa, Portugal
Predictive Medicine Using Interpretable Recurrent Neural Networks

17:35 - 17:45
Selected Short Talk
Jessica Torres
Stanford University, USA
Multi-task deep learning for cardiac rhythm detection in wearable devices

17:45 - 19:00
Virtual networking

OCTOBER 28 Day 02

Session 3:
AI in the Clinic

15:00 - 15:20
Zhenyu Xu
SOPHiA Genetics, Switzerland
Systematic in-silico determination of technical limitations enables reliable circulating tumour DNA profiling

15:20- 15:40
Supriyo Chatterjea
Philips Research Europe, The Netherlands
BigMedilytics: Experiences with characterizing hospital workflows

15:40 - 16:00
Benjamin Meder
University Hospital Heidelberg, Germany
AI in cardiovascular research: single molecules to patient care

16:00 - 16:20
Kristen Yeom
Stanford University, USA
Towards Precision in the Era of AI and Modern Medicine

16:20 - 16:40
Open discussion with all speakers from Session 3

16:40 - 16:50
Selected Short Talk
Tejaswini Mishra
Stanford University, USA
Early detection of COVID-19 using a smartwatch

16:50 - 17:00
Selected Short Talk
Adriano Lucieri
German Research Center for Artificial Intelligence, Germany
exAID - Explanations for AI in medical diagnosis

17:00 - 17:40
Coffee break and meet the speakers

OCTOBER 28 Day 02

Session 3:
AI in the Clinic

17:40 - 17:50
Selected Short Talk
Andrea Beccari
Dompé Farmaceutici, Switzerland
EXSCALATE: a smart in silico poly pharmacological drug design platform selecting molecules active against the ZIKA virus

17:50 - 18:00
Selected Short Talk
Benedikt Rauscher
EMBL Heidelberg, Germany
mitoWEAR: Monitoring of mitochondrial disorders using wearable activity trackers

18:05 - 18:50
Panel Discussion

Hosted by Russ Altman, Stanford University USA
The Future of AI in Healthcare: what does it look like and how do we get there?
Oliver Stegle, EMBL Heidelberg & the DKFZ
Christof von Kalle, Berlin Institute of Health & Charité Universitätsmedizin Berlin
Patrick Werner, MOLIT Institute for personalized medicine
Kristen Yeom, Stanford University

18:50 - 19:00
Closing remarks

19:00 - 19:30
Virtual Networking

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Markus List

Technical University of Munich, Germany

Big Data in Systems Medicine

October 27, 13:15 – 13:35

Modern medicine suffers from a conceptual crisis: diseases are defined and diagnosed based on symptoms (e.g., hypertension, depression) or affected organs (e.g., heart failure, nephropathy), complicating the use of therapies targeted at the causal disease mechanism. To mitigate this, the field of systems medicine aims to develop mechanistic disease definitions and to identify groups of patients that would benefit from targeted treatment with existing, new or repurposed drugs.

The basis for systems medicine are big biomedical data obtained through modern omics technologies as well as rich public databases on molecular interactions, comorbidities, drug effects, etc. Integrative artificial intelligence (AI) methods have the potential to leverage these big data to change future clinical decision-making. We will highlight emerging examples of big data in systems medicine ranging from de novo endophenotyping, i.e. the stratification of patients based not only on simple molecular markers, but on composite, network-based markers to *in silico* methods for discovering drug repurposing candidates. The success of systems medicine hinges on the availability of large data sets. Thus, we will also consider federated AI as a framework to overcome technological and legislative barriers that currently prevent data sharing across medical institutions.

Isidro Cortés-Ciriano

EMBL-EBI Hinxton, UK

What is realistic and what are illusions in Artificial Intelligence in drug discovery? A discussion on ways to impact, and why we are not there yet

October 27, 13:35 – 13:55

While Artificial Intelligence (AI) has had a profound impact on diverse scientific disciplines, such as computer vision, its contribution to the discovery of new drugs has been somewhat limited. In this presentation, I will firstly discuss in which stages of the drug discovery process improving either the time needed, the success rate of decisions, or decreasing cost would have the most profound impact on bringing new drugs to market. After cost of capital, changes in clinical success rates would have the strongest impact on improving success in drug discovery, indicating that the quality of decisions regarding which compound to take forward are more important than their speed or cost. Secondly, I will argue that while most efforts applying AI in the context of drug discovery have been centred around the question of ‚how to make new compounds', the question of ‚what compound to make' taking into account efficacy and toxicity endpoints has received comparatively less attention. As a result, the potential of AI to make significant progress in drug discovery is limited by the proxy data currently available, which are often of insufficient quality with respect to the in vivo assessment of efficacy and safety. Harnessing the power of AI to inform decision making at those stages of the drug discovery process with the strongest impact on bringing new drugs to market is thus contingent on the generation of practically relevant data in sufficient quantities to enable the discovery of novel chemistry with novel modes of action, and showing desirable efficacy and safety in the clinic.

Alexandra Reichenbach

Heilbronn University, Germany

Leveraging longitudinal phenotypic data for subtyping neurodegenerative disease

October 27, 13:55 – 14:15

Most diseases of the central nervous system are multicausal, affect multiple neural systems, and display highly heterogeneous symptoms. Neurodegenerative diseases, such as Alzheimer's or Parkinson's disease, are characterized by irreversible decline in neural and cognitive function. Stratification of patients with a common clinical diagnosis into homogenous subtypes of the disease is necessary to shed light on the biological mechanisms underlying these diseases and develop personalized treatments. Two patients, however, with very similar phenotypes, such as loss of a specific set of cognitive function or brain matter, may still experience different developments of the disease. Therefore, it is necessary to take the progression of phenotypic markers into account in order to comprehensively characterize subtypes of a neurodegenerative disease.

This talk will introduce and compare different approaches for subtyping neurodegenerative diseases based on longitudinal phenotypic data, such as neuropsychological tests or measurements of brain anatomy. The methods will cover several possibilities for feature engineering and a variety of supervised and unsupervised machine learning algorithms.

Hagai Rossman

Weizmann Institute of Science, Israel

Rapid deployment of a nationwide symptoms survey during the outbreak and spread of COVID-19 - framework and applications

October 27, 14:15 – 14:35

Policy makers and health providers around the world are struggling to contain the rapid spread of COVID-19. This talk will highlight the recent efforts of our team to assist in a national pandemic response, highlighting the importance of fast data-collection and data-driven decision making during times of uncertainty. We present a framework designed and deployed in the early stages of the coronavirus pandemic in Israel, which has already been adopted by several countries. This framework consists of an anonymous daily, population-wide, online questionnaire which can be utilized to detect coronavirus outbreak and spread, characterize and separate geographic areas by symptoms' prevalence and give new insights on the clinical course of COVID-19 on an individual level. Up to date, more than 2 million responses have been recorded in Israel. This, along with parallel initiatives from researchers around the world have also led to the establishment of a collaborative international consortium which will constitute as a hub for the integration of COVID-19-related data.

We present several applications and results of this framework: an assessment of the effect of national lockdown policies, a machine learning triage model for optimizing testing policy, insights on individual longitudinal symptom dynamics, and models for predicting hospitalized critical patients.

Christof von Kalle

Berlin Institute of Health
& Charité Universitätsmedizin Berlin, Germany

First principle thinking in translational data research

October 27, 15:45 – 16:05

Precision medicine, and in fact all of medicine, is hampered by the lack of access or the lack of digital availability of health data in most health systems. Data processing is often sectoral or even institutional only, and follow up at best incomplete. The COVID 19 epidemic has taught us very clearly that our inability to collect, process, and understand patient and disease data has cost patient lives in significant numbers around the world. We therefore continue to reason that legally and ethically correct data handling for precision medicine should be patient centered and sovereign. Both regular and academic data processes should regularly provide a patient with access to and decision power over their own health data. Data protection is synonymous with protection of the individuals described by the data, and therefore necessarily a judgment call between the dire risks of not processing data, which is rarely discussed but has a significant death toll, and the risks of processing data.

Funded by the Federal Ministry of Education and Research and the Federal Ministry of Health, the project „DataBox – Patient-centered Health Management through Digital Intelligence" we have piloted the development of a novel patient-centered model data space that can be used by patients to file, administer and share their medical data in. Instruments like DataBox allow patients, their doctors, or commissioned DataBox documentarists to add the data to the individual data store via smartphone app, email, or web tool. The patient journey through the health care system can then be organized as a continuous improvement, systemic learning and clinical research process, depending on patient needs, medical requirements and organizational capabilities for every participating patient. As cloud users, the patients can decide who is granted access to their data. Certified institutions may request pseudonymized data sets to find suitable participants for studies on new pharmaceuticals for personalized therapy, for instance. With their consent, the patients can also be contacted directly if they prove to be eligible for certain trials. We discuss how precision medicine in oncology can use umbrella trials and patient centered data spaces to connect modern patient care with research involving natural and artificial intelligence.

Patrick Werner

MOLIT Institute for personalized medicine, Germany

Structured data first – Implementing interoperability in clinical processes

October 27, 16:05 – 16:25

Structured, interoperable and semantically annotated data is the prerequisite for modern, ai based analysis approaches. Most oncological genomic reports today are PDF based, the lack of semantical interoperability and standardization of the reported variants hinders the utilization of modern AI methods and clinical decision support systems.

To enable analyzability of oncologic case data, including structured Genomic Diagnostic Reports, the MOLIT Institute, as part of the HL7 clinical genomics workgroup, participates in the creation of a FHIR based Genomic Report Implementation guide. Furthermore, several tools (VITU, Variant Browser, and Import/Export Interfaces were created. The aggregated case data is combined with patient reported outcomes and exports from the mandatory tumor registry system and stored in the HL7 FHIR format. This enables the analysis of the data via modern tools like Bunsen (SPARK) or fhirProto (protobuf).

Saila Rinne

European Commission, DG CNECT, eHealth Unit, Belgium

Data and AI for healthcare – EU policy and research initiatives

October 27, 16:25 – 16:45

The Commission Communication on enabling the digital transformation of health and care in the Digital Single Market, published in April 2018, proposed a set of actions to foster the provision of more preventive, personalised and responsive healthcare to European citizens. This initiative aims at increasing the efficiency, sustainability and resilience of and equitable access to health and care systems across Europe, stimulating growth and promoting European industry.
The availability of health data and the possibility to use, combine and re-use data from various sources in a GDPR compliant way are essential prerequisites for advances in digital health and care. Data is needed, among others, for detecting, preventing and treating diseases, for supporting research on new treatments and medicines and for data-driven innovations.

A European Health Data Space would improve safe and secure accessibility of health data, allowing for targeted and faster research, diagnosis and treatment. It builds upon previous EU initiatives and the most recent Commission Communication "A European Strategy for Data" published in February 2020, aiming at the creation of a single market for data, to foster innovative processes, products and services while establishing clear and fair rules on access and re-use of data.

Wendelin Schramm

GECKO Research Institute, Germany

Generic Health-Economic Disease Models - Intermediary Between Personalized Data and Societal Value

October 27, 16:45 – 17:05

Over the millennia, we have seen an unstoppable trend in the development of medical research, starting with the study of the symptoms of disease (phenomenology), through physiology and on to the molecular level, and only in recent decades to the genome. An exponential acceleration of knowledge and available medical data is evident. At the same time, the distance between basic research and practical application has widened. Urgent questions arise. Is it possible to investigate whether basic research is relevant and will enable practical application in the future? Are there more valuable or more rewarding areas of research when making a selection decision? The value of medical innovation is defined by health systems in terms of the added value generated for society. At the same time, this is compared with monetary expenditure.

Disease models are regularly used for technology assessment and health economics. These follow mathematical laws that can be derived from personalised data. Unsupervised machine learning methods such as clustering are already used to create disease models from personalised data. The results are generic models that can translate data into meaning. The need for research in this new discipline is great, but there is a potential worthy of discussion for bridging the gap between basic research and social value.

Zhenyu Xu

SOPHiA Genetics, Switzerland

Systematic in-silico determination of technical limitations enables reliable circulating tumour DNA profiling

October 28, 15:00 – 15:20

Liquid biopsies, such as next generation sequencing (NGS) assays of circulating tumour DNA (ctDNA), are a minimally invasive alternative to tumour biopsies enabling longitudinal monitoring and capturing tumour heterogeneity. As ctDNA constitutes a minority of plasma cell-free DNA (cfDNA), tumour-specific genomic alterations are challenging to detect. Limits of detection (LODs) of 0.1-1% are purported for NGS assays, but abundant false negatives and discordant results challenge this. We sought to improve the reliability of NGS testing by understanding and modelling factors governing LOD. Establishing a model system mimicking clinical ctDNA workflows uncovered a remarkably heterogeneous LOD landscape, defined by factors acting at assay, sample and nucleotide levels. We incorporated these insights into an LOD-aware variant calling framework that accurately predicts possible incorrect calls during clinical NGS testing.

Applying this to 580 clinical samples predicted all but one false negative call, resulting in an inter-assay concordance of 99%. Our approach improves the reliability, reproducibility and transparency of genetic testing, with widespread benefits for clinical trials, technology development and patient care.

Supriyo Chatterjea

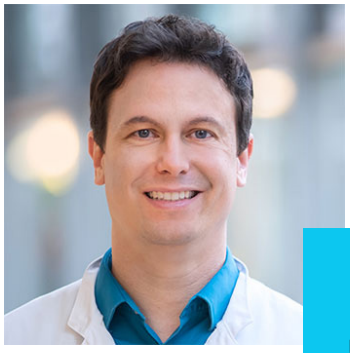
Philips Research Europe, The Netherlands

BigMedilytics: Experiences with characterizing hospital workflows

October 28, 15:20 – 15:40

There are currently several converging trends in the healthcare sector that threaten the future of the quality of healthcare provided by hospitals: an aging population, increasing incidence of chronic disease, dwindling number of care providers and shrinking healthcare budgets. One way to address this problem is to optimize workflows in hospitals. This will help improve the utilization of resources in the healthcare sector and thus improve productivity. Both patients and staff will be positively impacted and healthcare costs can be kept in check.

The BigMedilytics EU Lighthouse project aims to demonstrate how Big Data can have a transformational impact on the healthcare sector. The project has three main themes: Population Health, Oncology and Industrialization of Healthcare. This talk will give an overview of the BigMedilytics project and focus on the third theme by describing how data from real-time locating systems and Electronic Medical Records can be combined to accurately characterize workflows in hospitals. This information can then be used to identify bottlenecks and subsequently optimize workflows.



Benjamin Meder

University Hospital Heidelberg, Germany

AI in cardiovascular research: single molecules to patient care

October 28, 15:40 – 16:00

Precision Medicine is the evolution of empirical and evidence-based medicine. It attributes the individual variability in patients and the effect of these factors on health and disease. Deep phenotyping and genotyping are now possible in the clinical setting, laying the groundwork for such personalised decision making. To take full advantage of these high-dimensional datasets, machine learning and AI are critical.

In this talk I will highlight concepts and own studies from our network Informatics for Life that showcase the different components on the promising way „from data to patient care“.

Kristen Yeom

Stanford University, USA

Towards Precision in the Era of AI and Modern Medicine

October 28, 16:00 – 16:20

Advances in health technology and digital medicine offer integrated solutions for precision in clinical diagnostics and potential for layered approaches to early interventions, therapeutics, and disease prevention. Artificial intelligence has emerged as the new frontier to bolster this effort. In this talk, we will discuss how machine learning can engage and augment modern medicine with a special focus on computer vision and medical imaging.

We will examine specific clinical case scenarios that range from challenging to mundane, critical to routine, as well as COVID-19 pandemic. Brief discussion on cyber security and data privacy will be presented. Finally, we will explore pitfalls and current challenges to rapid AI translation, and potential future impact of AI in medicine.

Florian Huber

EMBL Heidelberg, Germany

Combining chemical genetics with machine learning to study antibacterial drug mode of actiont

October 27, 15:00 – 15:10

The rising threat of antibiotic resistance requires the development of fast and scalable approaches for determining antibacterial drug mode of action (MoA). Using chemical genetics data as input we trained several supervised classifiers in order to predict the main cellular process targeted by small molecules. A random forest classifier performed best with a classification accuracy of 70%. Further inspection of the model revealed that a small subset of genes contained most of the MoA-specific information and a model trained with these fingerprint features performed equally well on a test set. We used our model to predict the MoA of compounds whose target process is unclear in Escherichia coli. Surprisingly, our predictions indicated that thiolutin is a cell wall damaging agent. Thiolutin has long been used for its RNA synthesis inhibition properties in eukaryotes, which is thought to be a secondary effect of its zinc-chelating properties. We conducted follow-up experiments to investigate the connection of metal homeostasis to cell wall maintenance and structure and show data on how different metals and chelators impact cellular structure and lysis phenotypes.

In summary, our study gauges the potential of using chemical genetics for MoA prediction and shows a way how ML can be used to simplify future experiments by selecting only meaningful features. It also reveals a hitherto unknown MoA for thiolutin with implications for the study of other dithiolopyrrolones such as gliotoxin or aureothricin.

Theodore Alexandrov

EMBL Heidelberg, Germany

Spatial and single-cell metabolomics in the age of AI

October 27, 15:10 – 15:20

Recent discoveries put metabolism into the spotlight. Metabolism not only fuels cells but also plays key roles in health and disease in particular in cancer, inflammation, and immunity. In parallel, emerging single-cell technologies opened a new world of heterogeneous cell types and states previously hidden beneath population averages. Yet, methods for discovering links between metabolism, cell states, metabolic plasticity and reprogramming on the single-cell level and in situ are crucially lacking. Our research aims to bridge this gap. First, I will explain how the emerging technology of imaging mass spectrometry can be used for the spatial profiling of metabolites, lipids, and drugs in tissues. I will present our cloud and Artificial Intelligence-powered platform METASPACE which is increasingly used across the world. In the second part of my talk I will focus on our method SpaceM for spatial single-cell metabolomics in situ. We applied SpaceM to investigate hepatocytes stimulated with fatty acids and cytokines, a model mimicking the inflammation-associated transition from the fatty liver disease NAFLD to steatohepatitis NASH. We characterized the metabolic state of steatotic hepatocytes and metabolic plasticity associated with the inflammation. We discovered that steatosis and proliferation take place in distinct cell subpopulations, each with a characteristic spatial organization and metabolic signatures. Overall, such methods open novel avenues for understanding metabolism in tissues and cell cultures on the single-cell level.

André Ferreira

Instituto Superior Técnico – Universidade de Lisboa, Portugal

Predictive Medicine Using Interpretable Recurrent Neural Networks

October 27, 17:25 – 17:35

Deep learning has been revolutionizing multiple aspects of our daily lives, thanks to its state-of-the-art results. However, the complexity of its models and its associated difficulty to interpret its results has prevented it from being widely adopted in health-care systems. This represents a missed opportunity, specially considering the growing volumes of Electronic Health Record (EHR) data, as hospitals and clinics increasingly collect information in digital databases. While there are studies addressing artificial neural networks applied to this type of data, the interpretability component tends to be approached lightly or even disregarded. Here we demonstrate the superior capability of recurrent neural network based models, outperforming multiple baselines with an average of 0.94 test AUC, when predicting the use of non-invasive ventilation by Amyotrophic Lateral Sclerosis (ALS) patients, while also presenting a comprehensive explainability solution. In order to interpret these complex, recurrent algorithms, the robust SHAP package was adapted, as well as a new instance importance score was defined, to highlight the effect of feature values and time series samples in the output, respectively. These concepts were then combined in a dashboard, which serves as a proof of concept in terms of a AI-enhanced detailed analysis tool for medical staff.

Jessica Torres

Stanford University, USA

Multi-task deep learning for cardiac rhythm detection in wearable devices

October 27, 17:35 – 17:45

Wearable devices enable theoretically continuous, longitudinal monitoring of physiological measurements such as step count, energy expenditure, and heart rate. Although the classification of abnormal cardiac rhythms such as atrial fibrillation from wearable devices has great potential, commercial algorithms remain proprietary and tend to focus on heart rate variability derived from green spectrum LED sensors placed on the wrist, where noise remains an unsolved problem. Here we develop DeepBeat, a multi-task deep learning method to jointly assess signal quality and arrhythmia event detection in wearable photoplethysmography devices for real-time detection of atrial fibrillation. The model is trained on approximately one million simulated unlabeled physiological signals and fine-tuned on a curated dataset of over 500K labeled signals from over 100 individuals from 3 different wearable devices. We demonstrate that, in comparison with a single task model, our architecture using unsupervised transfer learning through convolutional denoising autoencoders dramatically improves the performance of atrial fibrillation detection from a F1-score of 0.54 to 0.96. We also include in our evaluation a prospectively derived replication cohort of ambulatory participants where the algorithm performed with high sensitivity (0.98), specificity (0.99), and F1-score (0.93). We show that two-stage training can help address the unbalanced data problem common to biomedical applications, where large-scale well-annotated datasets are hard to generate due to the expense of manual annotation, data acquisition, and participant privacy.

Tejaswini Mishra

Stanford University, USA

Early detection of COVID-19 using a smartwatch

October 28, 16:40 – 16:50

Consumer wearables that continuously measure vital signs have been used to monitor the onset of infectious disease. Here, we show that data from consumer smartwatches can be used for the pre-symptomatic detection of COVID-19. We analysed physiological and activity data from 32 individuals infected with COVID-19, identified from a cohort of nearly 5,300 participants, and found that 26 of them (83%) had alterations in heart rate, number of daily steps or time asleep. Of the 25 COVID-19 cases with detected physiological alterations for which we had symptom information, 22 were detected before (or at) symptom onset, with three cases detected at least nine days earlier. By using retrospective smartwatch data, we show that 63% of the COVID-19 cases could be detected before symptom onset in real time via a two-tiered warning system based on the occurrence of extreme elevations in resting heart rate relative to the individual baseline. Our findings suggest that activity tracking and health monitoring via consumer wearables may be used for the large-scale real-time detection of respiratory infections, often pre-symptomatically.

Adriano Lucieri

German Research Center for Artificial Intelligence, Germany

exAID - Explanations for AI in medical diagnosis

October 28, 16:50 – 17:00

The symbiosis of medical professionals and intelligent algorithms is a first, palpable step towards increased trust in AI-based healthcare applications. Despite outstanding diagnostic performances, current Computer-Aided Diagnosis systems often lack the ability to provide satisfying and complete decision explanations that can be easily understood by doctors. This negatively affects their acceptance among medical specialists. With exAID we present a new framework that is based on post-hoc explanation methods to support practitioners by enriching diagnostic decisions with human-understandable explanations using textual, conceptual and visual modalities. The framework allows to explain arbitrary, pre-trained Deep Learning models with a small amount of annotated data. Justifying medical diagnosis decisions is often not straightforward, due to the complexity of the underlying tasks. Therefore, exAID provides explanations in four different levels of granularity. Textual explanations using doctors-defined disease criteria provide understandable, high-level decision explanations. Second, concept scores quantifying the presence or absence of important criteria provide richer information. Additionally, exAID localizes the regions on the input image, where single criteria appear most salient to the AI. This helps doctors to efficiently verify the given prediction with less effort within their clinical workflow. Lastly, the framework quantifies the influence of single disease criteria on the AI's decision, based on the evaluation of all collected patient data. An Analytic Mode allows for facilitated training of prospective physicians and provides novel insights for medical researchers. Tools for systematical navigation through patient data and exploration of the input as well as the AI's representational space promote the discovery of previously unknown disease patterns exploited by the AI. The framework is currently being applied to the classification of dermoscopic skin lesions but can be adapted with minimal efforts for all kinds of use cases like the classification of histopathological skin lesions, diabetic retinopathy or the detection of COVID-19 in X-ray images.

Andrea Beccari

Dompé Farmaceutici, Switzerland

EXSCALATE: a smart in silico poly pharmacological drug design platform selecting molecules active against the ZIKA virus

October 28, 17:40 – 17:50

The EXSCALATE platform, leveraging the most powerful computing resources in Europe to empower the drug discovery process, is a fully integrated AI driven drug design infrastructure. Key elements of the platform are the exa-scale ready virtual screening tool and the poly pharmacological approach to correct the pathological phenotype. For its validation we started analyzing the Zika virus (ZikV) infection. ZikV infection is predominantly asymptomatic, nevertheless, severe neurological manifestations are associated , leading the World Health Organization to declare a public health emergency in 2016. Unfortunately, there are no FDA-approved treatments and vaccines for Zika virus, making the drug-discovery research crucial. The simulation was performed using LiGen™, to virtual screen a comprehensive database of investigational and marketed drugs (>10K) versus the following ZikA proteins: NS2B-NS3, NS3, NS5-MT, NS5-RdRp, Envelope and NS1.

Through this approach 83 molecules were predicted to be active on ZikV and the 12 top scored were selected for further validation. Interestingly, 8 compounds have an effective antiviral activity at a concentration lower than 10uM, assessed by different cellular-based approaches. Among them, the best hit is the Dactolisib that is active as inhibitor in the nanomolar range (0.01uM). Moreover, Dactolisib is able to overcome BBB and effectively reach the brain , becoming a promising compound for the treatment of ZikV infection. Preclinical in vivo studies to evaluate prophylactic and therapeutical activity of Dactolisib are ongoing.

Benedikt Rauscher

EMBL Heidelberg, Germany

mitoWEAR:

Monitoring of mitochondrial disorders using wearable activity trackers

October 28, 17:50 – 18:00

eHealth and the emergence of sophisticated devices for remote patient monitoring are paving the way to radically improve detection and treatment of disease, as well as promote wellness. A key hurdle for wider adoption of these devices, however, is a convincing demonstration of their reliability and utility. Mitochondrial disease patients frequently present with exercise intolerance that manifests after various periods of exertion. Exercise-related tests to measure these symptoms are notoriously difficult to perform in the clinic due to time constraints, variability of symptoms and influence from learned patient behaviors. mitoWEAR is a clinical study, where we provide a small cohort of mitochondrial disease patients with activity tracking devices to monitor daily exertion, day-to-day physiological variation and protracted response to exercise tests. Patient performance on established exercise tests will be benchmarked with clinical data to establish the validity of recorded activity measurements for diagnosing mitochondrial diseases. Both test-specific and daily activity measures will be correlated with additional factors, including type, etiology, severity and progression of the mitochondrial disease. Our goal is to determine whether fitness measures are accurate enough for clinically relevant classifications, and whether they can be used to accurately capture exercise intolerance symptoms that are difficult to measure in the clinic. The successful completion of this study can initiate a transformation in the way mitochondrial diseases are diagnosed and monitored in the clinic but will also set a precedent for other diagnostic studies employing wearable devices.

Yasmin Hollenbenders

Heilbronn University, Germany

Modelling progression of Alzheimer's disease with Hidden Markov Models based on cognitive and neuroanatomical data

October 27, 15:20 – 15:45 and October 28, 19:00 – 19:30

Alzheimer's disease (AD) is a neurodegenerative disorder and the most common type of dementia. Symptoms of AD include cognitive decline in various domains, which is caused by damage in neural tissue. The progression of the disease is highly heterogeneous and therefore prognosis and personalized treatment is challenging. This study models AD progression with Hidden Markov Models (HMMs) using cognitive and neuroanatomical data. The disease stages revealed with this technique are further analyzed as well as the transitions between these stages.

Longitudinal data from 1017 subjects from the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort with diagnoses healthy, mild cognitive impairment, or AD was used to generate (I) a cognitive and (II) a neuroanatomical HMM without restrictions on the model's structure. The cognitive model is based on the 11 sub-scores of the ADAS-cog assessment and the anatomical model is based on the thickness or volume, respectively, of 14 cortical and subcortical regions associated with AD.
The two models complement each other. The neuroanatomical model already differentiates early stages in which a cognitive decline cannot be observed yet. The cognitive model, on the other hand, structures the heterogeneity in later stages on a more fine grained level. The eight states of the neuroanatomical model are organized in two parallel progression pathways with little crossing between them. One pathway is characterized by decreasing precuneus thickness while the other one is driven by decreases in hippocampus and amygdala volumes. The five stages of the cognitive model are best differentiated by decline in the memory domain but the structure is less ordered than in the neuroanatomical model.
To conclude, this study sheds light on the diverse progression pathways of AD and presents different perspectives on them by taking cognition and neuroanatomy into account.

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Discovering Novel Therapeutic Targets Using Deep Learning and Large Biomedical Knowledge Graphs

October 27, 15:20 – 15:45 and October 28, 17:00 – 17:40

One of the challenges in drug discovery is the high attrition rate late in development. Lack of efficacy is one of the main reasons for failures in late-stage clinical trials. However, drugs for targets supported by genetic evidence are more likely to succeed clinically. Therefore, using the increased amount of human genetic data available today to prioritise the best drug targets can improve the success rate of new drugs development. The goal of the study is discovering new therapeutic targets using machine learning approaches to accelerate the process of developing new or repurposing existing drugs. We apply knowledge graph analysis to exploit heterogeneous data to find novel targets. Nodes in the knowledge graph represent biological entities (e.g., targets, diseases, drugs, variants, pathways, etc.), and edges represent their relationships. We incorporated data from the Open Targets Platform, ChEMBL, UniProt, and IntAct, and Reactome databases, and EFO and GO ontologies. The resulting knowledge graph contains 45,614 targets, 18,332 diseases, 416,333 nodes, and ~15 million edges. Graph embedding algorithms are applied to create feature vector representations of nodes in the graph, which represent semantic relationships between entities. We used graph convolutional network algorithm to generate the embeddings, and a neural network classifier to predict edges between pairs of nodes. The accuracy of the model is assessed using a hold-out testing set, and the model achieved 91% accuracy in predicting edges between targets and diseases. Overall, this study provides a large-scale knowledge graph created for the purpose of target discovery and provides model for predicting associations between targets and diseases. The computational approach applied in this study is generic in nature and can be applied or extended to find associations between other biological entities as well.

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