PRISME FORUM
BASEL 2015

THE HUMAN BRAIN PROJECT

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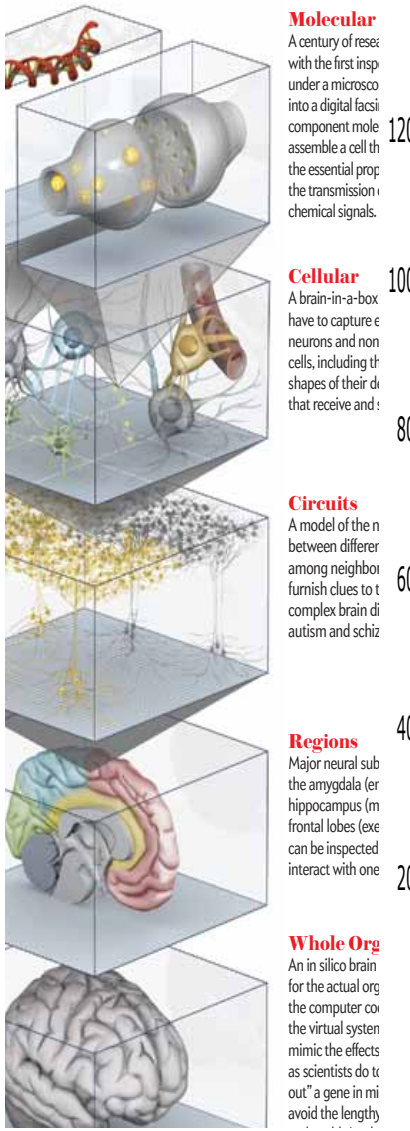
MOTIVATION 1 - DATA FEDERATION & INTEGRATION

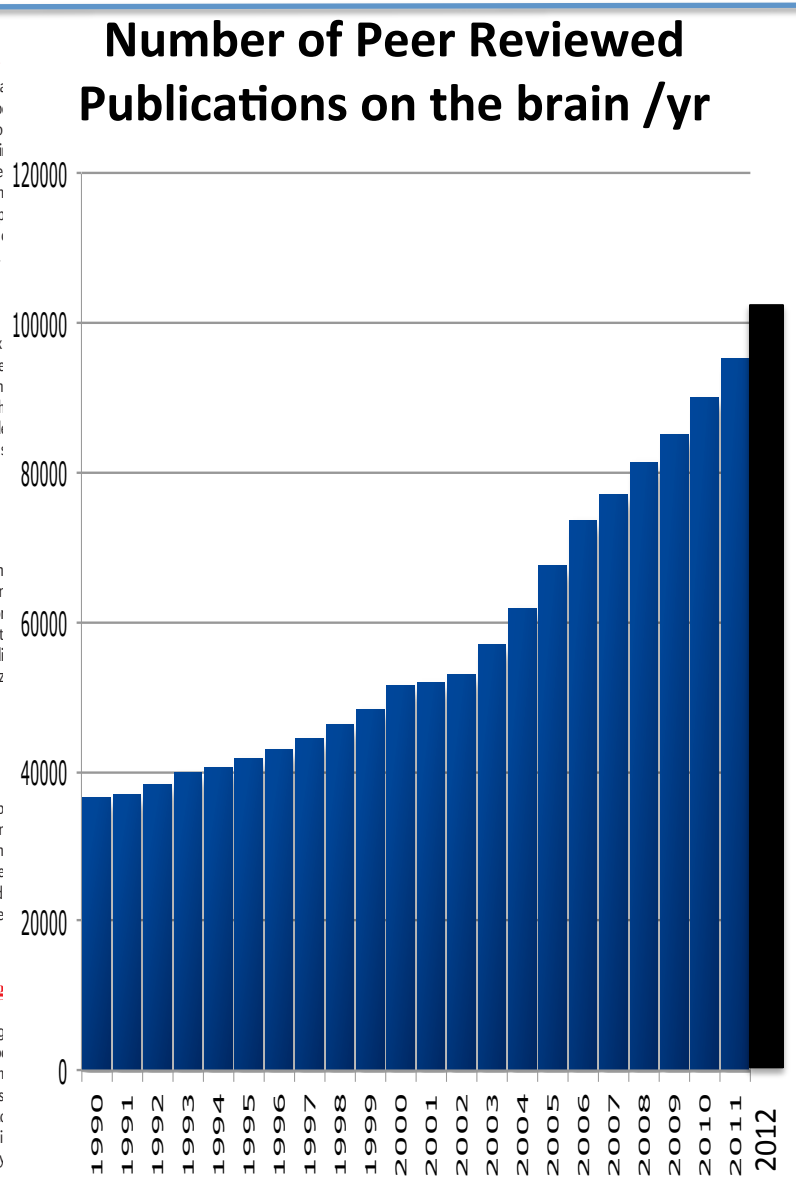
The facts:

1. Data and knowledge is **growing** exponentially
2. Data and knowledge are increasingly **fragmented**
3. Benefits for society seem to be **decreasing**
4. Economic burden increasing to **unsustainable** levels

The causes:

1. No integration plan
2. No data curation plan
3. No plan to link across levels
4. No plan to transfer knowledge from animal model to human
5. No plan to go beyond traditional classification of diseases





MOTIVATION 2 – THE MEDICO-SOCIAL CHALLENGE

Alzheimer's disease: **20 per cent** beyond the age of 80; dependent within 3-5 years of onset.

Depression: the second most common condition in the world (WHO): **6 per cent** of the population in the Western world.

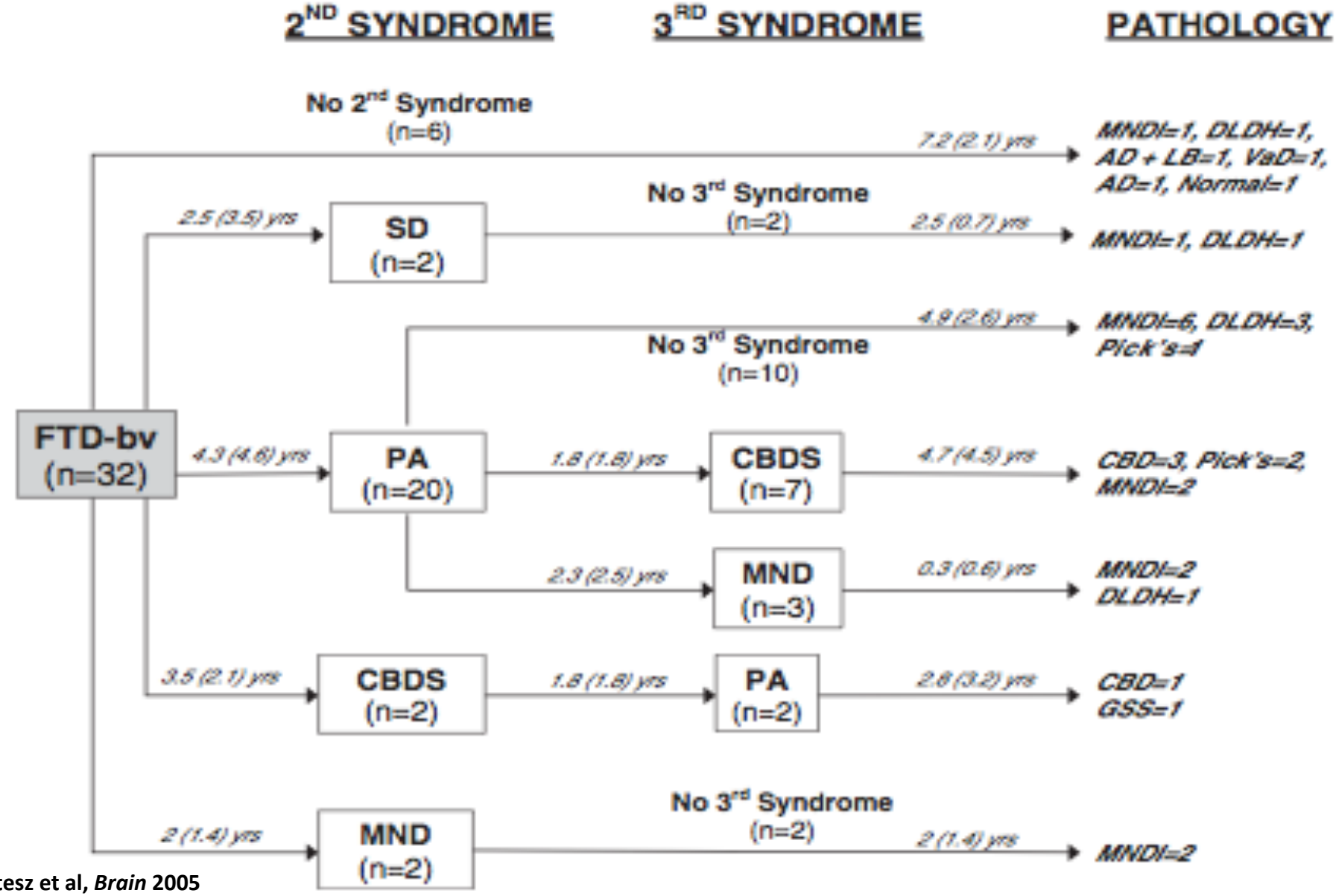
Cerebral vascular accidents: first cause of adult motor disability. **75 per cent** suffer residual disability.

Parkinson's disease: second cause of motor disability. Affects **0.2 per cent** of the population.

Multiple sclerosis: mainly young people with dependency in **30 per cent**.

Epilepsy: 50 million people globally of which almost **50 per cent** are aged < 10 years**.** Social and familial repercussions are **lifelong.**

HAS PHENOMENOLOGY REACHED A DEAD END?



Kertesz et al, *Brain* 2005

MOTIVATION 3 – DISCOVERING CAUSES OF DISEASE

WHAT CAUSES IT?

What mechanisms?
Role of genes?
Abnormal proteins – amyloid?
Abnormal neurotransmission – acetyl choline?

What pathophysiological abnormalities are causes and which are effects?

- **US President 1981-1989**
- **Oldest US President**
- **1994: AD admitted publicly**

HOW DO WE PREVENT IT? AND TREAT IT?

Can we diagnose it?	- **NO**
Do symptoms matter?	- **A LITTLE**
What weight to pathology?	- **END STAGE**
Do we compensate?	- **REDUNDANCY**
What about pre-symptomatic diagnosis?	- **???**
Why don't the treatments work?	- **TREAT WHAT**
And what about preventive treatment?	- **???**

WHAT IS A FLAGSHIP OF ENTERPRISE AND TECHNOLOGY

Future and Emerging Technology Flagships (FET)

Are ambitious large-scale, informatics-driven, research Initiatives that aim to achieve a visionary goal.

The scientific advance should provide a strong and broad Basis for future technological innovation and economic Exploitation in a variety of areas, as well as novel benefits for society.

The research is collaborative, internally non-competitive, inter- and trans-disciplinary, driven by a commonly agreed road-map

EUROPEAN COMMISSION

FET FLAGSHIPS

BLUE BRAIN PROJECT + NEUROIMAGING COMMUNITY

IMPACT OF ICT

VON NEUMANN MACHINES

MOORE'S LAW

ENERGY LIMITATIONS

INTERNET

DATABASE MANAGEMENT

CLOUD ENVIRONMENT

DATABASE QUERYING & ADDRESSING

REAL-TIME VISUALISATION

SUPERCOMPUTING

BEYOND EXASCALE

BANDWIDTH & ROUTING [**HTML5, Cisco**]

DISTRIBUTED [**Oracle**]

SECURITY [**Amazon, Dropbox, iCloud**]

LOCAL [**Google**] vs REMOTE [**EPFL**]

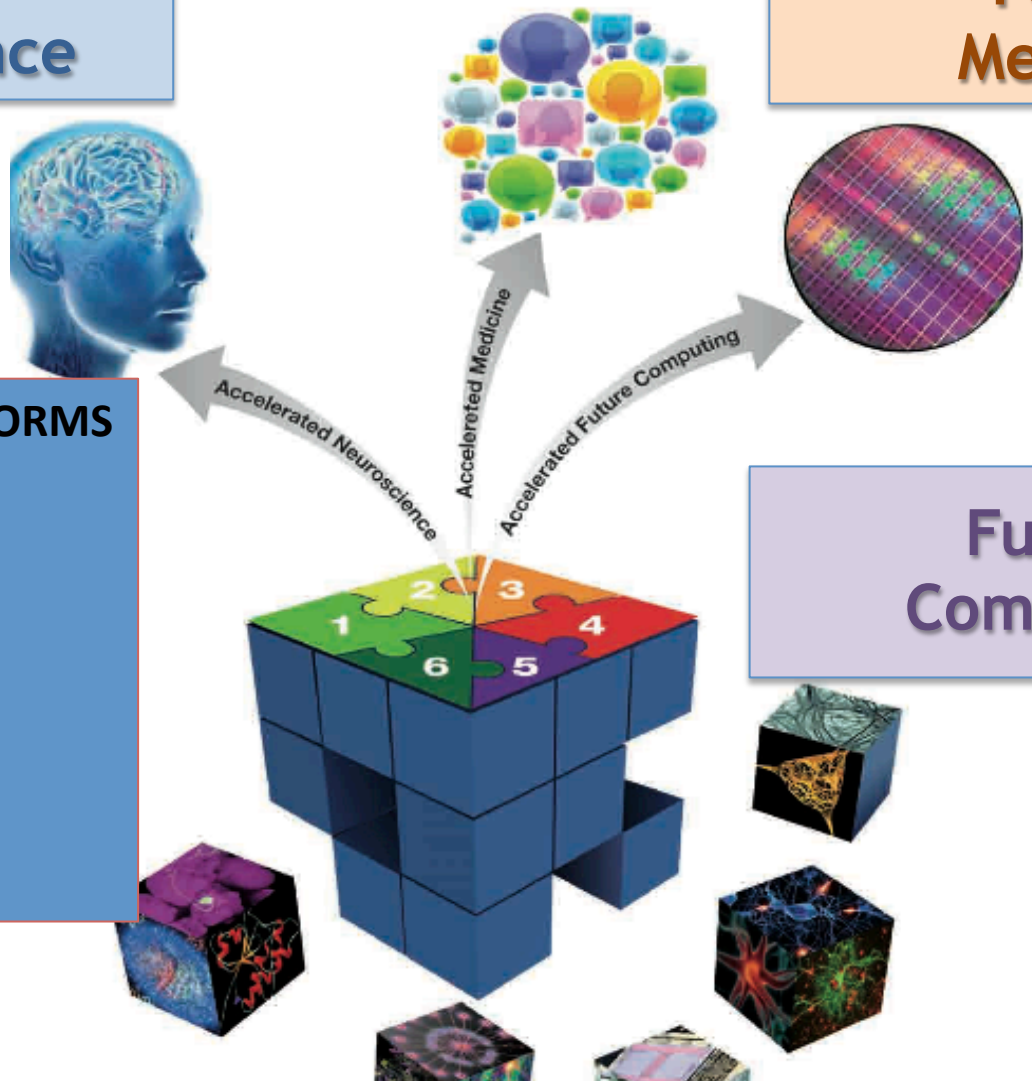
FOR SUPERCOMPUTING [**IBM, CRAY**]

NEUROMORPHIC COMPUTING

HBP – A NEUROINFORMATICS PROJECT

Future Neuroscience

Future Medicine



Future Computing

6 OPEN ACCESS PLATFORMS

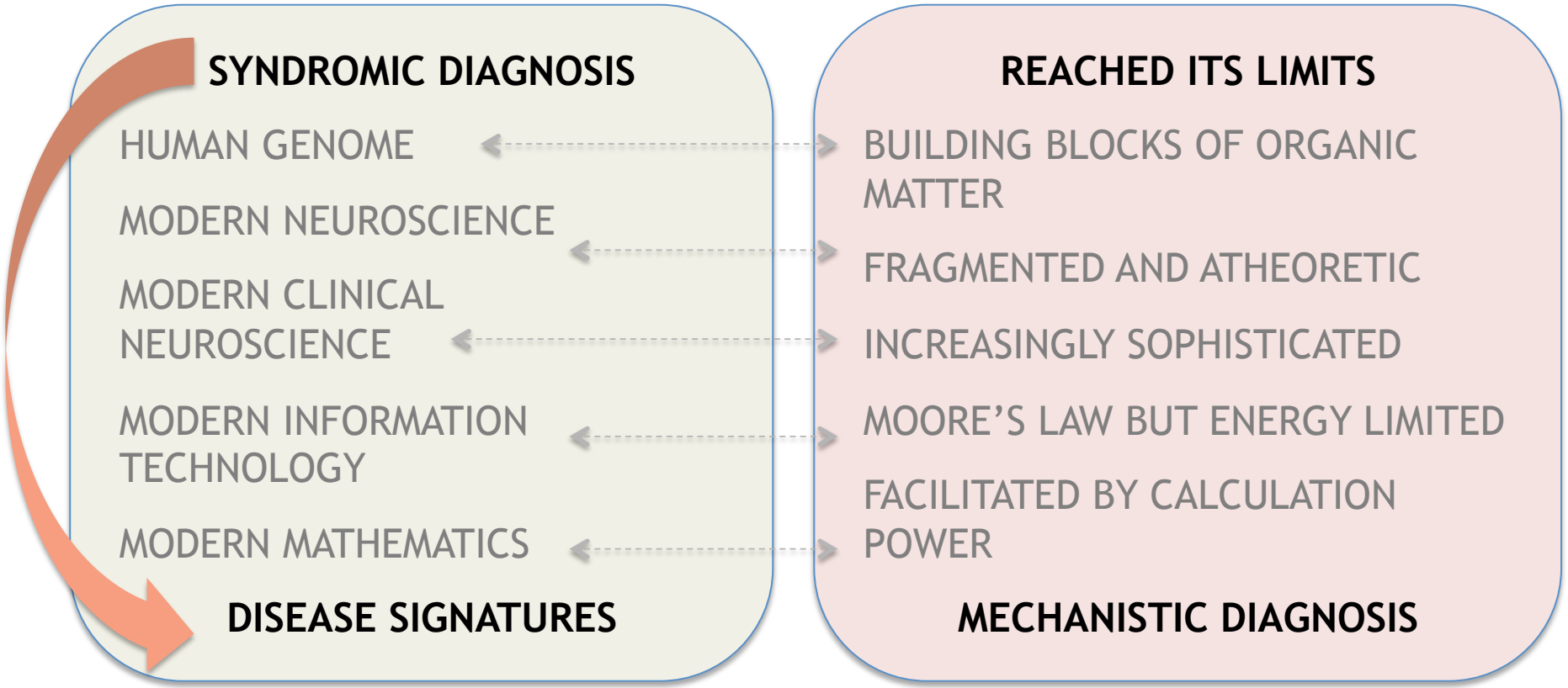
HIGH PERFORMANCE COMPUTING
NEUROMORPHIC COMPUTING
NEURAL THEORY (EIT)
SIMULATION
NEUROINFORMATICS
MEDICAL INFORMATICS

CONTRACT

ACCREDITATION

FUTURE MEDICINE

The Medical Informatics Platform



CONFRONTING PARADIGMS

CARTESIAN MODEL (TOP DOWN)

Mental theory
Mathematically expressed model
Confrontation with “relevant” data
Parameterisation and optimisation of model
Facts

SIMULATION MODEL (BOTTOM UP)

Multimodal and multivariate data
Mining to demonstrate structures by correlation &/or classification
Mathematically expressed model
Exploration of structures to generate hypotheses
Investigation of hypotheses
Knowledge

THE MEDICAL INFORMATICS PLATFORM

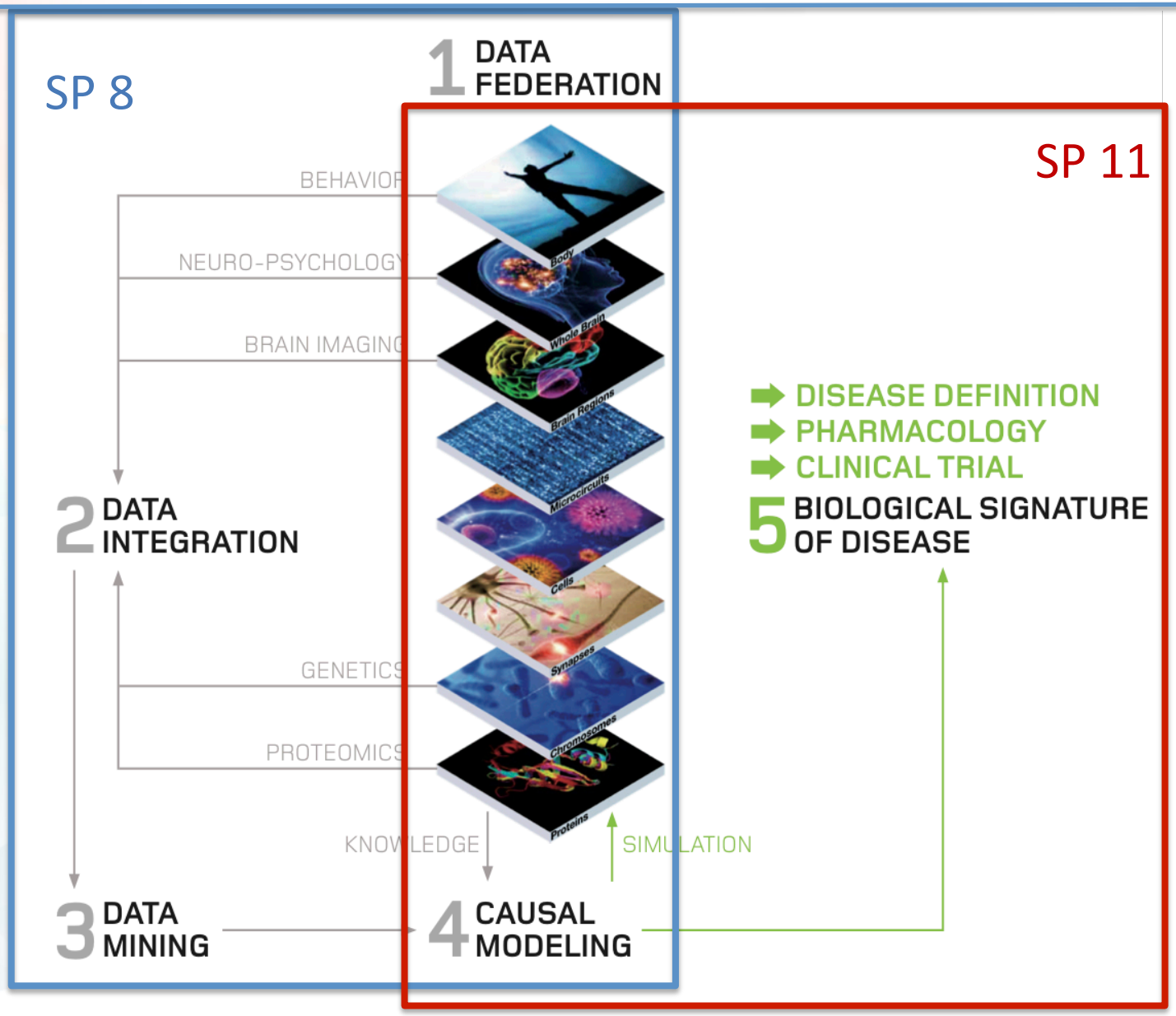
A TIPPING POINT FOR BRAIN MEDICINE

THE ROLE OF COMPUTER SCIENCE

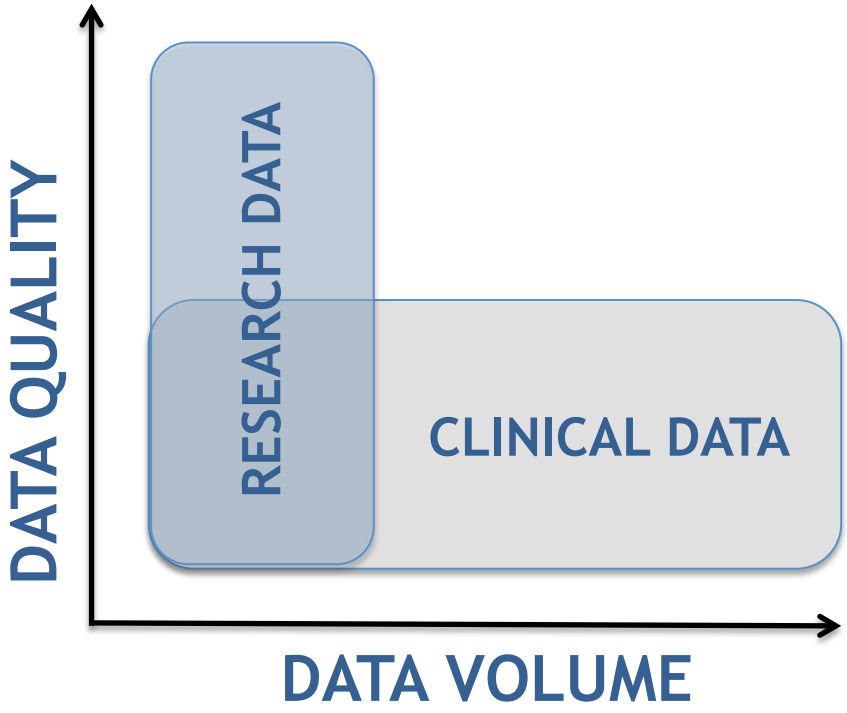
A CHANGING DEONTOLOGICAL PARADIGM

IMPLEMENTATION OF NEW TECHNOLOGY

THE EXAMPLE OF THE MIP



DATA SOURCES AND CHALLENGES



HOSPITAL DATABASES

- NOT COMPLETE
- NOT STRUCTURED
- NOT STANDARDISED
- NOT CLEAN
- PROTECTED FOR PRIVACY
- PROTECTED AGAINST CORRUPTION

RESEARCH DATABASES

- PROTECTED CULTURALLY

PHARMACEUTICAL DATABASES

- PROTECTED COMMERCIALLY

ETHICAL CHALLENGES

PRIVACY

- DE-PERSONALISATION
- AGGREGATION

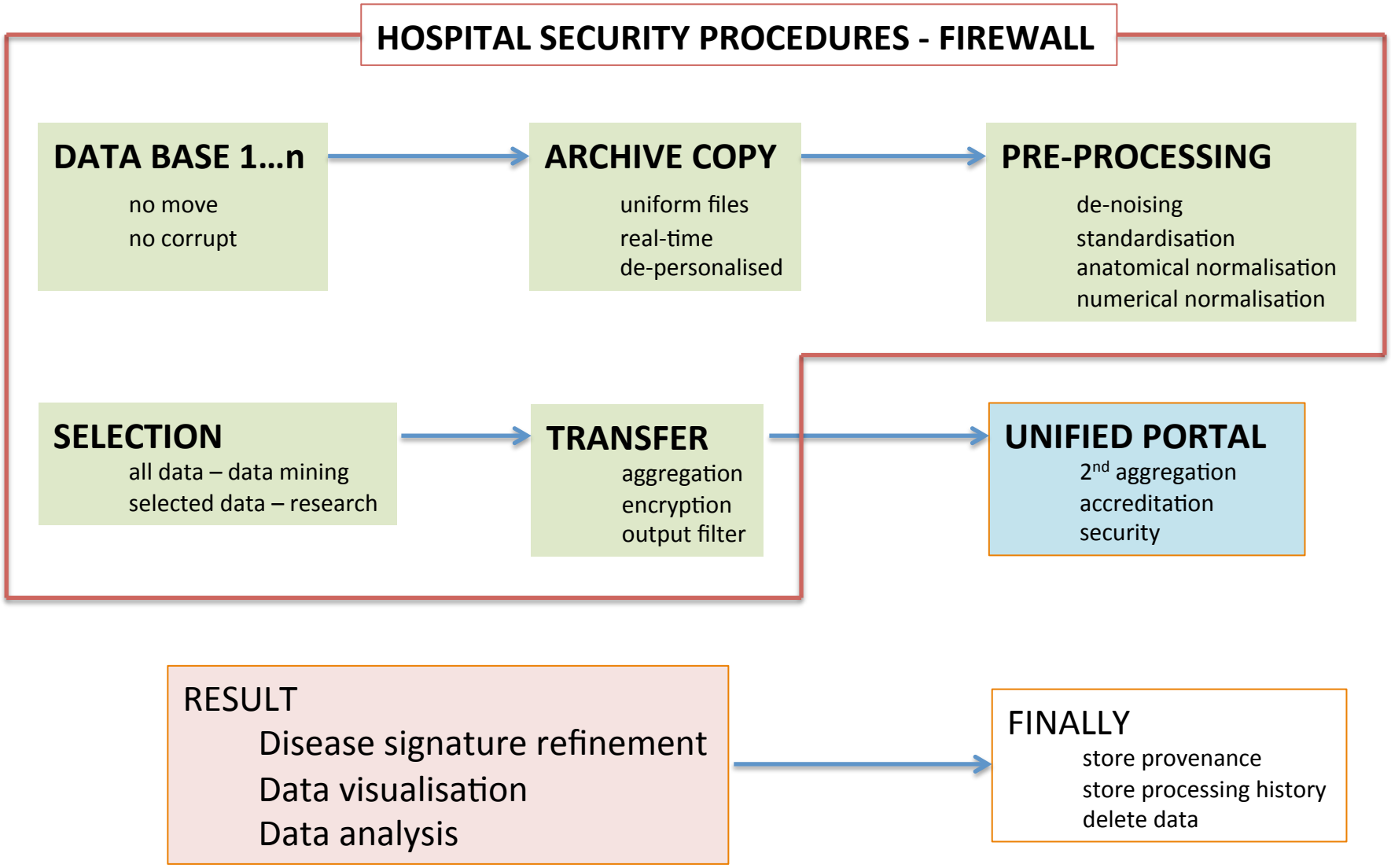
CONSENT

- BROAD CONSENT
- RETROSPECTIVE – PROSPECTIVE

MANAGEMENT OF ETHICS

- LOCAL ETHICS COMMITTEES
- VALUE AND CREDIBILITY OF SCIENCE

MEDICAL INFORMATICS PLATFORM



DATA ANALYSIS OPPORTUNITIES

DISEASE SIGNATURES

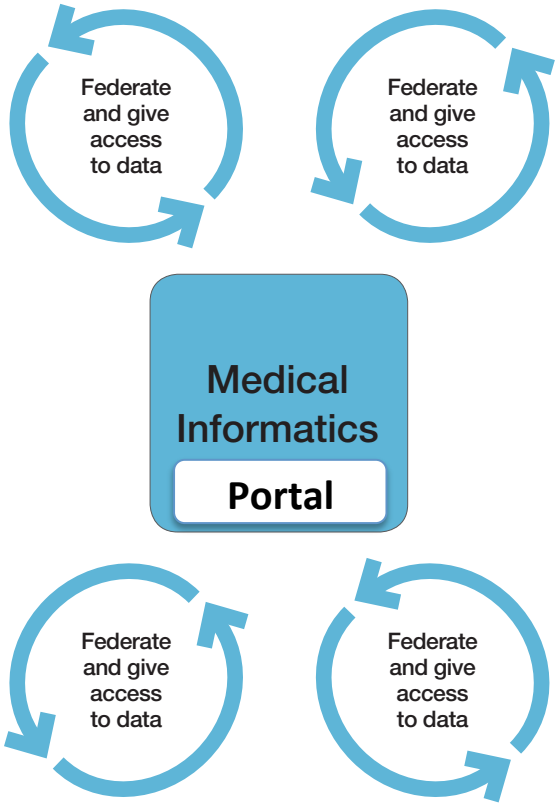
- DATA MINING
- REAL-TIME
- CONTINUOUS
- ITERATIVE

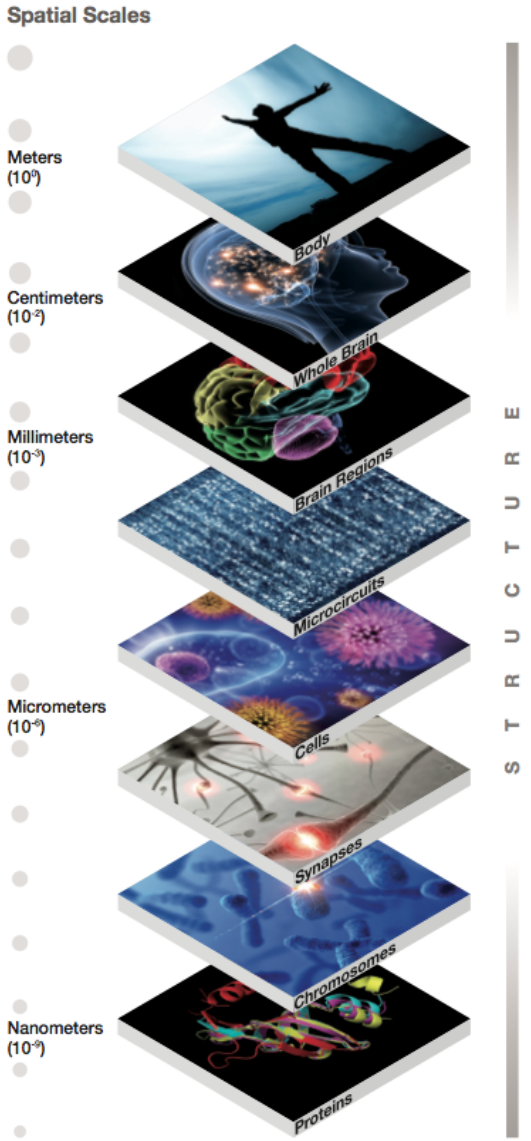
DATA VISUALISATION

- EPIDEMIOLOGY
- HEALTH SERVICES

RESEARCH

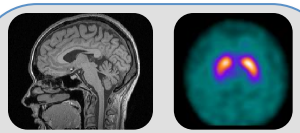
- HYPOTHESIS TESTING
- CLINICAL TRIALS

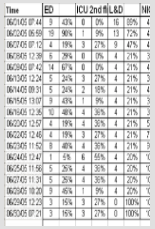


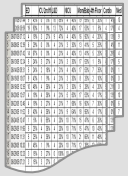


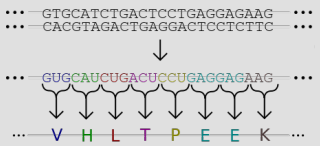
FEATURE EXTRACTION – DATA REDUCTION

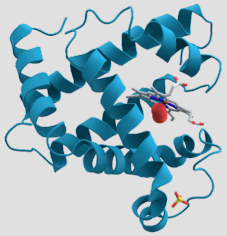
DATA





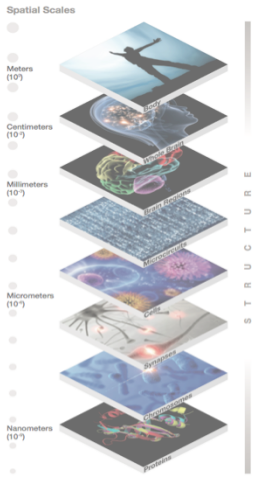






SCALE

- Genetic
- Molecular
- Cellular
- Circuits
- Systems

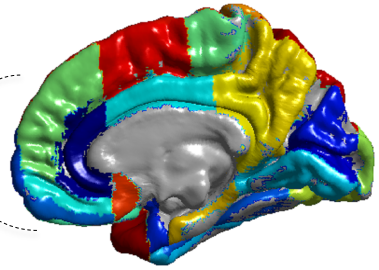


TIME

- Cross-sectional
- Longitudinal

SPACE

- Brain anatomy



PATHOLOGY

- Pathology confirmed diagnosis
- Risk factors

DEMOGRAPHICS

- Age, gender …

VARIABLES

MEDICAL EPIDEMIOLOGY

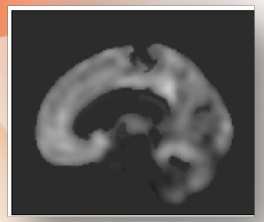
Submit Query

Hide Legend

- Diseases of the nervous system
- Certain disorders involving the immune mechanism
- Certain infectious and parasitic diseases
- Diseases of the respiratory system
- Diseases of the digestive system
- Congenital malformations, deformations and chromosomal abnormalities
- Injury, poisoning and certain other consequences of external causes
- Diseases of the musculoskeletal system and connective tissue
- Diseases of the skin and subcutaneous tissue
- Diseases of the circulatory system
- Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
- Diseases of the genitourinary system
- Unspecified mental disorder
- Diseases of the blood and disorders of the immune mechanism
- Mental and behavioural disorders
- External causes of morbidity and mortality
- Diseases of the ear and mastoid process
- Factors influencing health status and contact with health services
- Neoplasms
- Endocrine, nutritional and metabolic diseases
- Diseases of the eye and adnexa
- Codes for special purposes
- Pregnancy, childbirth and the puerperium

DATA INTEGRATION

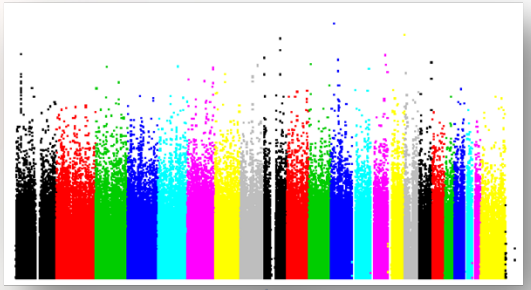
BRAIN IMAGING



PET

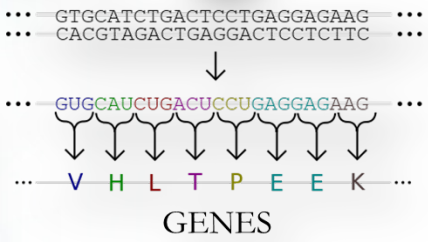
MRI

CLINICAL SCALES & MEASUREMENTS

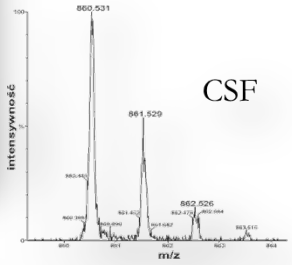


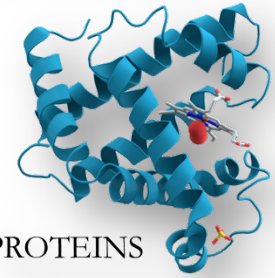
Organising Tabulating

Processing…

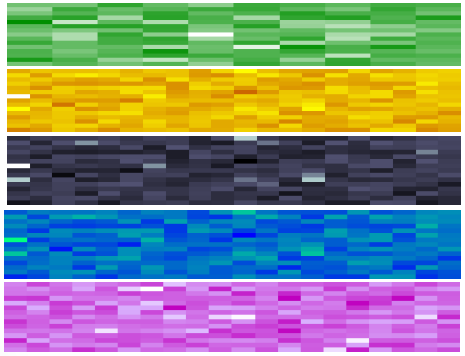


GENES





PROTEINS



MRI data

PET data

Gene data

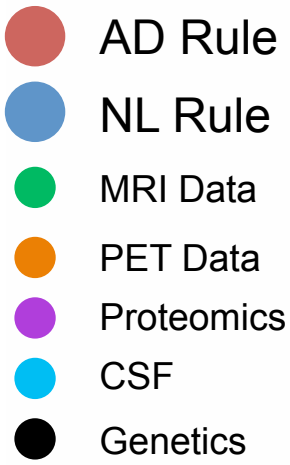
CSF data

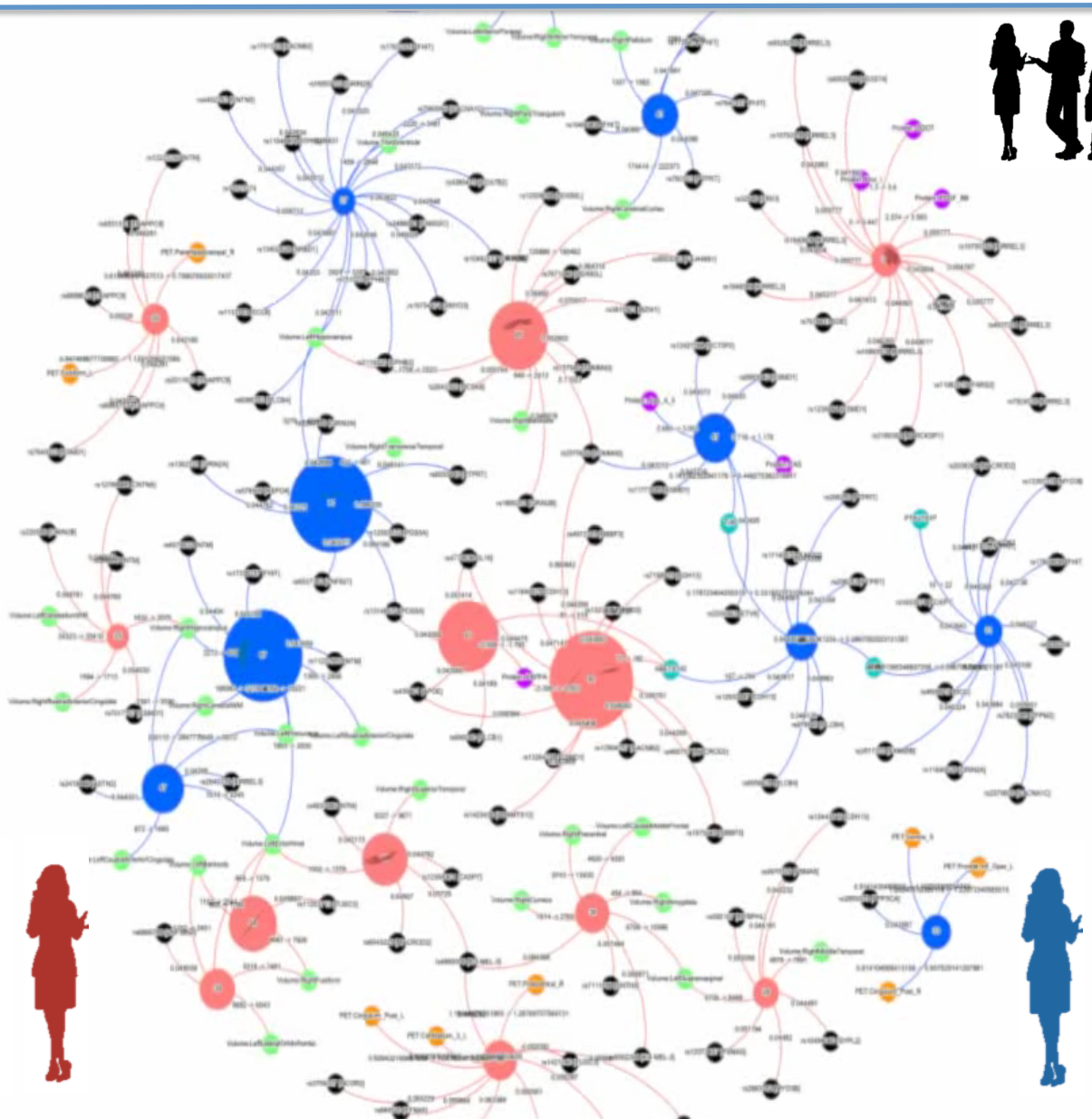
Protein data

912 Alzheimer's patients
5566 Healthy controls

- **Phenotype led semi-supervised clustering**
- **Biologically led classification**
- **High dimension and feature learning**

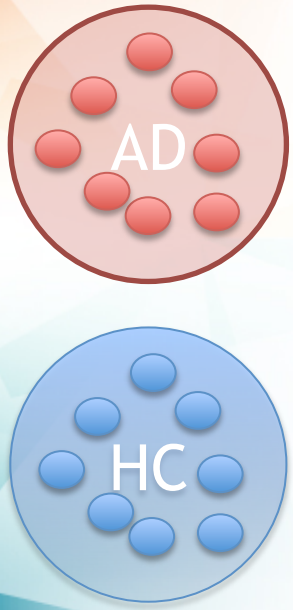
LINKS BETWEEN PHENOMENOLOGY & BIOLOGY



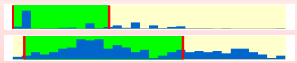


FINDING CAUSAL RULES

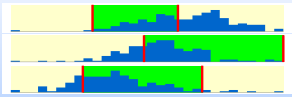
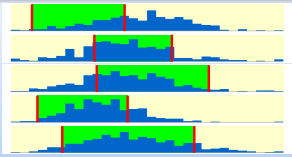
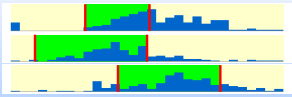
- Phenotype-led semi-supervised clustering



• AD RULES

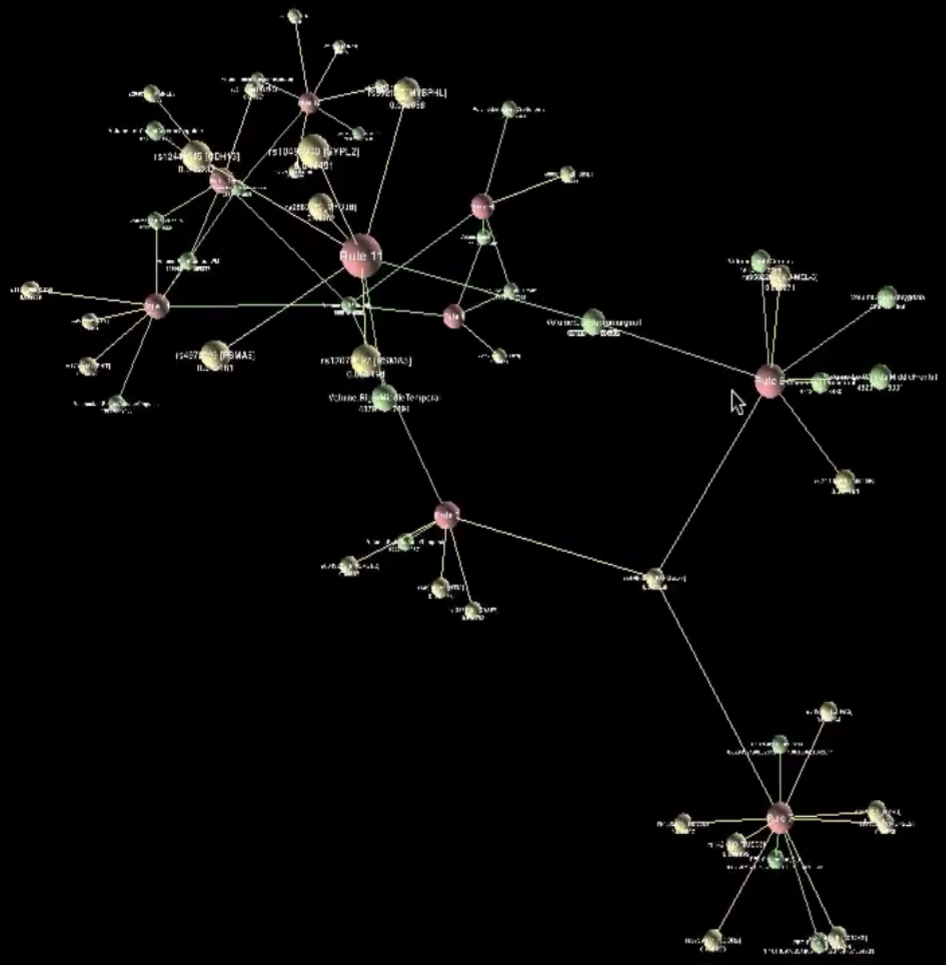
1	ABETA142 Protein: PAPPA	
2	Protein: PAPPA ABETA142	
3	Volume:LeftHippocampus Volume:RightCerebralCortex Volume:RightBankssts	
4	Volume:LeftEntorhinal Volume:RightFusiform Volume:LeftBankssts	

• HC RULES

PET:Cingulum_Post_L PET:Cerebelum_3_L PET:Postcentral_R	
Volume:RightAmygdala Volume:LeftCaudalMiddleFrontal Volume:RightPrecentral Volume:RightCuneus Volume:LeftSupramarginal	
Protein: Prol_I Protein: SGOT Protein: PDGF_BB	
PET:ParaHippocampal_R PET:Fusiform_L	

- New disease classification.
- Standard Format

LINKS BETWEEN PHENOMENOLOGY & BIOLOGY



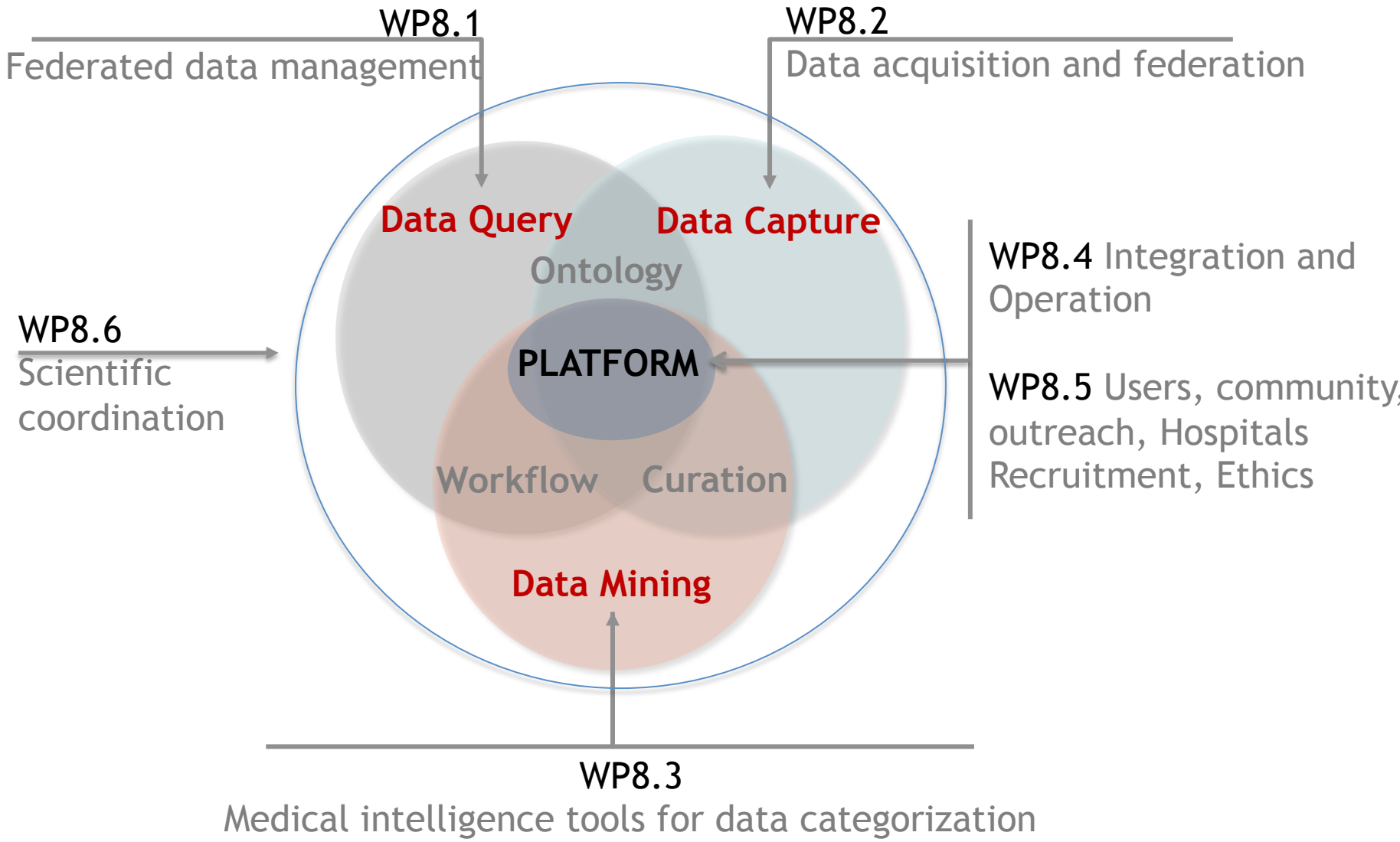
INFORMATICS BASED APPROACH

Informatics-based characterisation of brain diseases

- **Unlock** added value of clinical records & data
- **Catalyse** a major collaboration of hospitals
- **Federate and integrate** knowledge and data about human diseases – IT based atlas-encyclopedia
- **Analyse and Derive** biologically-grounded brain disease signatures for new diagnostic classification

- **Understand** the biological similarities and differences between brain diseases
- Provide **new discovery** pipelines to prevent, diagnose and treat brain disorders

MIP INTEGRATED VIEW



THANKS FOR LISTENING

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JF Demonet
Sara Lorio

www.unil.ch/lren

www.humanbrainproject.org