



PRISME FORUM
BASEL 2015

THE HUMAN BRAIN PROJECT



Richard Frackowiak (CHUV & EPFL Lausanne)



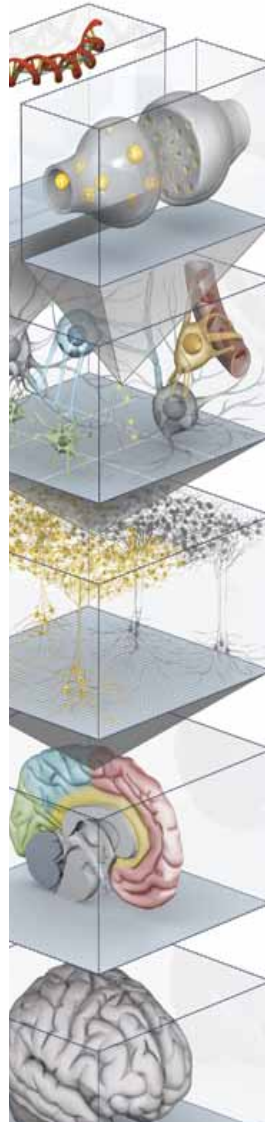
MOTIVATION 1 - DATA FEDERATION & INTEGRATION

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



Molecular

A century of resear with the first insp under a microsc into a digital facsi component mole assemble a cell th the essential prop the transmission chemical signals.

Cellular

A brain-in-a-box have to capture e neurons and non cells, including th shapes of their di that receive and :

Circuits

A model of the n between differer among neighbor furnish clues to t complex brain di autism and schiz

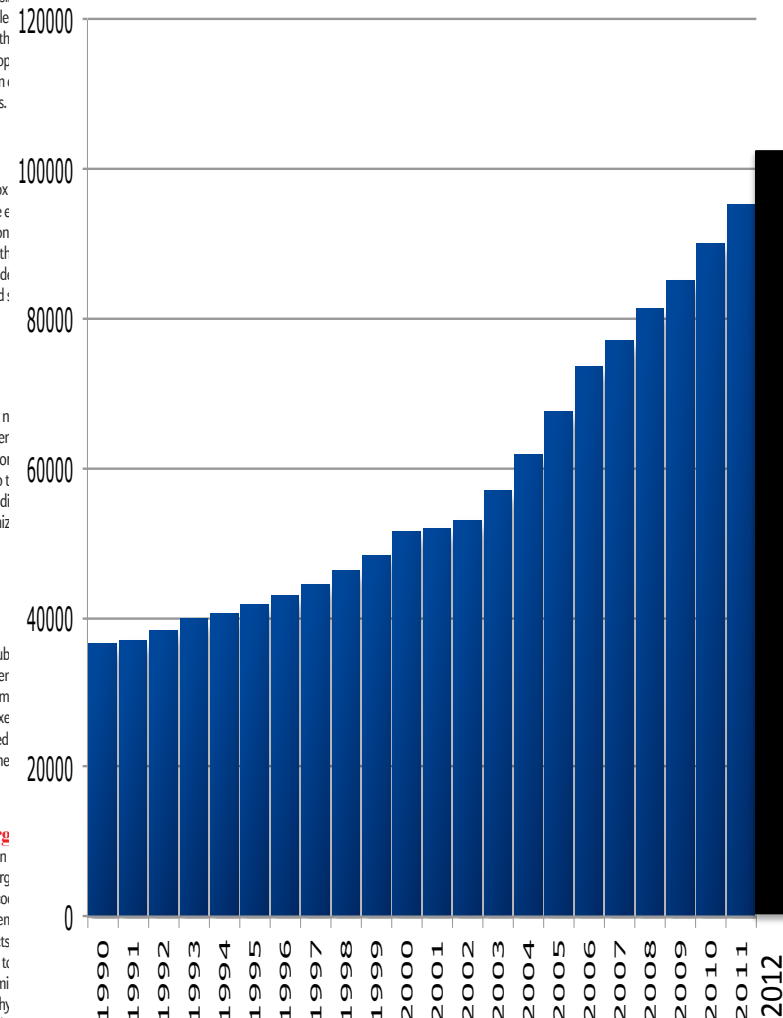
Regions

Major neural sub the amygdala (er hippocampus (m frontal lobes (ex can be inspected interact with one

Whole Org

An in silico brain for the actual org the computer co the virtual system mimic the effects as scientists do t out" a gene in mi avoid the lengthy

Number of Peer Reviewed Publications on the brain /yr





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.



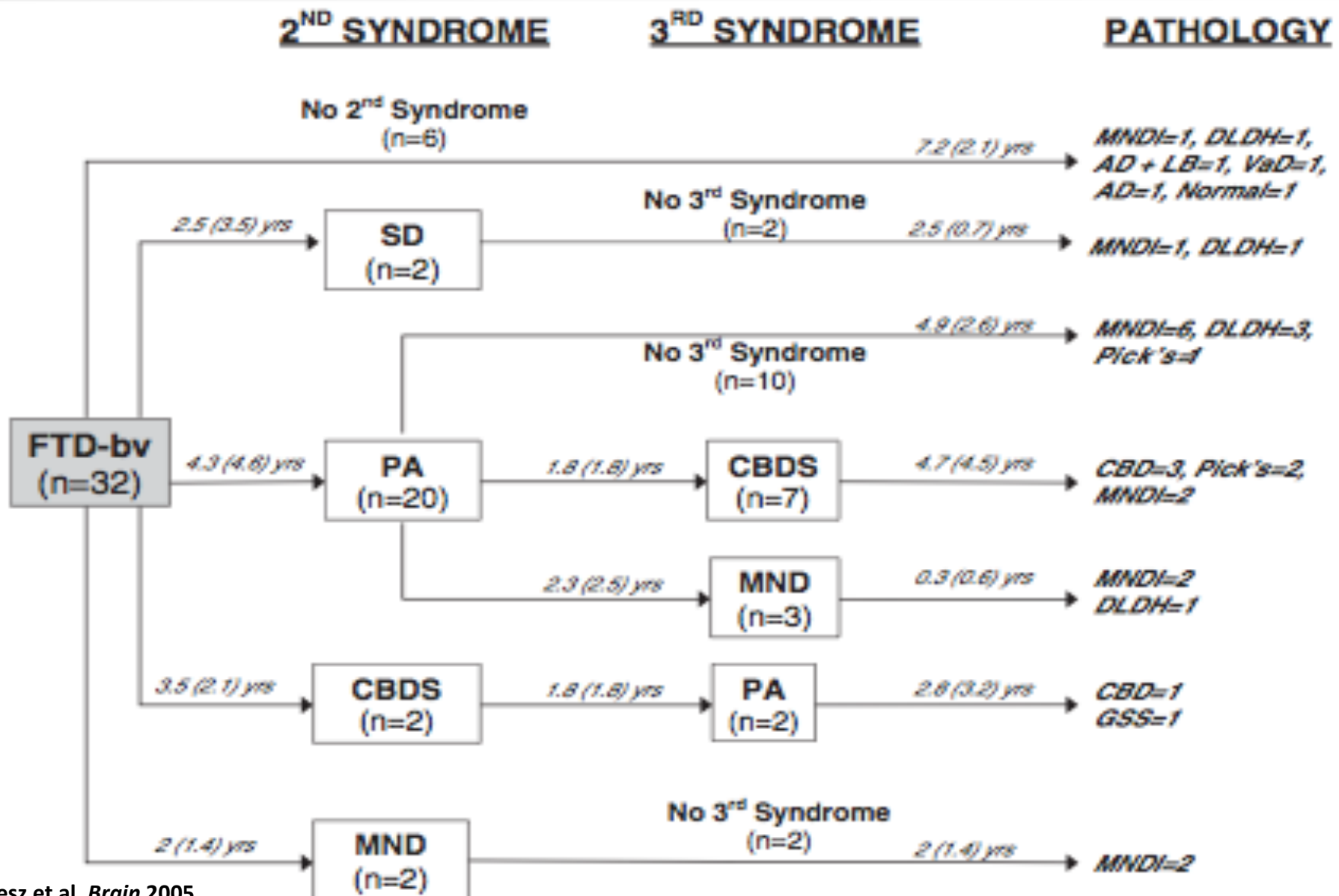
Multiple sclerosis: mainly young people with dependency in **30 per cent**.



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?





MOTIVATION 3 – DISCOVERING CAUSES OF DISEASE

WHAT CAUSES IT?

What mechanisms?

Role of genes?

Abnormal proteins – amyloid?

Abnormal neurotransmission – acetyl choline?



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

What pathophysiological abnormalities are causes and which are effects?

HOW DO WE PREVENT IT? AND TREAT IT?

Can we diagnose it?

Do symptoms matter?

What weight to pathology?

Do we compensate?

What about pre-symptomatic diagnosis?

Why don't the treatments work?

And what about preventive treatment?

- **NO**
- **A LITTLE**
- **END STAGE**
- **REDUNDANCY**
- **???**
- **TREAT WHAT**
- **???**



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

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**

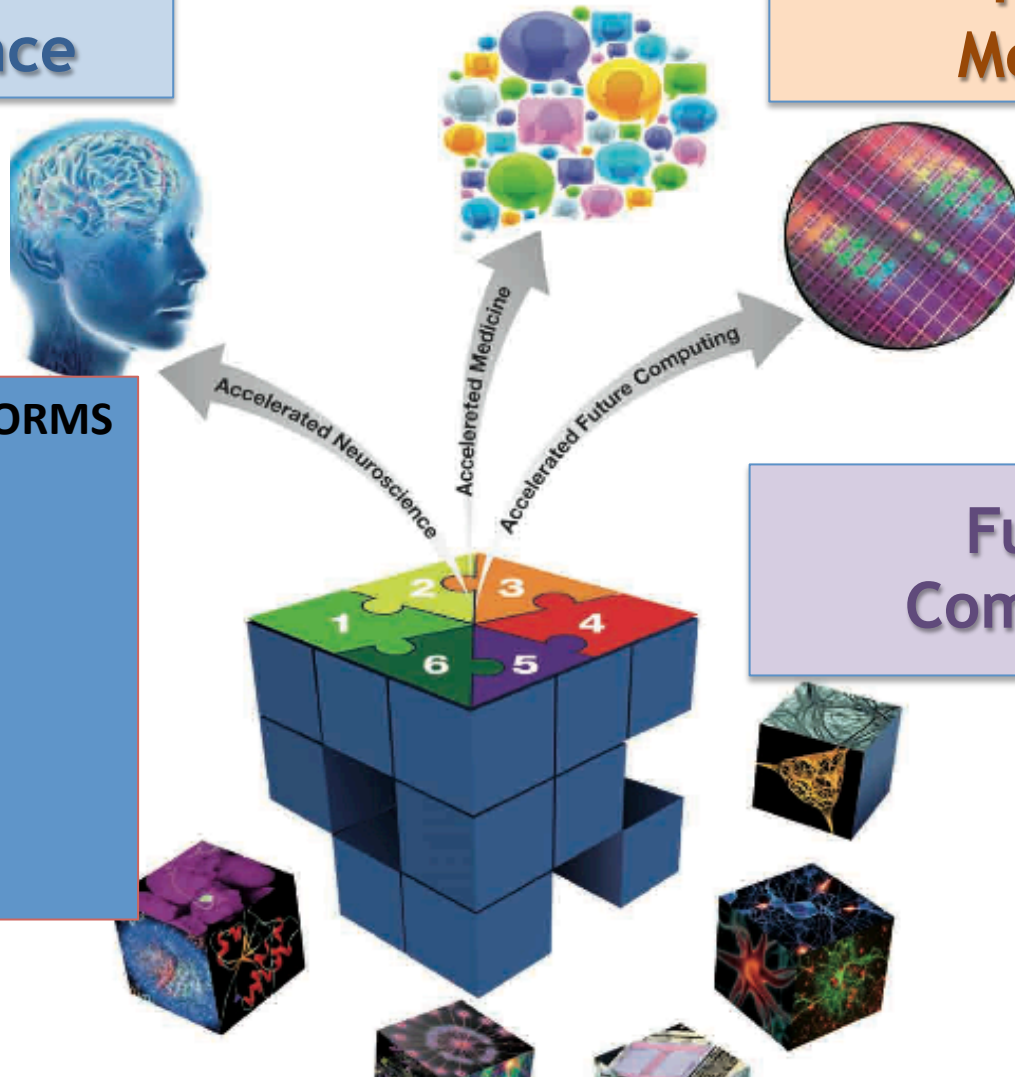
**Future
Medicine**

6 OPEN ACCESS PLATFORMS

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

CONTRACT

ACCREDITATION



**Future
Computing**



FUTURE MEDICINE

The Medical Informatics Platform

SYNDROMIC DIAGNOSIS

HUMAN GENOME

MODERN NEUROSCIENCE

MODERN CLINICAL
NEUROSCIENCE

MODERN INFORMATION
TECHNOLOGY

MODERN MATHEMATICS

DISEASE SIGNATURES

REACHED ITS LIMITS

BUILDING BLOCKS OF ORGANIC
MATTER

FRAGMENTED AND ATHEORETIC

INCREASINGLY SOPHISTICATED

MOORE'S LAW BUT ENERGY LIMITED

FACILITATED BY CALCULATION
POWER

MECHANISTIC DIAGNOSIS



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

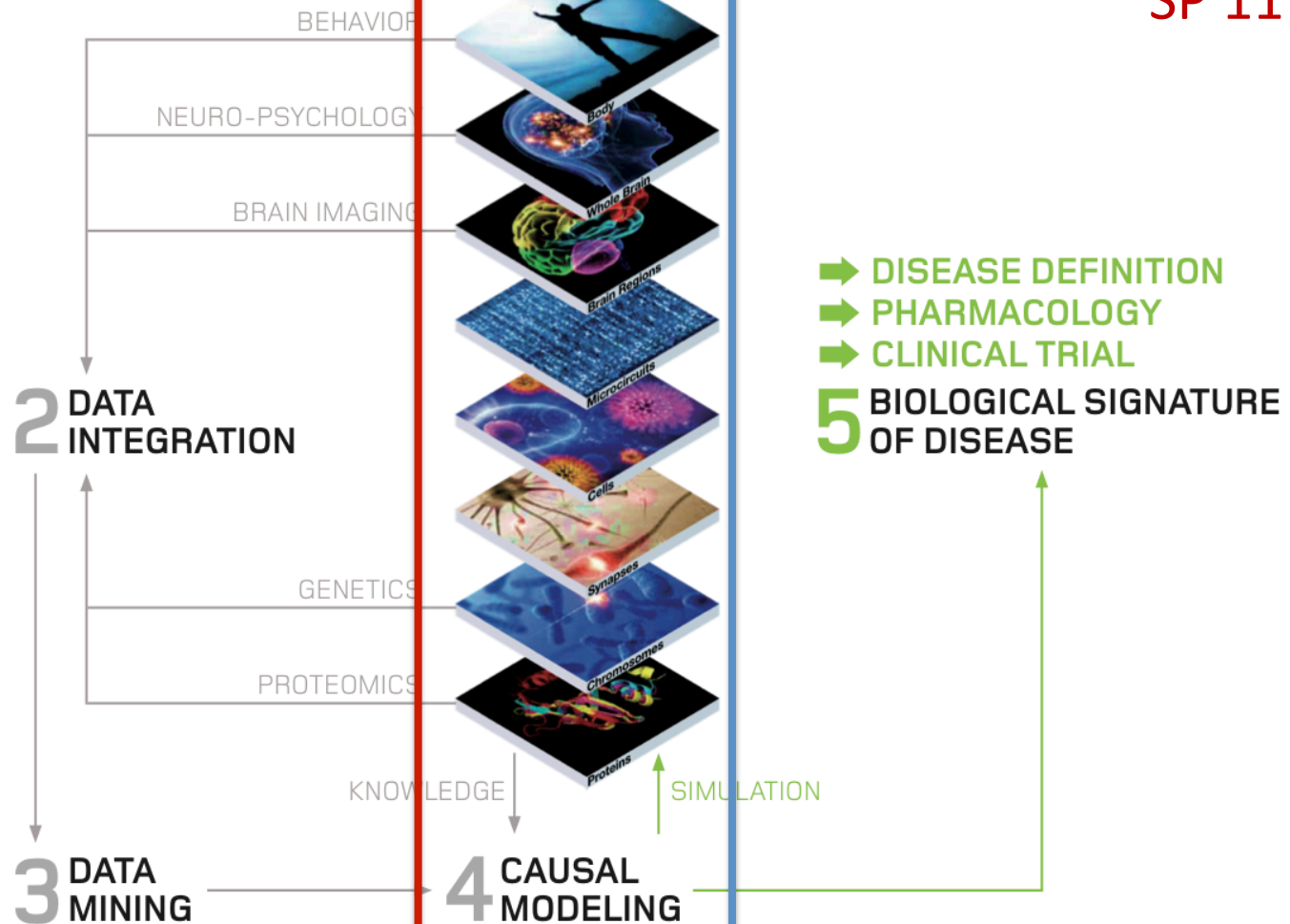


THE EXAMPLE OF THE MIP

SP 8

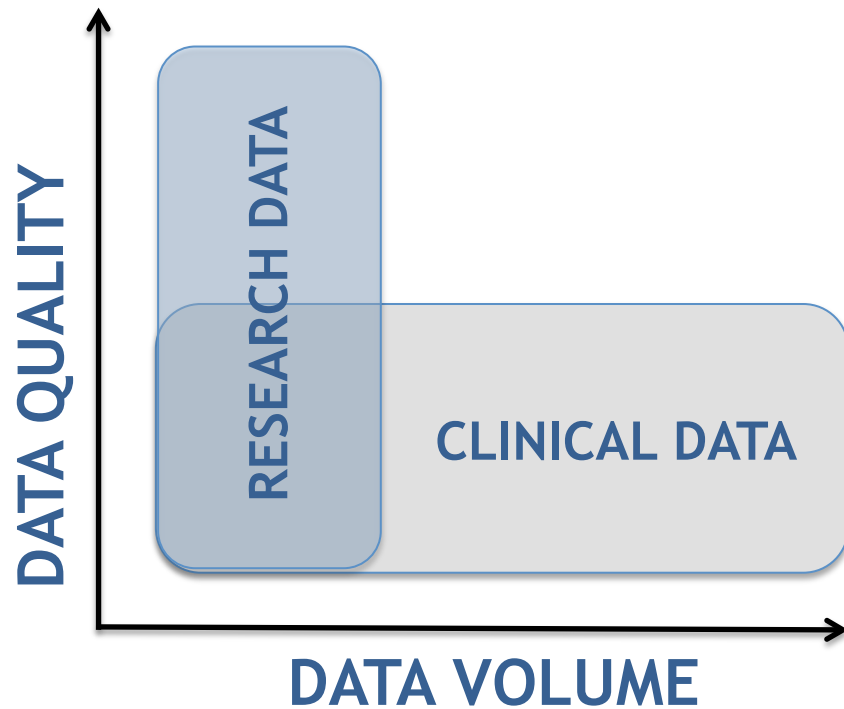
1 DATA
FEDERATION

SP 11





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 COMMERCIALY



ETHICAL CHALLENGES

PRIVACY

- DE-PERSONALISATION
- AGGREGATION

CONSENT

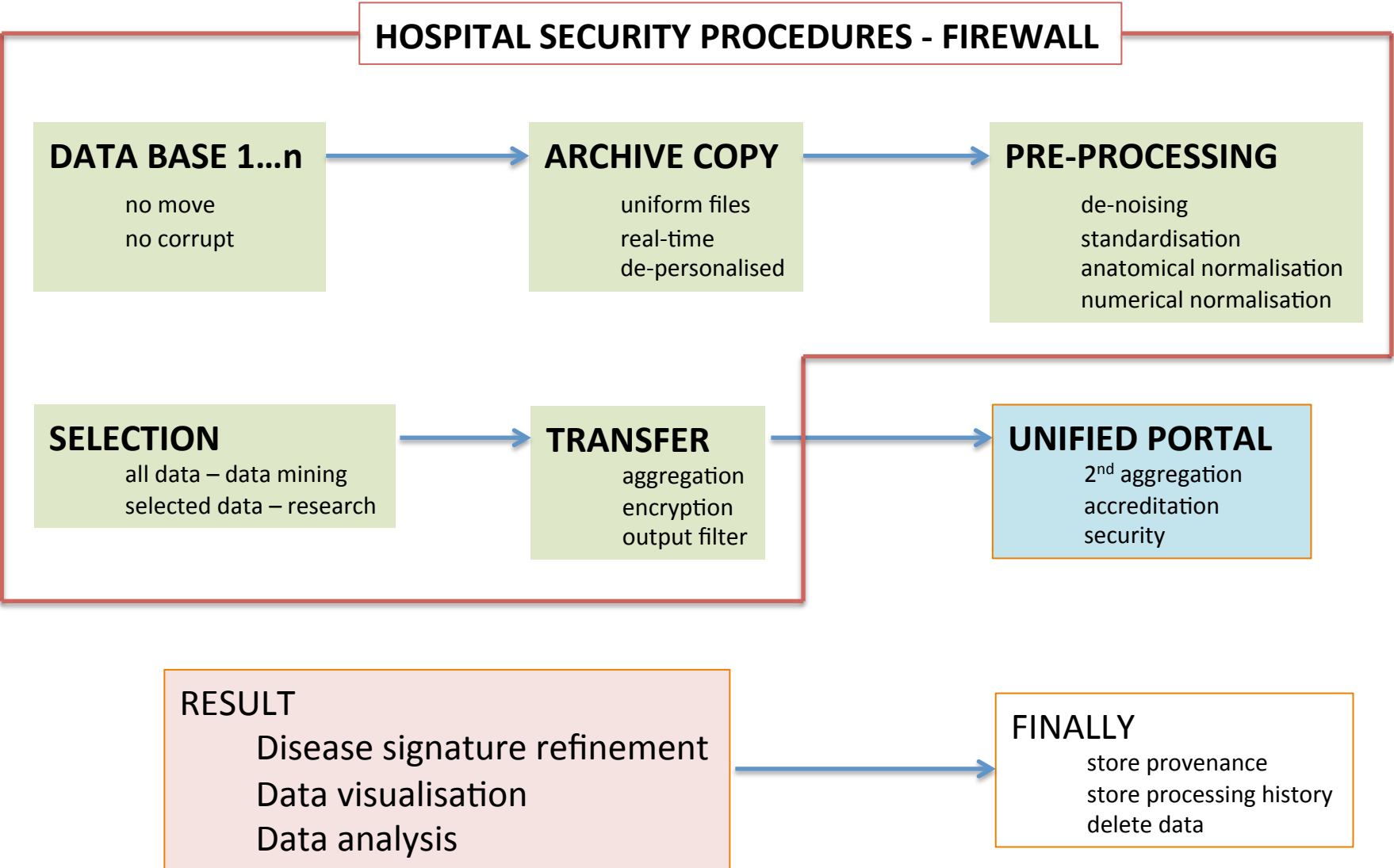
- BROAD CONSENT
- RETROSPECTIVE - PROSPECTIVE

MANAGEMENT OF ETHICS

- LOCAL ETHICS COMMITTEES
- VALUE AND CREDIBILITY OF SCIENCE



MEDICAL INFORMATICS PLATFORM





DATA ANALYSIS OPPORTUNITIES

DISEASE SIGNATURES

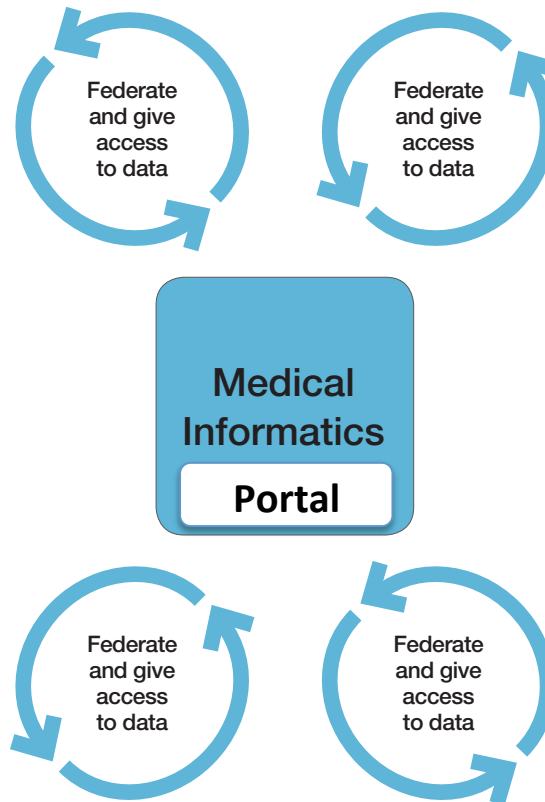
- DATA MINING
- REAL-TIME
- CONTINUOUS
- ITERATIVE

DATA VISUALISATION

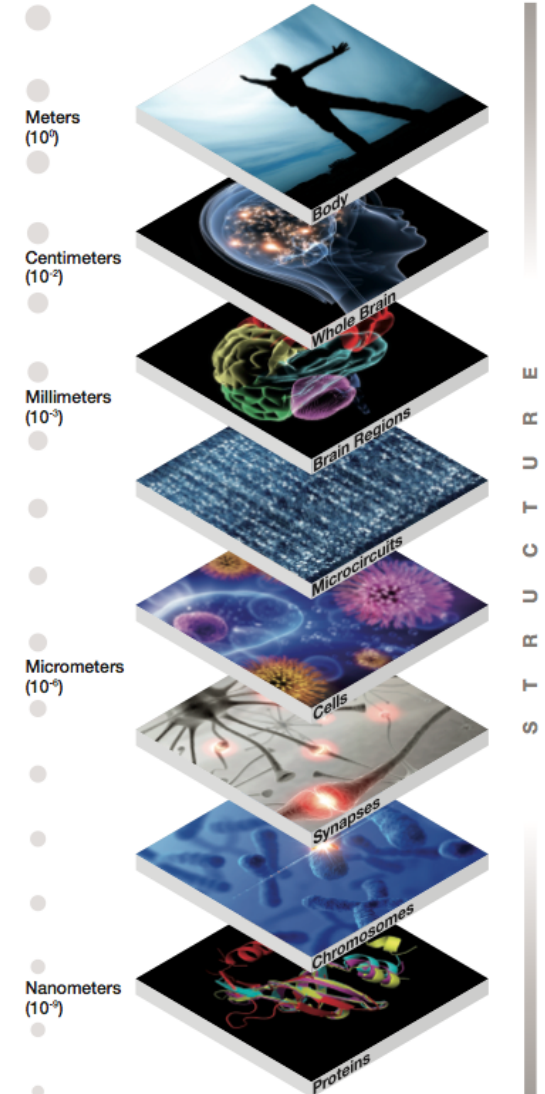
- EPIDEMIOLOGY
- HEALTH SERVICES

RESEARCH

- HYPOTHESIS TESTING
- CLINICAL TRIALS

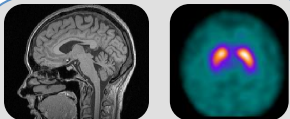


Spatial Scales





DATA

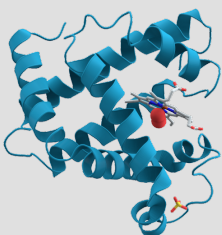


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 ...CACGTAGACTGAGGACTCCTCTTC...

...—GUGCAUCUGACUCCUGAGGAGAAG—...

... V H L T P E E K ...



SCALE

TIME

SPACE

PATHOLOGY

DEMOGRAPHICS

Genetic
Molecular
Cellular
Circuits
Systems

Cross-sectional

Longitudinal

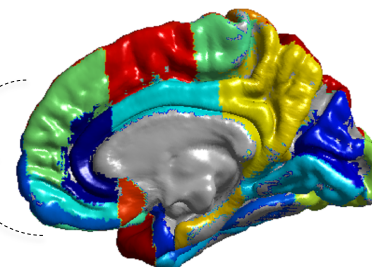
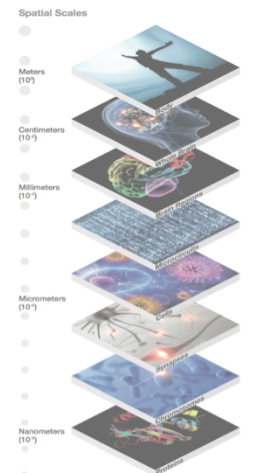
Brain anatomy

Pathology confirmed diagnosis

Risk factors

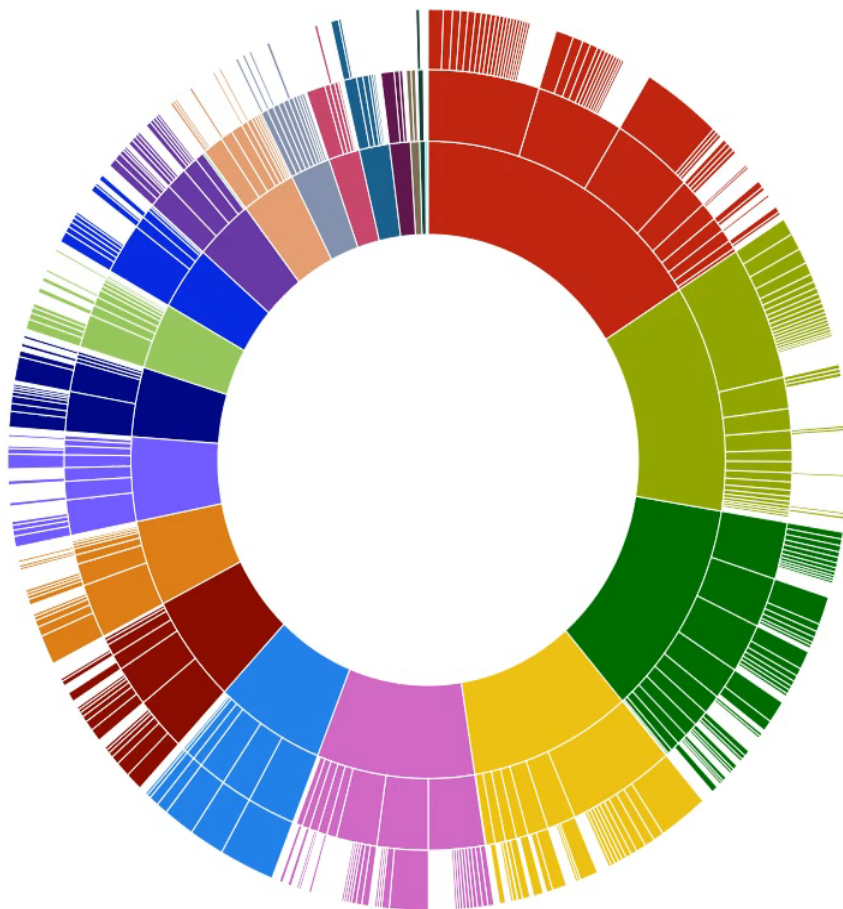
Age, gender ...

VARIABLES





MEDICAL EPIDEMIOLOGY



☐ 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

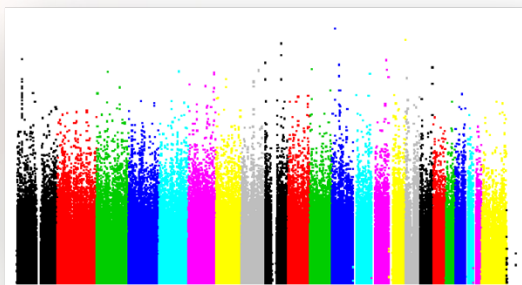


PET



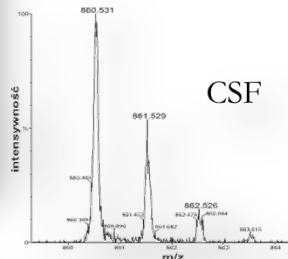
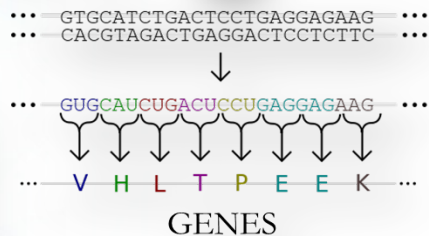
MRI

CLINICAL SCALES
&
MEASUREMENTS

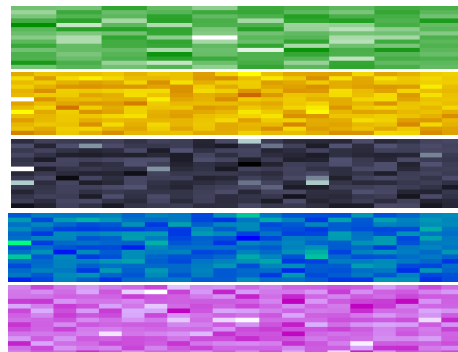
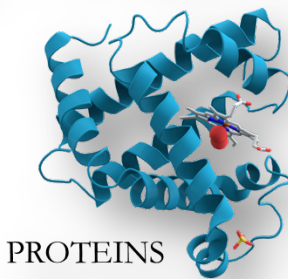


Organising
Tabulating

Processing...



CSF



MRI data

PET data

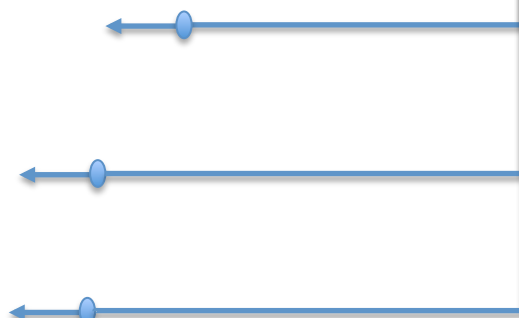
Gene data

CSF data

Protein data

912 Alzheimer's patients
5566 Healthy controls

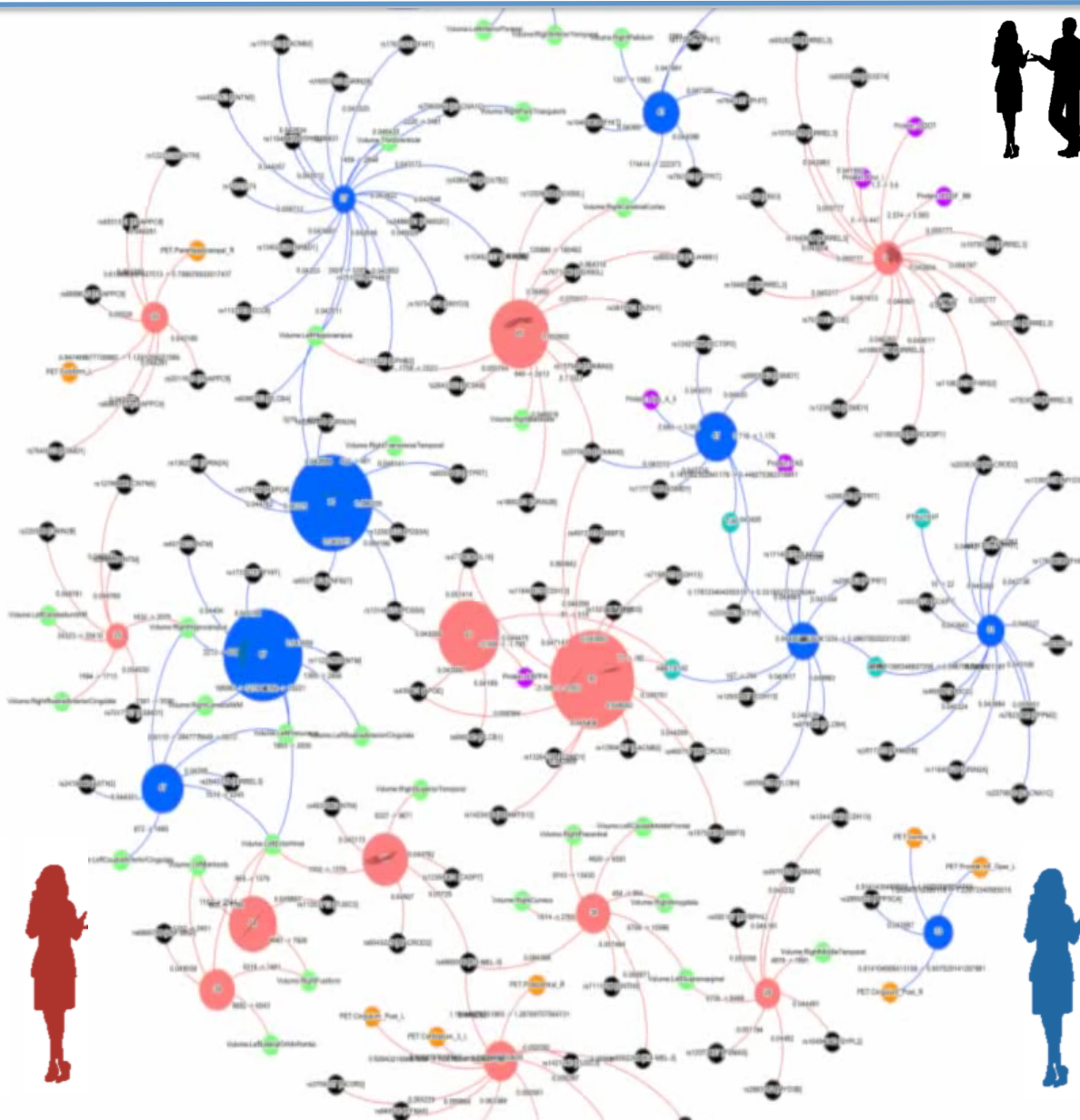
- Phenotype led semi-supervised clustering
- Biologically led classification
- High dimension and feature learning





LINKS BETWEEN PHENOMENOLOGY & BIOLOGY

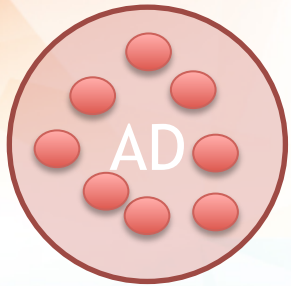
- AD Rule
- NL Rule
- MRI Data
- PET Data
- Proteomics
- CSF
- Genetics





FINDING CAUSAL RULES

- Phenotype-led semi-supervised clustering



• AD RULES

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

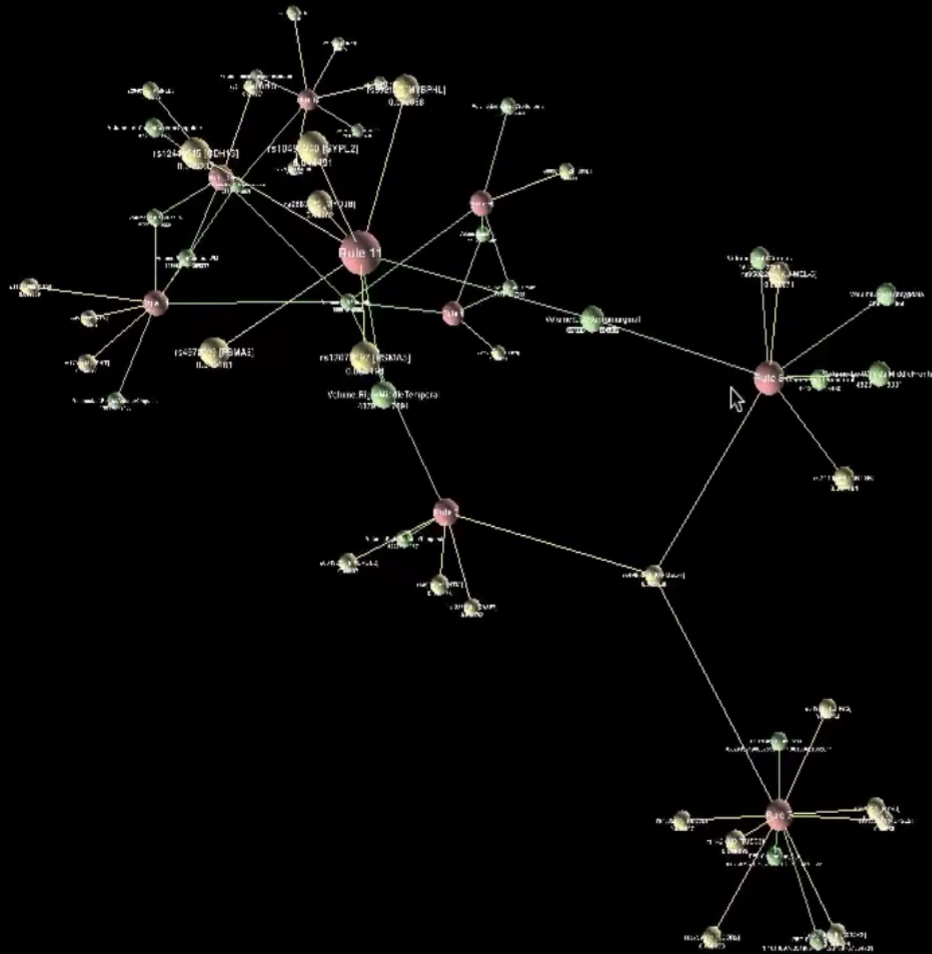
• HC RULES

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

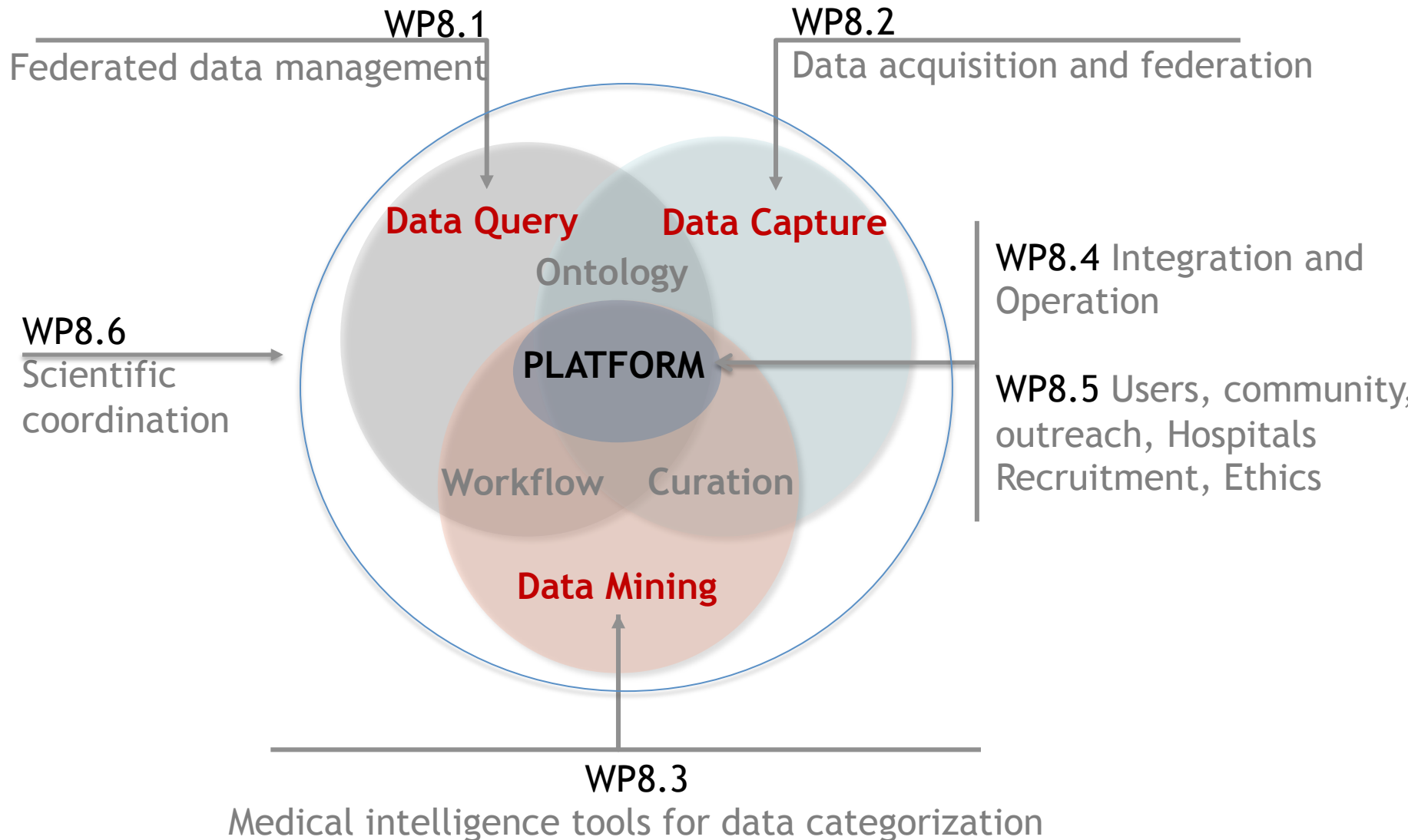
- **Unlock** added value of clinical records & data
- **Catalyse** a major collaboration of hospitals
- **Federate and integrate** knowledge and data about human diseases - IT based atlas-encyclopedia
- **Analyse and Derive** biologically-grounded brain disease signatures for new diagnostic classification



- **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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www.unil.ch/lren

www.humanbrainproject.org