Digital Biology & Digital Health: a major actor

Michel Dojat
Deputy Scientific Director of Inria for Digital Biology and Digital Medicine
Philippe Gesnouin
e-health Program Director

The main driving forces behind biology and health

Computer science

1990s: medical images

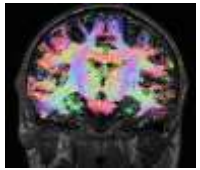
1995s: bioinformatics

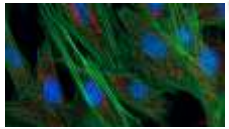
Models

2005s: biomechanics

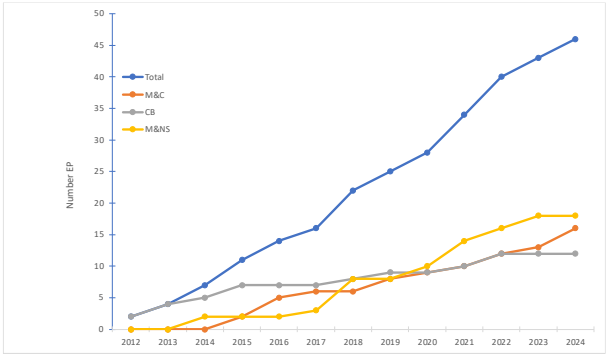
2020s: massive data

Machine learning





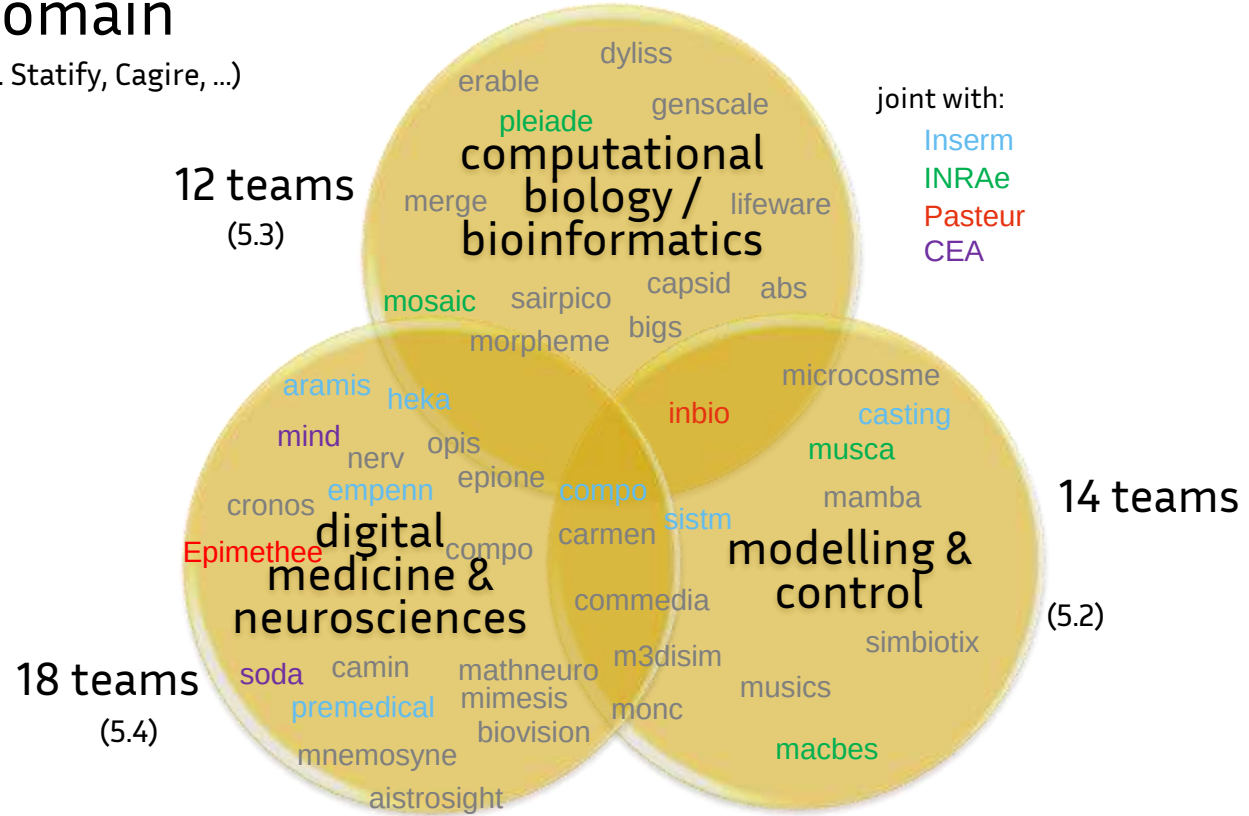
Links with Hospitals & Inserm



The themes in the domain

44 teams in the domain

+ EP with medical applications (e.g. Statify, Cagire, ...)



15 joint labs

- 7 Inria-Inserm
- 4 Inria-Inrae
- 2 Inria-Pasteur
- 2 Inria-Cea

Main methodologies: applied maths for biomedicine

PDEs, meshes

Biophysical models, dynamical systems

Multi-scale, Mean field

Model reduction, Reduced order

Inverse problem, data assimilation

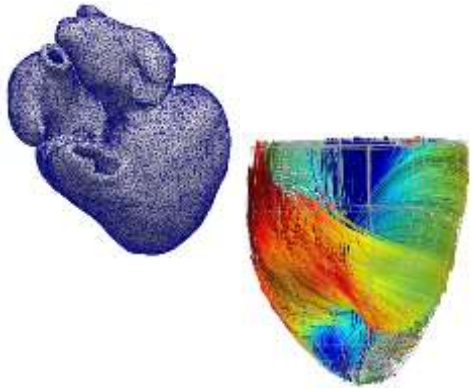
Riemannian geometry

Graph theory, network analysis

Theoretical biology

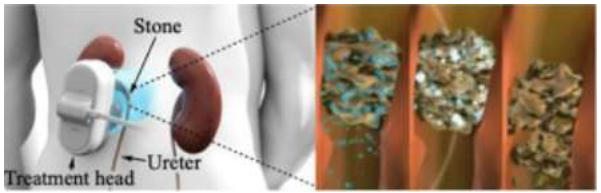
Biomechanics

Computational Neurosciences



Cardiac motion model

Epione



Shock waves

Cagire

Main methodologies for CS in biomedicine

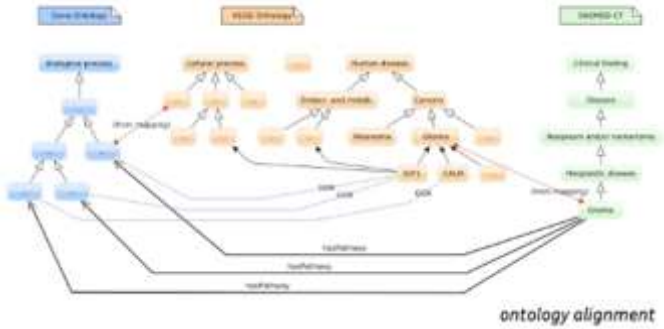
Algorithmics, combinatorics, Optimization

Knowledge representation, semantic web, ontology, data integration

Logic, constraint programming

Phylogenies, trees

HPC, parallelism, federated learning



ontology alignment

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX bp3: <http://www.biopax.org/release/biopax-level3.owl#>

SELECT DISTINCT ?invalidComplex
WHERE {
 ?invalidComplex rdf:type bp3:Complex .
 ?invalidComplex bp3:component ?complexComponent .
 ?complexComponent rdf:type bp3:Complex .
 ?complexComponent bp3:component ?componentOfComplexComponent .
}
```

SparkQL query

Dyliss

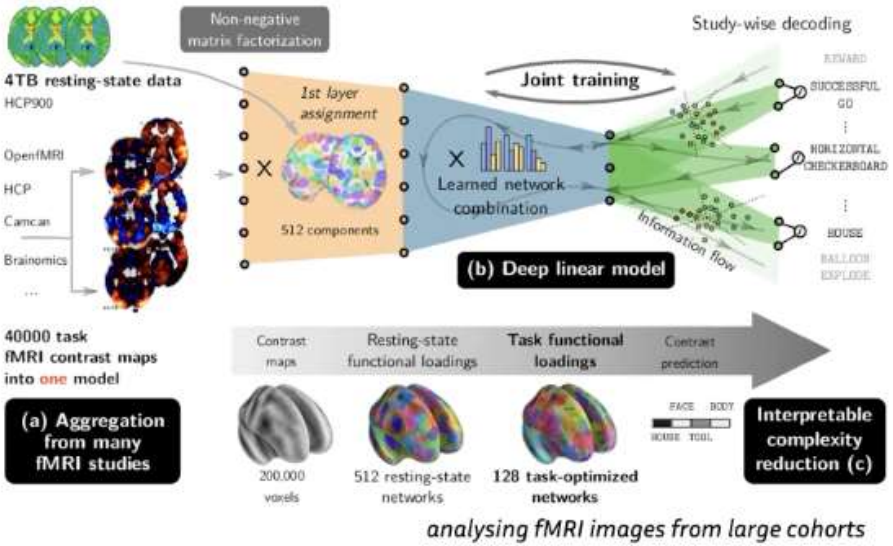
Main methodologies: Statistics for biomedical data

Statistics, machine/deep learning,

High dimension, few shot learning

Frugal approaches

Hybridation ML-AI with mechanistic modellin



Main medical applications

Neurodegenerative diseases, aging
- support to diagnostic, prediction,...

Oncology
-mechanisms, new treatment

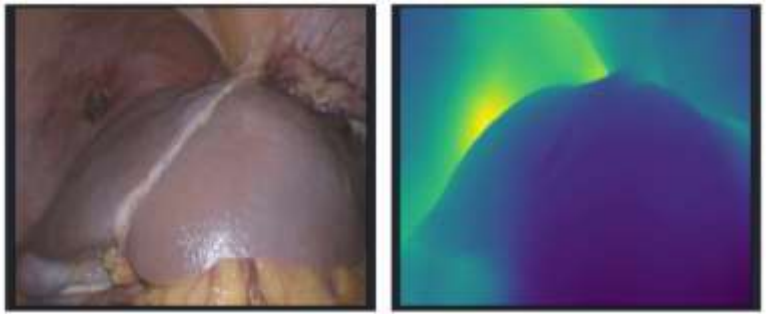
Handicap, rehabilitation,
- neuroprothesis, BCI

Pharmacology, drug resistance
-math. epidemiology

Public health
-clinical trials, patients pathways

Medical robotics
-surgery, endoscopy

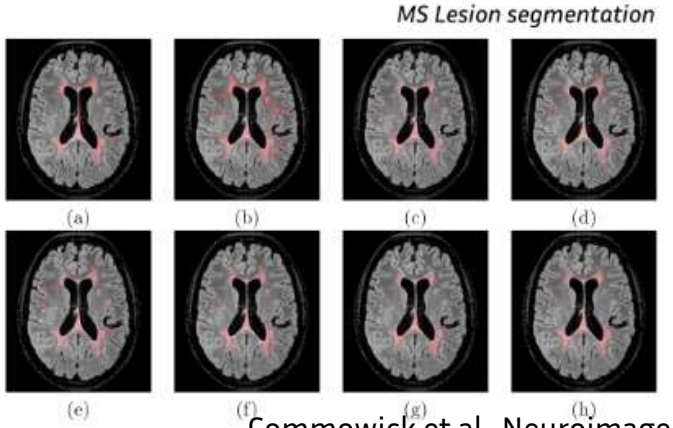
Illustrative examples



Mimesis

Acidi et al. (J. de Chirurgie Viscérale, 2023 160 128-37)

HumanCenteredRobotics

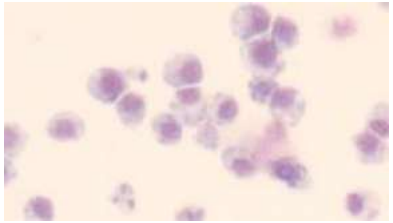


Commowick et al., Neuroimage, 2021 244)

Empenn, Statify

Computational Biology

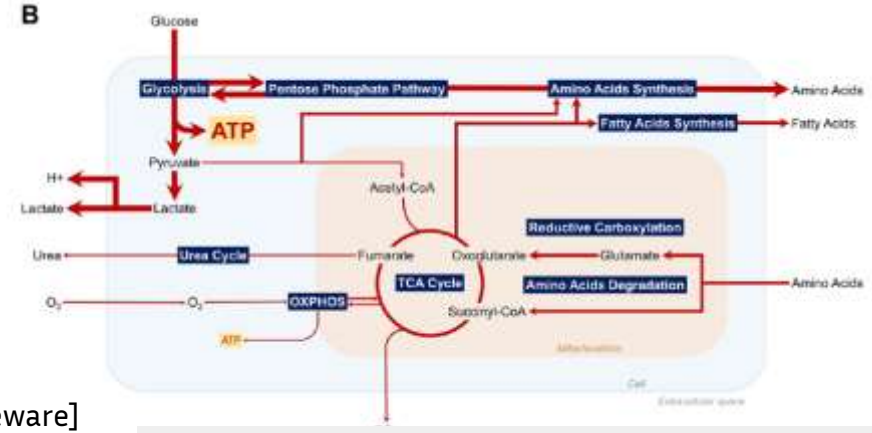
Dynamic modeling



How the cell's behavior emerges from genes interactions?

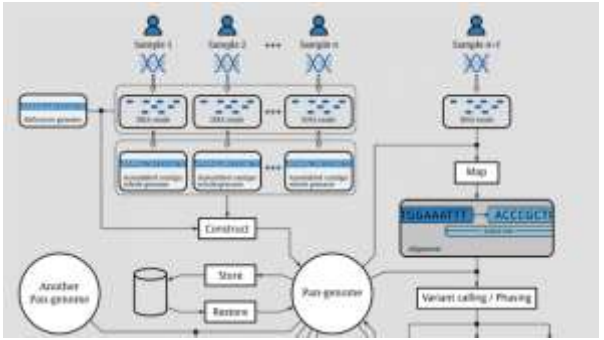
How the cells population behavior emerges from cells interactions?

[InBio, Microcosme, Capsid...]



[Lifeware]

The major active pathways of central metabolism in rhumatoid arthritis



[Genscale]

Tools for DNA Data deluge analysis

50 patients included 2023

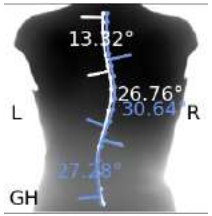
Hybrid, courtesy A. Lecuyer

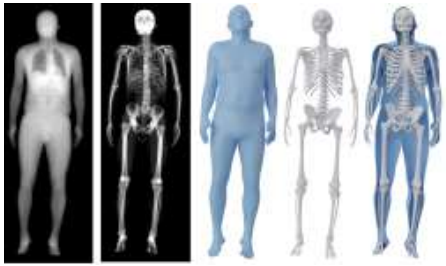
Kinovis plateform - Morpheo

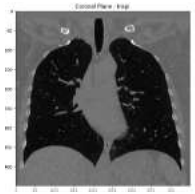
Movement disorders studies

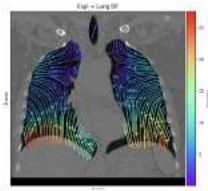
Inside Vision

Relation external form and inside anaotomy









Computer science & Applied Maths

Digital science

- Modeling & Simulation
- Robotics
- Digital security
- Data sciences, AI
- Internet of things
- High performance computing

Biology. & medical sciences

Healthcare

Digital Biology & Digital Health

Strategic partnerships: Inria-Inserm

> yearly open call for joint Inria-Inserm PhD grants:

- 4 joint **PhD grants co-funded per year** since 2016

> yearly open call for new **joint Inria-Inserm teams**

- 3 under study for 2024
- several located within Inserm/clinical premises (COMPO, HeKA, Aramis)

> co-steering of the **PEPR "Digital Health"** 2022

2023: RHU 6th call

Inria is partner of 4 of the 19 accepted projects

Ecan – Chu Nantes – Empenn *Intra cranial Aneurysm patient trajectory*
Rebone – CHU Nice – Epione – *Automated fracture modeling*
Talent – Chu Bordeaux– Epione *Prediction of Stroke risk*
LUCA- pi – APHM – Compo *Lung cancer prevention and interception*

Strategic partnerships: Largest French University Hospitals

> **APHP** *:* Paris, 39 University Hospitals, largest in EU

- Bernoulli Lab, since end 2020 (head Dominique Chapelle)
- facilitate bringing together researchers in digital sciences and healthcare professionals
- co-funding of 2 chairs and one joint Challenge, URGE (co-funding 1M€, started Oct 2022)

https://www.bernoulli-lab.fr

> **HCL** : Lyon, 14 University Hospitals, 2nd largest in fr, in progress

- a common technology development service for medical AI
- first ever joint team between Inria and an hospital

Strategic partnerships: PariSanté Campus

https://parisantecampus.fr

> a digital health development centre to federate the French health tech ecosystem

> cooperation between Inria, Inserm, PSL University, Health Data Hub, Agence du Numérique en Santé and private partners:

- startups (~100)
- MGEN (health insurance)
- Doctolib
- J&J

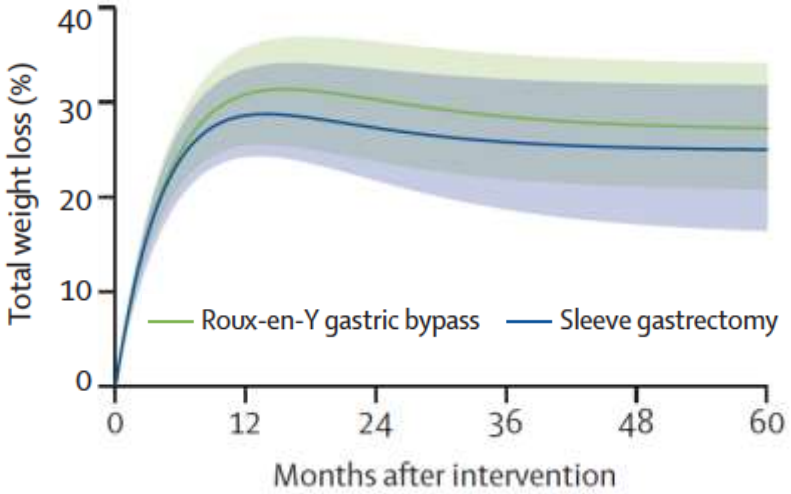
More quantitative assessment: publications

Field	Venues	# for 2018-2022 (2013-2017)
Biology	Nature, Science	**7** (4)
	PNAS, eLife, Neuron, Cell, Nature *X*, NAR, PLoS Biol, Curr Biol	**66** (32)
Medicine	BMJ, NEJM, JAMA, Lancet, Nature Medicine	**1** (2)
	Circulation, Blood, Hepatology, Brain, Physiol Rev, Stroke, Lancet *X*, JAMA *X*, BMJ *X*	**21** (7)
ML/IA	NeurIPS, ICML, AISTATS, AAAI	**51** (18)

Themes “computational biology”, “modelling and control for life sciences” & “computational neuroscience and medicine”: total of 35 (31) EPIs

Development and validation of an interpretable machine learning-based calculator for predicting 5-year weight trajectories after bariatric surgery: a multinational retrospective cohort SOPHIA study

Patrick Saux*, Pierre Bauvin*, Violeta Raverdy, Julien Teigny, Hélène Verkindt, Tomy Soumphonphakdy, Maxence Debert, Anne Jacobs, Daan Jacobs, Valerie Monpellier, Phong Ching Lee, Chin Hong Lim, Johanna C Andersson-Assarsson, Lena Carlsson, Per-Arne Svensson, Florence Gaitier, Gudarzeh Dezfoulian, Mihaela Moldovanu, Severine Andrieux, Julien Couster, Marie Lepage, Erminia Lembo, Ornella Verrastro, ph Peterli, Ricardo V Cohen, Carlos Zerrweck, David Nocca, Carel W Le Roux,



Lancet Digit Health 2023; 5: e692–702
Published Online
August 29, 2023
https://doi.org/10.1016/S2589-7500(23)00135-8

Examples of successful software

scikit-learn

> a Machine Learning library in python
> started 2010 by Parietal, to promote python for neuroscience
> #3 most-downloaded ML/AI on GitHub, used by many companies
> 2024: :Probal. creation

https://scikit-learn.org

Plant@Net

> collaborative app to identify a plant from a mobile phone
> funded 2009 with Cirad, INRAe, IRD
> 10^4 users per day, 2 M downloads
> deep learning + very large database fed by users (Zenith)
> leveraged for research purposes (biodiversity, conservation, species distribution)

Pl@ntNet
https://plantnet.org

Fed-BioMed

> open-source federated learning framework, Epione
> friendly user interface for federated learning experiments
> deployed on Nice Center for cancer research, in progress CHU Lille-Caen
> used in a set of related projects : AEx Flamed, challenge Fed-Malin

https://fedbiomed.gitlabpages.inria.fr

Inria StartupStudio
https://www.inriastartupstudio.fr/

biotech-medtech ≃ 20% of the startup studio since 2017 (25/129)

RebrAIn
https://rebrain.eu/

RebrAIn *Carmen*

> treatment of Parkinson's and essential tremor by deep brain stimulation
> use AI and shared data (OptimDBS) for precision -personalized- localization of the areas to stimulate (STN or VIM), clinical trial ongoing
> with Bordeaux University Hospital

PIXYL
pixyl.ai

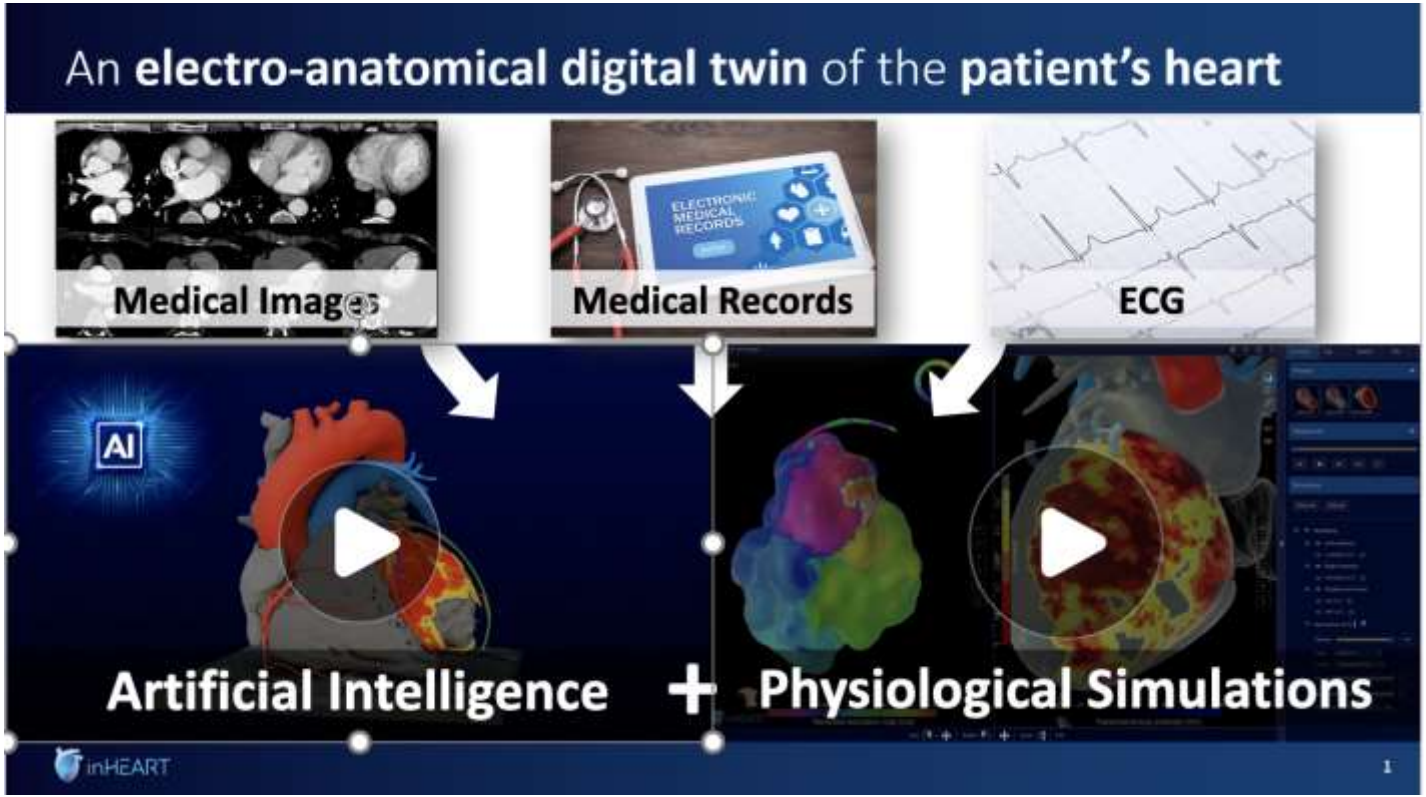
Pixyl *Statify* (2015)

> AI solutions for medical imaging
> With Inserm (GIN)

AnaestAssist *M3DISIM*

> improve cardiovascular monitoring of anesthetized patients under surgery or in ICU
> augment available data with patient-specific biomechanical models of her/his cardiovascular system
> can be used to predict the risks of cardiovascular and neurocognitive complications
> with Lariboisière University Hospital (APHP) and Bernoulli Lab (Chair BigData & Medicine)

InHeart


An electro-anatomical digital twin of the patient's heart
Medical Images
Medical Records
ELECTRONIC MEDICAL RECORDS
ECG
AI
Artificial Intelligence
+
Physiological Simulations
inHEART
1

Inria challenges : in-house incentive funding

5 Inria Challenges funded in the domain in the period (≈5 M€)

FedMalin (epione): **Federated MAchine Learning over the INternet (FedMalin) 2022-26**

to address a number of challenges that arise when FL is deployed over the Internet, including privacy & fairness, energy consumption, personalization, and location/time dependencies. FedMalin will also contribute to the development of open-source tools for FL experimentation and real-world deployments, and use them for concrete applications in medicine and crowd sensing.

COATI, COMETE, DYOGENE, EPIONE, MAGNET, MARACAS, NEO, SPIRALS, TRIBE, WIDE

Exploratory Actions : In-house incentive funding

18 Actions Exploratoires (AEx) funded in the domain in the period (4 M€)

Discotik (Mosaic): **Discrete geometry applied to morphomechanics of plant tissues (2022-25)**

GRASP (Empenn): **Generalizing Results Across Scientific Pipelines (2022-25)**

EyeSkin-NF (Empenn): **Eye-tracking and skin conductance measures for neurofeedback analysis and validation (2021-24)**

OcéanIA (Biocore, Ange, Tau) **Artificial Intelligence, Data, and Models for Understanding Oceans and Climate Change (2022-24)**

….

A focus on clinical trials

Simulation and new designs

> Simulation of clinical trials (Monolix/Simulx, Xpop → Lixoft → SimulationsPlus)

> New designs (in silico, adaptive doses): HeKA, SISTM

https://www.simulations-plus.com

Some of the clinical trials we participated

> 15 + vaccine trials (Ebola, HIV, Hepatitis, phase I to IV): SISTM

- head of Inserm's CT methodology and management center
- coordination EBOVAC2 (IMI, Janssen, Phase II, children+adolescents)

> Brain diseases: Carmen (DBS), Aramis (opening BBB in AD)

> Oncology: COMPO (Pioneer, lung immuno-onco)

> Neuroprosthetics: Camin (5 CT on clinicaltrial.gov)

> Sophia study: gastric surgery

Prospective 2023-2027: structuring objects

2022: Official announcement of the PEPR “Digital Health”

a 60 M€ governmental research program to structure/support french research in digital health
Inria designated by the gov to co-supervise it with Inserm

PEPR Digital Health Inria-Inserm

> **heka aramis epione compo premedical parietal empenn mind casting dyliss**
> multimodel multiscale data integration
> data/knowledge integration, FAIRification
> longitudinal data for precision medicine
> statistical and AI for advanced clinical trials
> e-healthcare patient pathways
> secure, safe and fair machine learning for healthcare
> applications to pharmacology, cardiomyopathies, stroke, neuroscience

Prospective 2023-2027: structuring objects

PEPR Digital agronomy Inria-INRAe

> **beagle genscale dyliss pleiade**
> policies, breeding, agrodiversity, holobionts, models of crop plants

PEPR MolecularXiv CNRS

> **genscale**
> data storage into DNA molecules

MediTwin

> industrial cooperation supported by the French State, *(120 M€, +80M€ funding)*
> with Dassault Systemes, Inria (10 EPI), 7 IHU, inHeart...
> digital twins for oncology, cardiology, neurology inside a platform for practitioners

Premyom

> digital twin of the vision
> with EssilorLuxottica, Inria (4 EPI), IMT, hospitals, Insimo...

Prevention ?

Prospective 2023-2027: structuring objects

New IHUs (vague 3, starting 2023)

> the mere assembling of the application has a strong local structuring effect

- VBHI, Bordeaux, maladies vasculaires cérébrales, IHU
- Prism, Villejuif, oncologie, IHU
- re-Connect, Paris, troubles de l'audition, IHU
- Prometheus, Garches, sepsis, IHU
- Thema-2, Paris, hématologie, IHU
- Cancers des femmes, Paris, cancers gynécologiques, IHU
- Everest, Lyon, pathologies hépatiques, IHU
- RespirERA, Nice, pathologies respiratoires, IHU
- IMMUN4CURE, Montpellier, immunothérapies, IHU
- InovAND, Paris, neuro-développement pédiatrique, IHU
- HealthAge, Toulouse, gérontologie et vieillissement, IHU émergent
- Infiny, Nancy, maladies inflammatoires de l'intestin, IHU émergent

Hospital data warehouses (EDS)

> strong implication for the software infrastructure

- ongoing: Paris (APHP), Oura (HCL, Chuga, St-Etienne, ClerFerd), Bordeaux

3R: reduction, replacement, refinement of animal experiment

> a strong societal demand and a clear role for Inria

> Inria funding member of the FC3R.

AI clusters

- **With a digital health program**

What INRIA can bring to our project:

- ➔ **A well-defined scientific position, clear project visibility and a reinforced attractivity**
- ➔ **High level expertise in ML/AI linked with the biological and health questions**
- ➔ **A strong support for research products valorisation**
- ➔ **A network and development support**

Vielen Dank für Ihre Aufmerksamkeit!

www.inria.fr

https://tinyurl.com/Michel-Dojat

Michel.Dojat@inria.fr

Philippe.Gesnouin@inria.fr
+33 6 08 46 04 72