Imagerie médicale et apprentissage automatique :
vers une intelligence artificielle ?

Patient numérique & intelligence artificielle

Nicholas Ayache

2 mai 2018

informatiques mathématiques

COLLÈGE DE FRANCE 1530

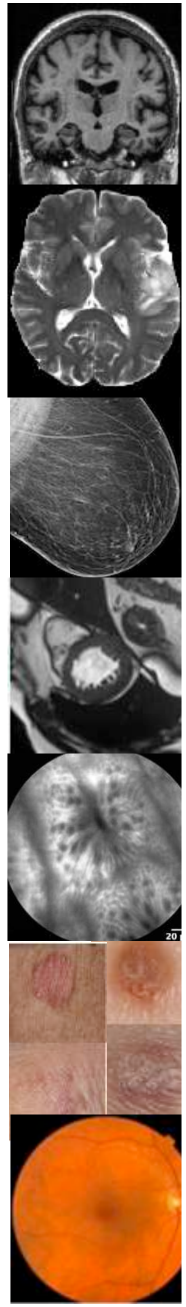
Intelligence Artificielle pour l'imagerie médicale

- **Une définition ?**
  - Algorithmes, modèles et données
    - pour **analyser** les **images médicales** aussi bien qu'un expert
    - afin de guider diagnostic, pronostic, et thérapie : outils de **médecine numérique**

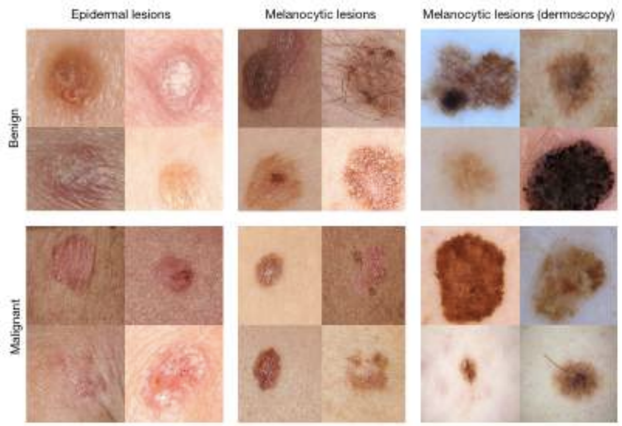
MICCAI depuis 20 ans

- **Pourquoi IA ?**
  - Capacités d'**apprentissage**
  - sur des **données** de plus en plus **complexes**, **hétérogènes**, et/ou **massives** :

quelques exemples récents…



Fév. 2017 Dermatologie



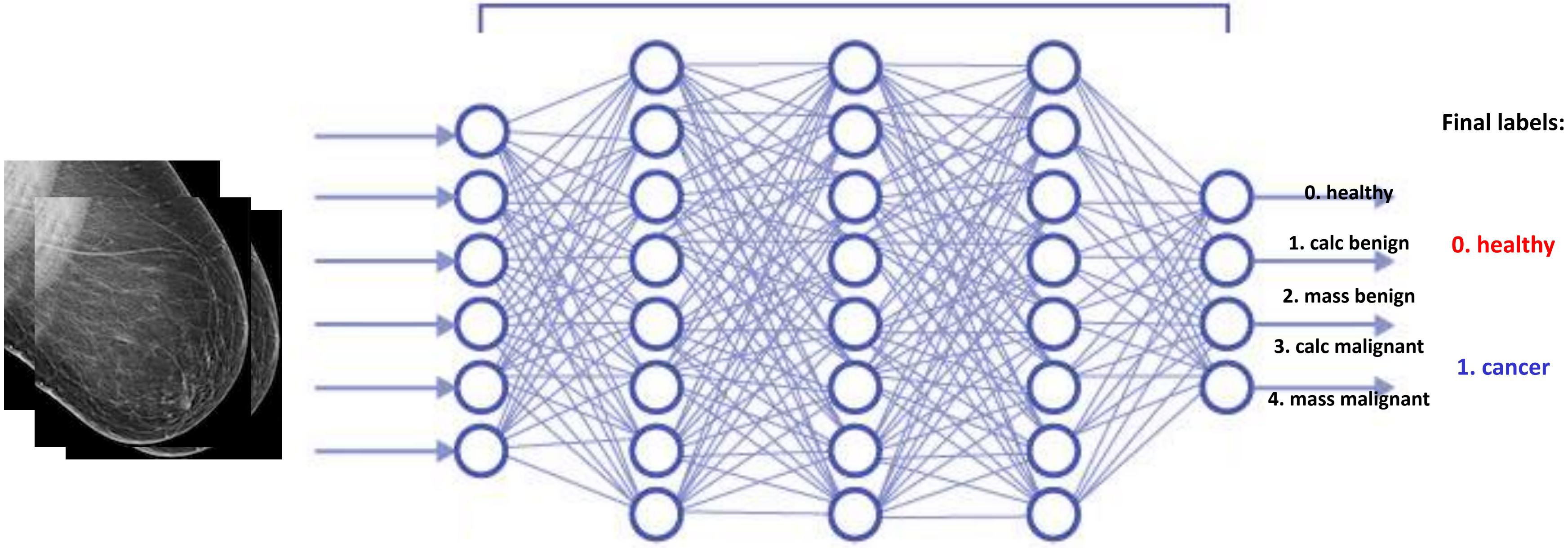
https://cs.stanford.edu/people/esteva/nature/

- **réseaux de neurones profonds**
- Classification de lésions (bénignes, cancéreuses)
- performances = dermatologues confirmés.
- Pré-entrainement: 1.3 Million d'images naturelles
- Apprentissage final :
  - ~130.000 lésions couvrant 2000 pathologies

Juin 2017

Radiologie

Deep Neural Network



The Digital Mammography DREAM Challenge

Apprentissage : ~640.000 mammographies

1.200+ participants

1 Therapixel

Funded by

Enabled by

Courtesy of Therapixel

Apprentissage profond : la solution universelle ?

- **Boîte noire**
  - Manque d'explication
  - Erreurs grossières possibles

M. Kwiatkowska

- **Immenses bases de données**
  - Pas toujours disponibles
  - Coût de l'étiquetage (experts)
  - Représentativité : cas rares ? sujets sains ? biais ?
  - Ethique : confidentialité

Patient numérique et IA

- Exploiter modèles anatomie & physiologie pour profiter des outils modernes d'apprentissage en surmontant certaines difficultés

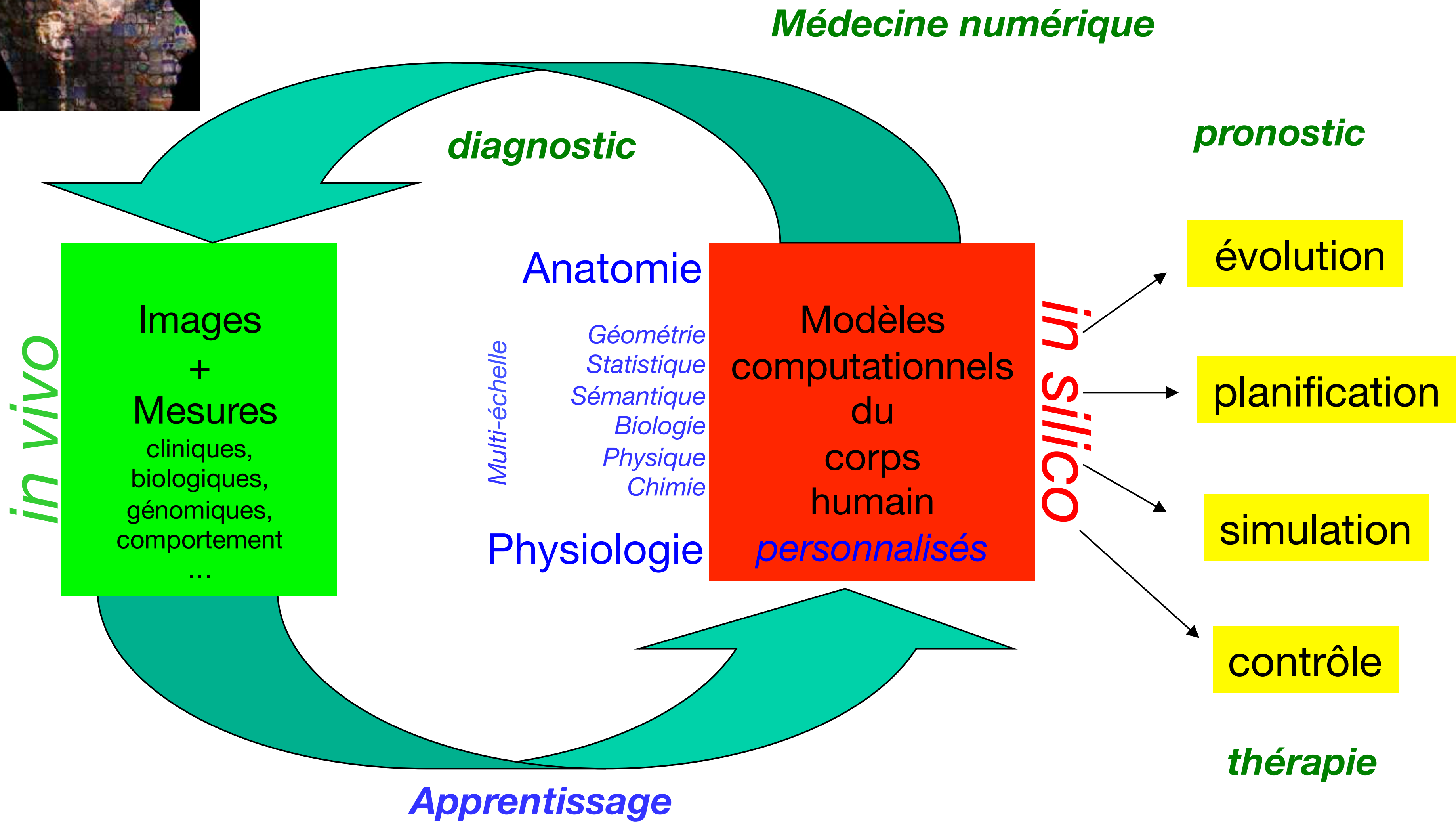
  - Contraindre l'apprentissage aux paramètres de modèles prédéfinis

    donner un sens aux paramètres
    réduire l'ensemble d'apprentissage

  - Simuler des images dont l'acquisition réelle est délicate et/ou l'étiquetage coûteux.

    compléter bases de données existantes

Le patient numérique personnalisé



N. Ayache, Leçons inaugurales du Collège de France, Fayard 2015

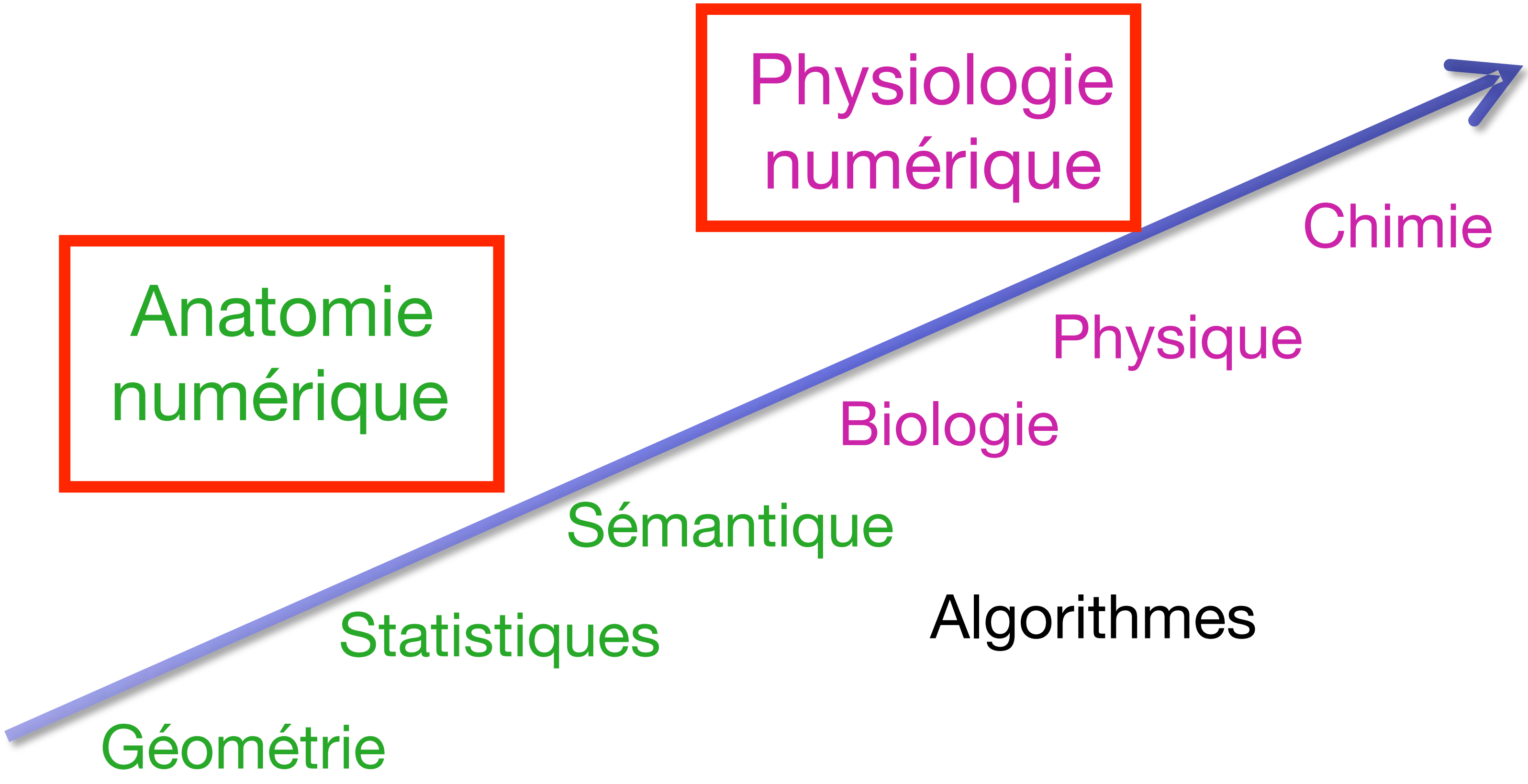
Illustrations

Quelques exemples mêlant

images, patient numérique, apprentissage

tirés des recherches « en marche » de notre équipe *Epione* avec ses partenaires académiques, cliniques et industriels

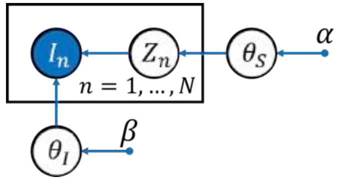
Patient numérique



N Ayache. *Towards a Personalized Computational Patient.* IMIA Yearbook of Medical Informatics, 2016

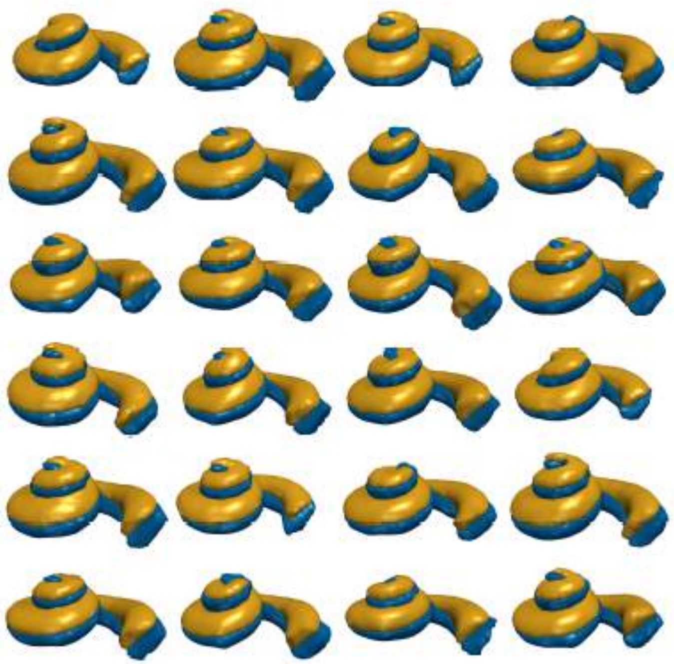
Inria
IUFC
Oticon

1. Implants cochléaires

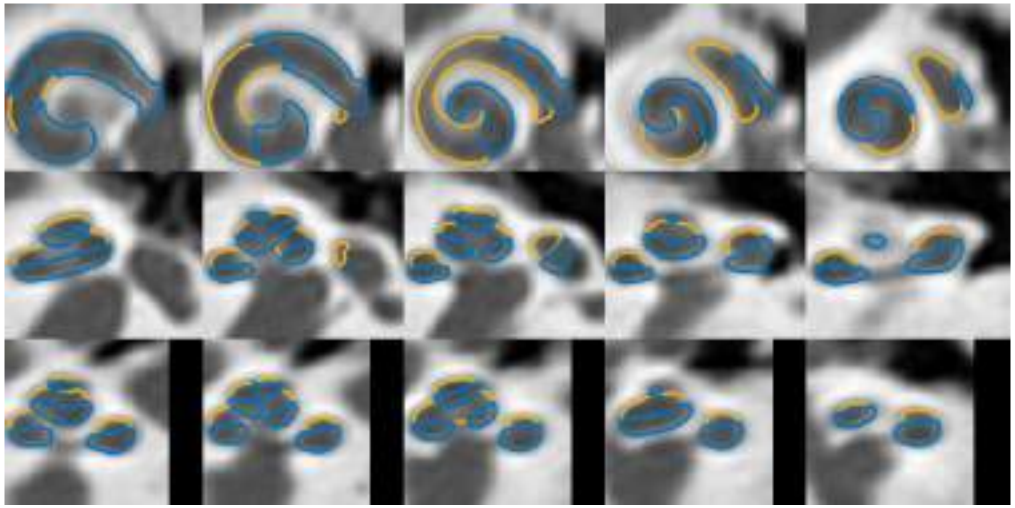


Modèle géométrique

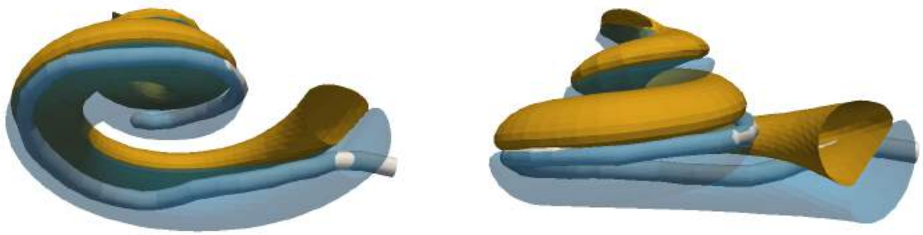
Analyse statistique ~1000 sujets



Segmentation Bayesienne



Insertion électrode

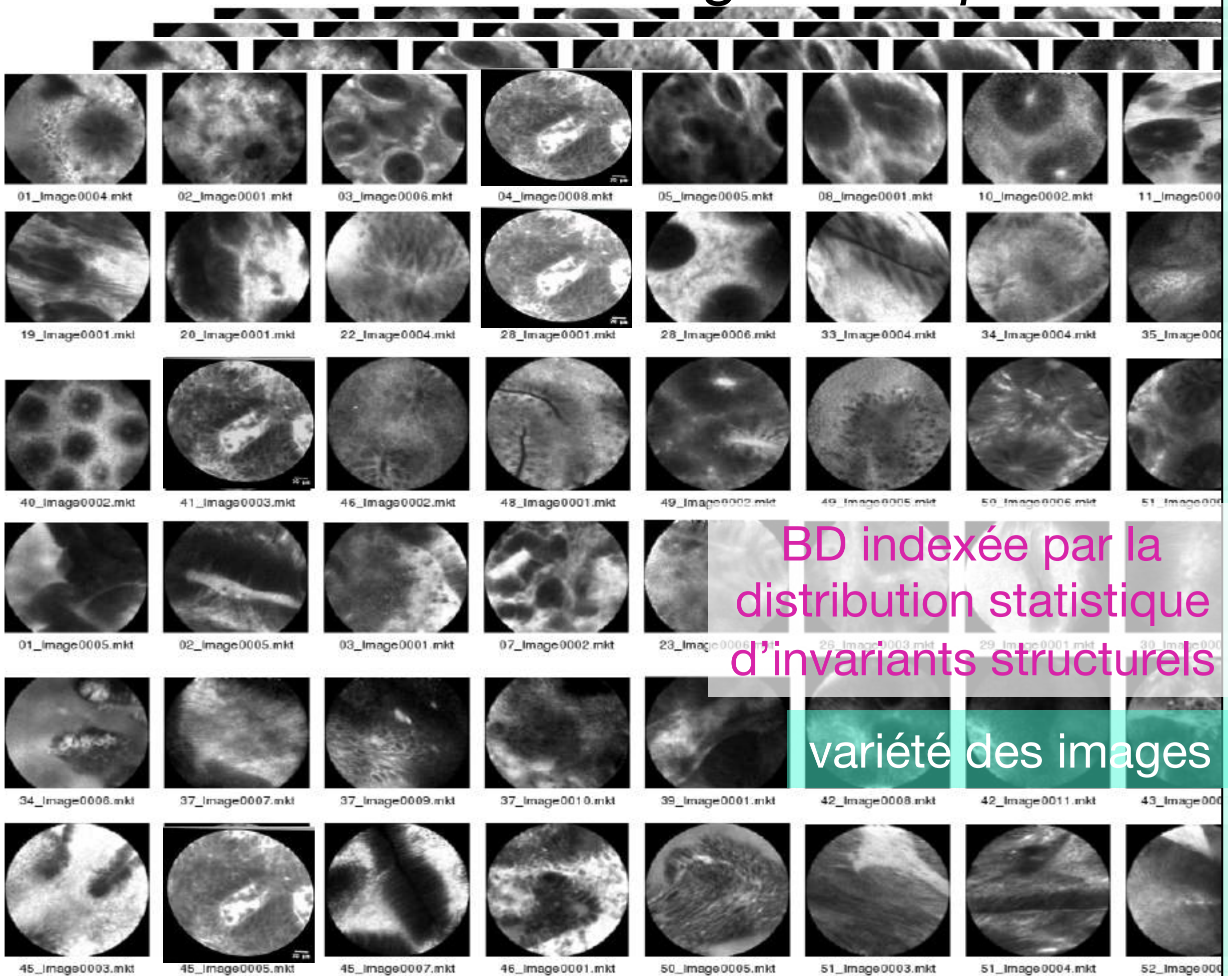


T. Demarcy, C. Vandersteen, N. Guevara, C. Raffaelli, D. Gnansia, N. Ayache, H. Delingette, *Automated analysis of human cochlea shape variability from seg. μ CT images* **Comp. Medical Imaging & Graphics 2017**

Mauna Kea Technologies

2. Endomicroscopie

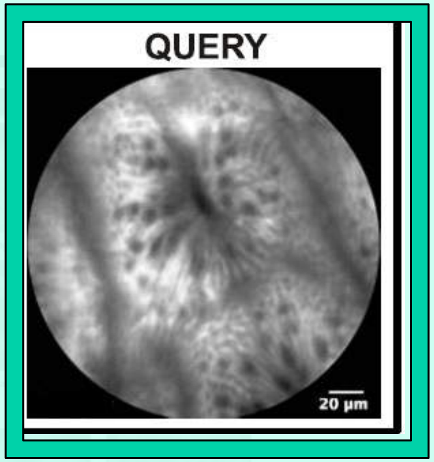
~4500 Images et expertises



BD indexée par la distribution statistique d'invariants structurels

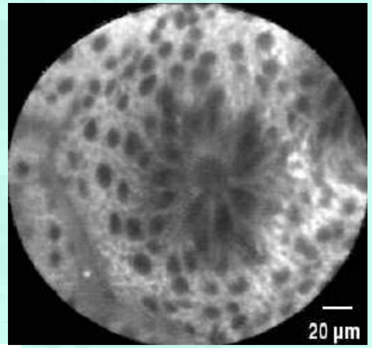
variété des images

Nouvelle image



Atlas Intelligent

Colon



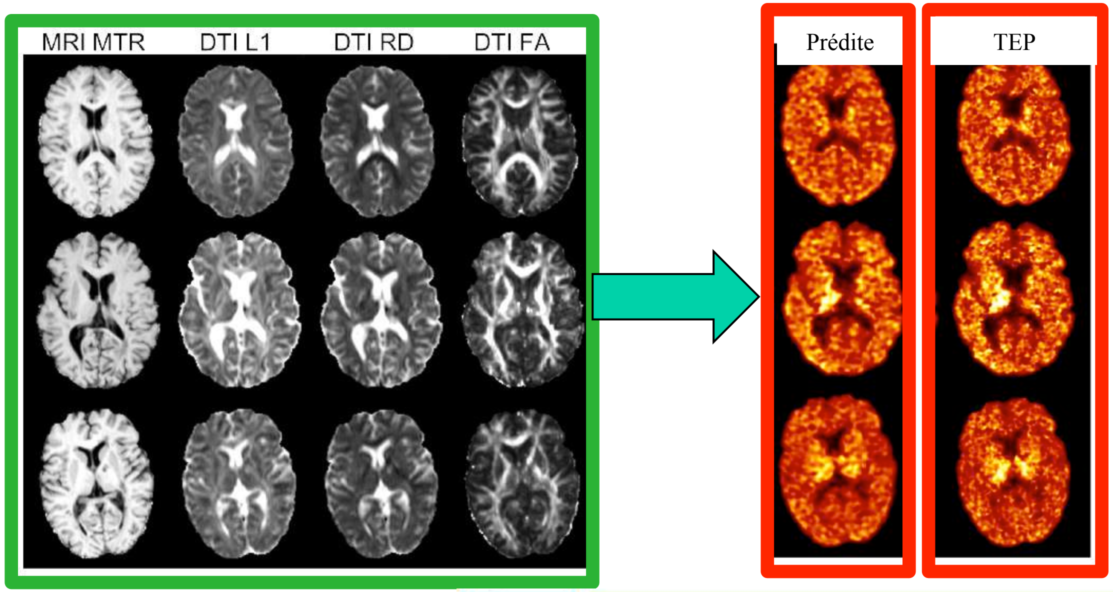
Pathology: Purely Benign
Semantic features: Round crypts, Medium lumen, Normal Goblet Cells

- André, Vercauteren, Wallace, Buchner, Ayache. IEEE TMI 2012
- M Kohandani Tafreshi et al., Digestive Disease Week, DDW 2014

3. Lésions cérébrales

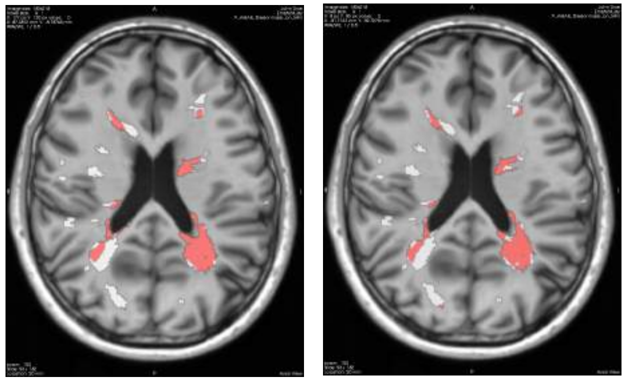
- Sclérose en plaques
- Tumeurs cérébrales

IRM pour apprendre TEP



Sclérose en plaques

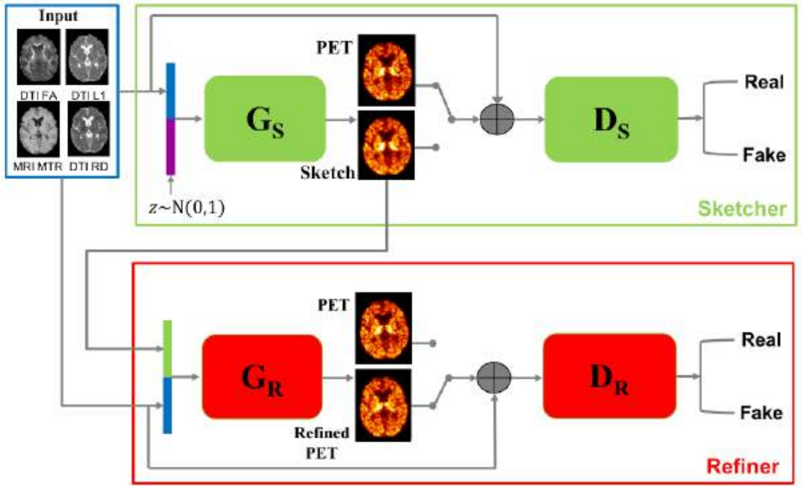
Démyélinisation



Prédiction IRM

Marqueur TEP

$[^{11}C]PIB$



Réseaux génératifs adversaires

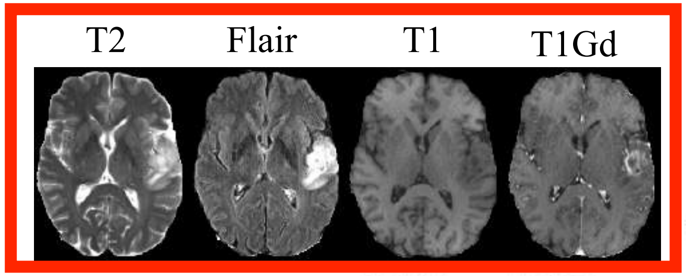
Entrainement :
28 sujets
(millions de voxels)

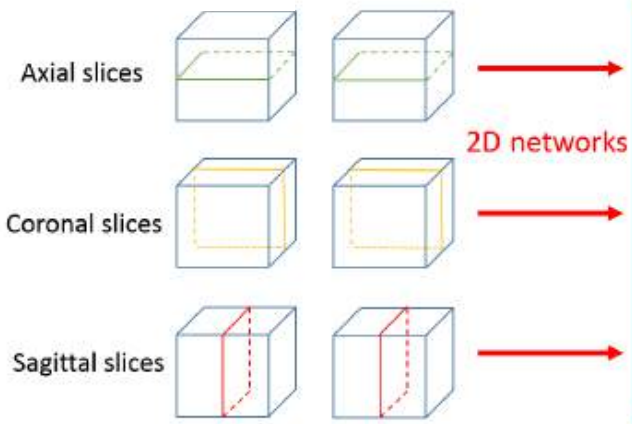
W. Wei, E Poirion, B Bodini, S Durrleman, N Ayache, B Stankoff, O Colliot. Learning Myelin Content in Multiple Sclerosis from Multimodal MRI through Adversarial Training. ArXiv 2018

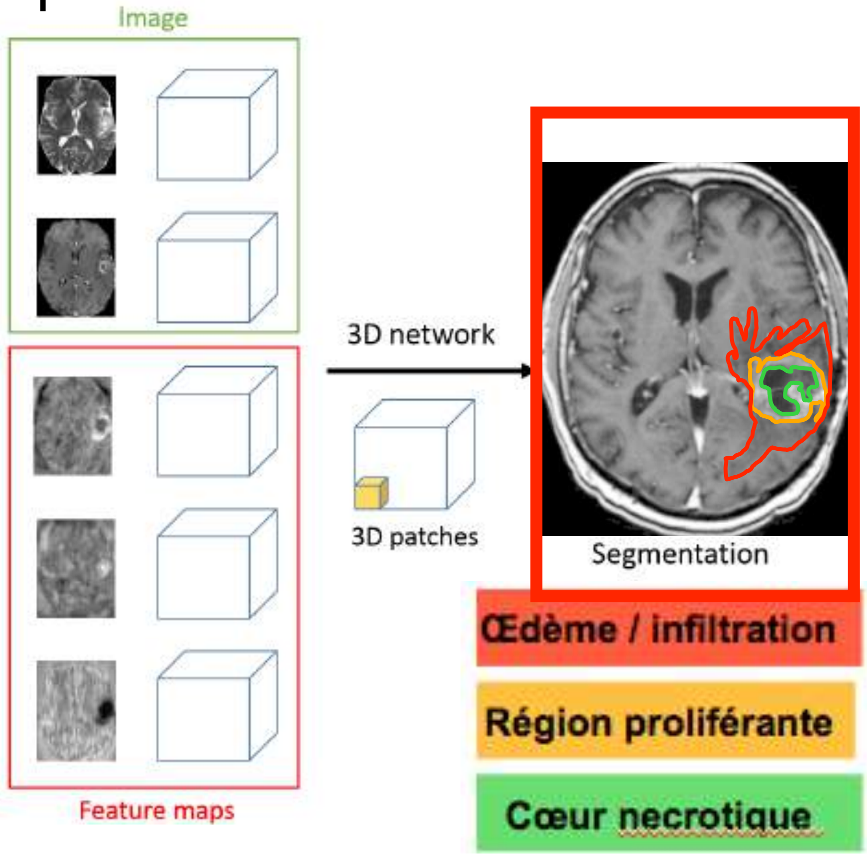
Tumeurs cérébrales

Segmentation par apprentissage profond

IRM



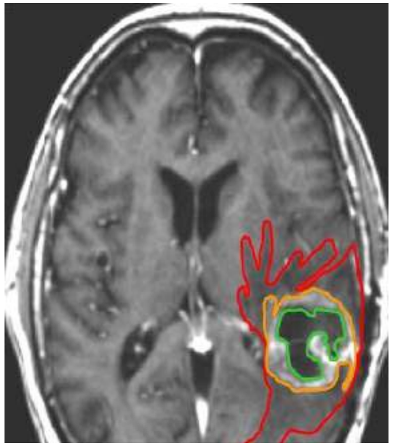




- Données : BRATS 2017
- 285 patients
- Supervision **forte**
- Supervision **faible**

P. Mlynarski, H Delingette, A Criminisi, and N Ayache. Fusion of 2D and 3D Neural Networks for Tumor Segmentation in Multisequence MR Images. IEEE Tr.. on Medical Imaging, under revision, 2018.

Modèle biophysique

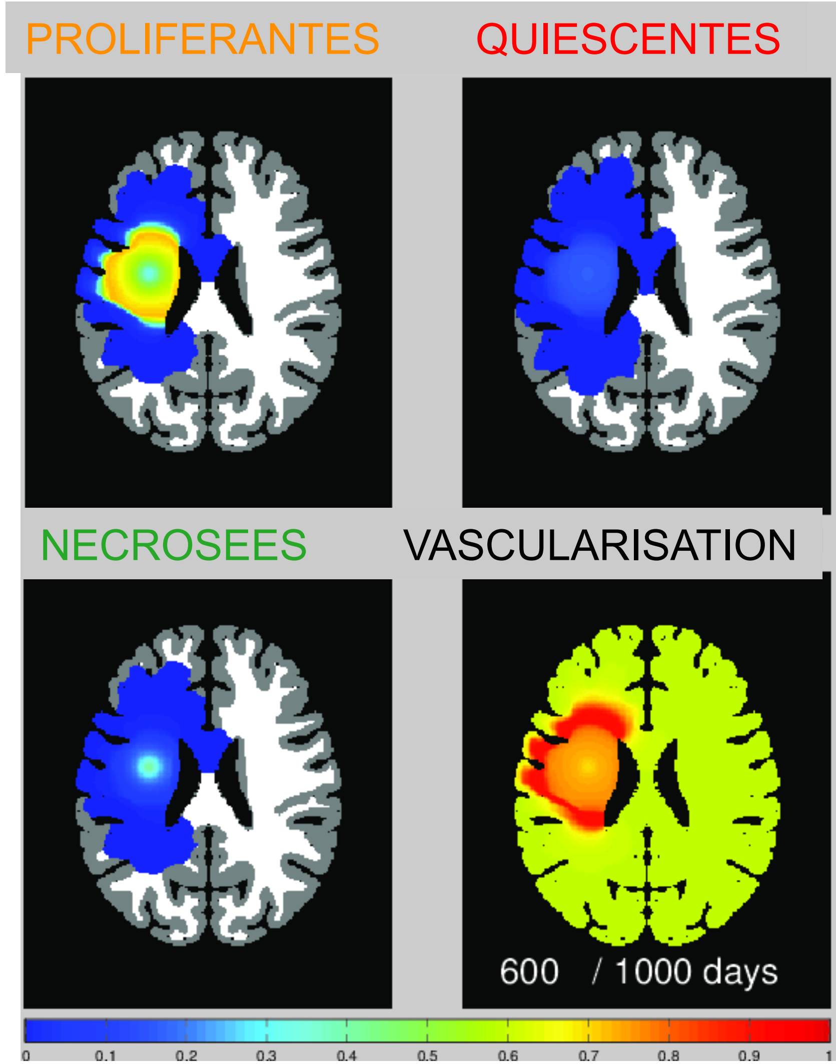


Cellules tumorales

Proliférantes

Quiescentes

Nécrosées



T. Colin, O. Saut et al., M. Le 2012

Evolution densité :

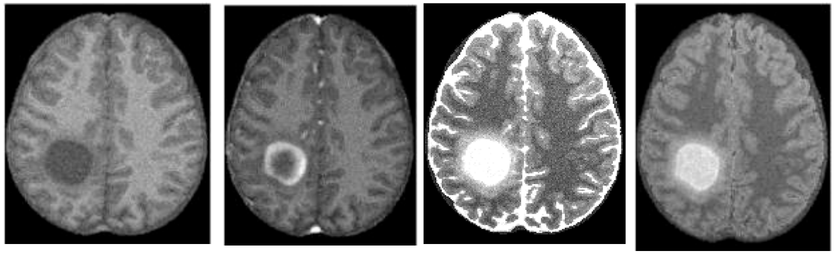
réaction- diffusion + transitions statistiques (vascularisation)

$$\frac{\partial P}{\partial t} = \nabla.(D_P(1-T)\nabla P) \quad +\rho P(1-T)$$
$$-\lambda_{P\to Q}P - \lambda_{P\to N}P + \lambda_{Q\to P}Q$$
$$\frac{\partial Q}{\partial t} = \nabla.(D_Q(1-T)\nabla Q)$$
$$-\lambda_{Q\to P}Q - \lambda_{Q\to N}Q + \lambda_{P\to Q}P$$
$$\frac{\partial N}{\partial t} = +\lambda_{P\to N}P + \lambda_{Q\to N}Q$$

Apprendre densité tumorale

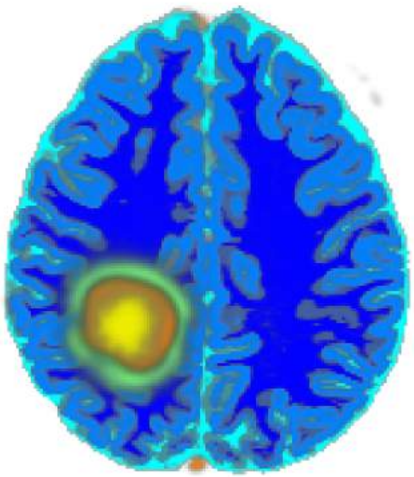
erc MedYMA
+ Microsoft Research

4 x 500 IRM Simulées



T1 T1+Gad T2 Flair

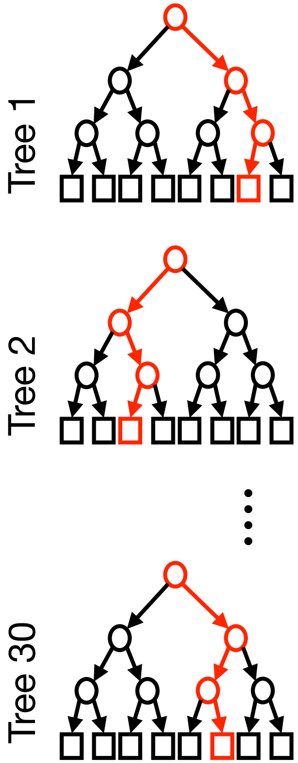
Simulateur



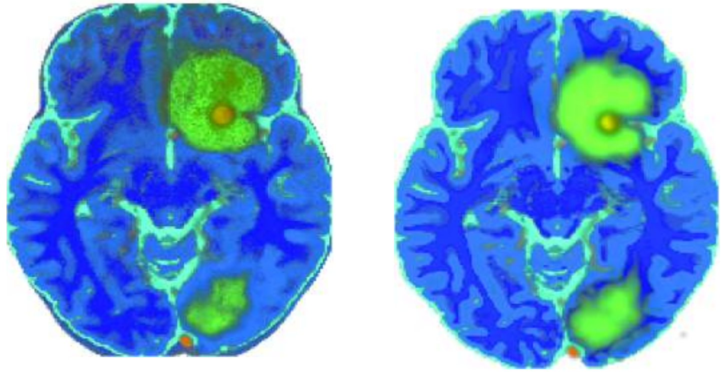
- Grey matter
- White matter
- LCR
- necrosis
- vessels
- œdema

Univ Utah

Apprentissage statistique

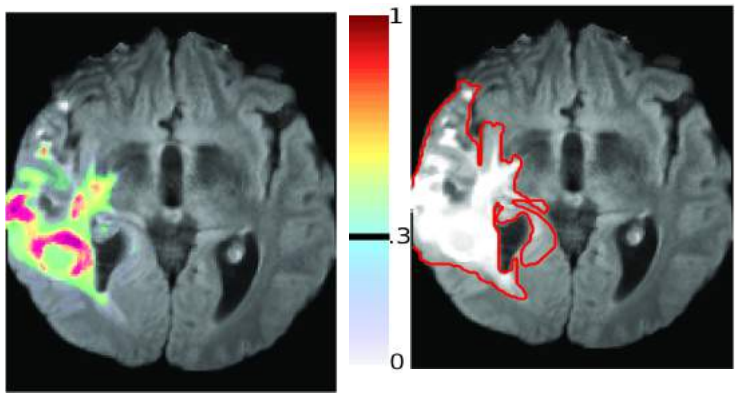


Validation sur 200 IRM simulées



prediction vérité

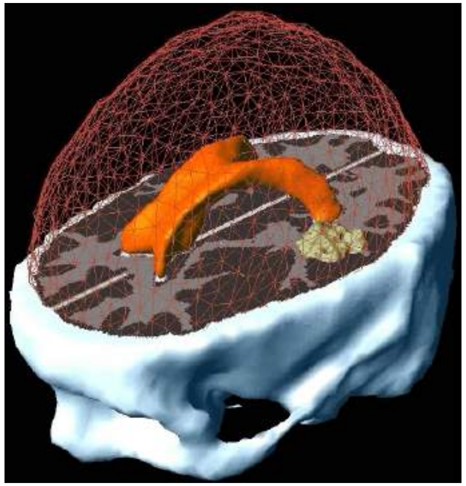
Transfert aux images réelles



E Geremia, B H. Menze, M Prastawa, MA Weber, A Criminisi, and N Ayache. LNCS, 2012.
N. Cordier, H Delingette, M Lê, N Ayache. IEEE Tr. on Medical Imaging, 2016.

Radiothérapie personnalisée

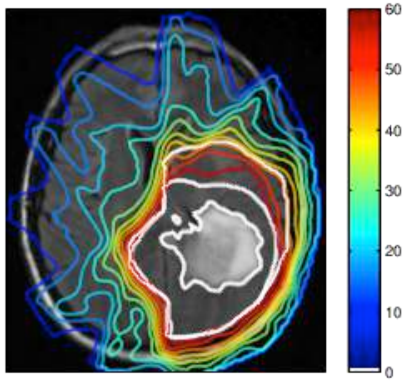
erc MedYMA



0. Clatz

Mass. General Hospital, Boston

Dosimétrie standard



GTV : 60 Gy - *T1Gd + 2cm*
CTV 46 Gy - *T2Flair + 1.5cm*

Migration + prolifération

$$\boxed{\frac{\partial c}{\partial t} = \nabla.\left(D\nabla c\right) + \rho c\left(1-c\right)}$$

Fisher-Kolmogorov

Modèle densité cellules tumorales

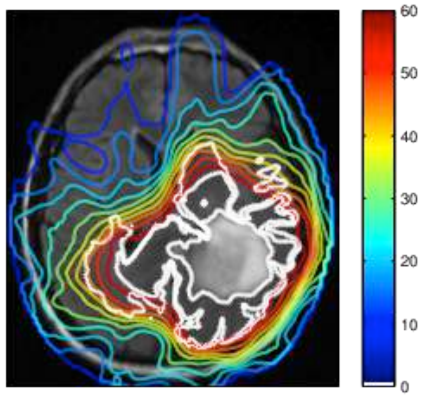
$$\min_{d} \sum_{i \in T} \boxed{c_i} \boxed{\exp\left(-d_i\left(\alpha + \frac{\beta}{\alpha N_f} d_i\right)\right)}$$

Modèle de radiothérapie

$$\text{subject to } \frac{1}{N_T} \sum_{i \in T} d_i \leq \boxed{d^p}$$

Dose maxi autorisée

Dosimétrie optimisée

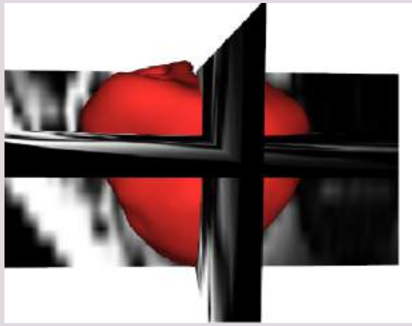


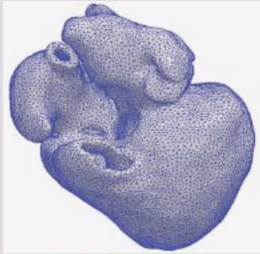
Traitement personnalisé

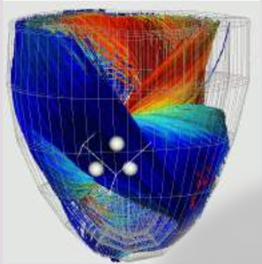
- M Lê, H Delingette, …, J Unkelbach, N Ayache. IEEE Tr. on Medical Imaging 2016

4. Cardiologie

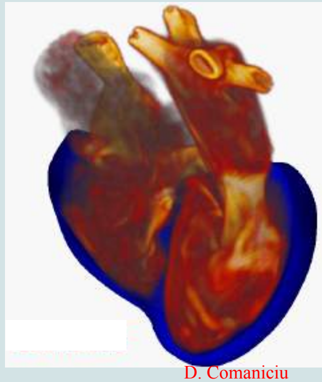
1. Structure



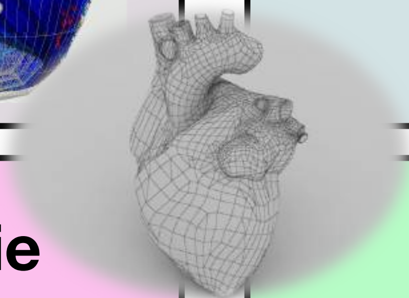




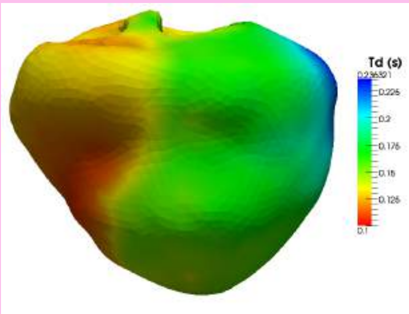
4. Hémodynamique



D. Comaniciu

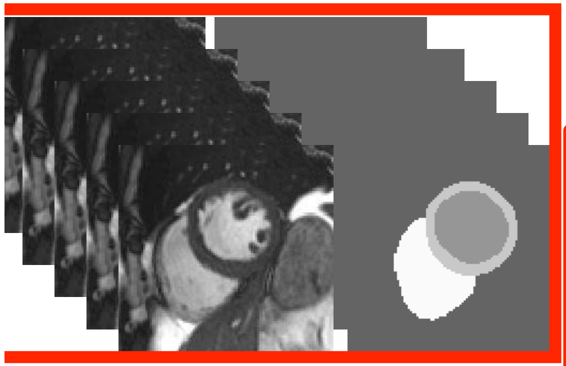


2. Electrophysiologie

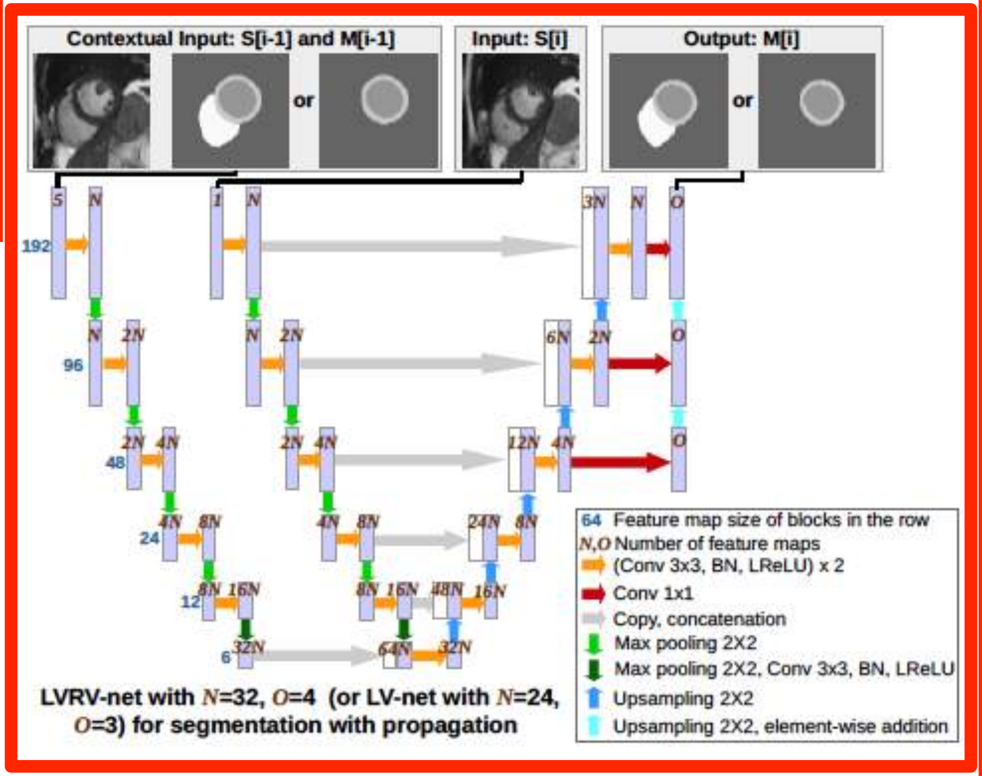


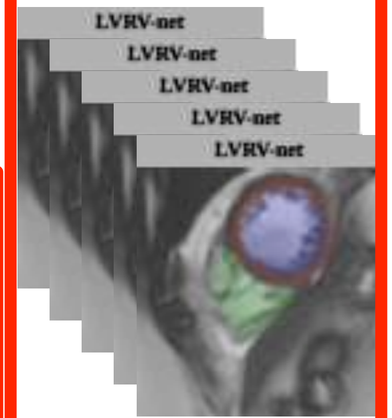
3. Mécanique

Géométrie des ventricules



Apprentissage profond





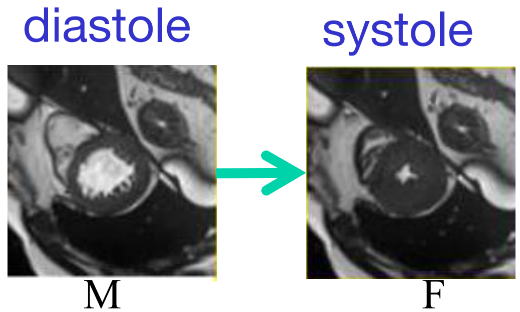
- **Entrainement** :
  UK Biobank :
  4000 sujets

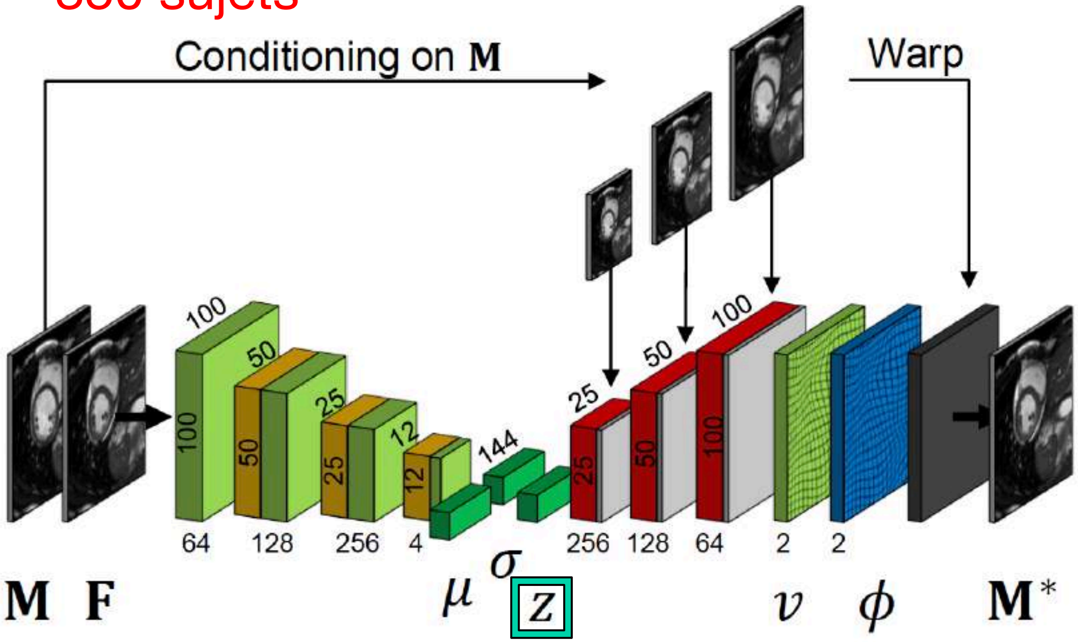
- Thanks to :
  - S Petersen
  - D. Rueckert et al.

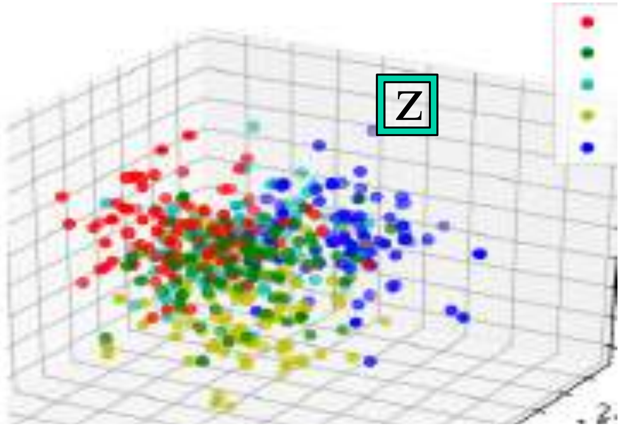
Q. Zheng, H Delingette, N Duchateau, N Ayache. 3D Consistent & Robust Segmentation of Cardiac Images by Deep Learning with Spatial Propagation. IEEE Transactions on Medical Imaging, 2018.

Apprendre les déformations ?

- Recalage entre images diastole et systole
- Auto Encodeur Variationnel Conditionnel
- 350 sujets





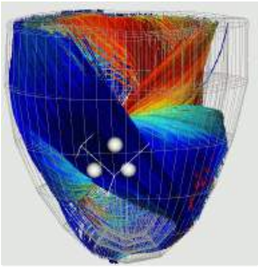


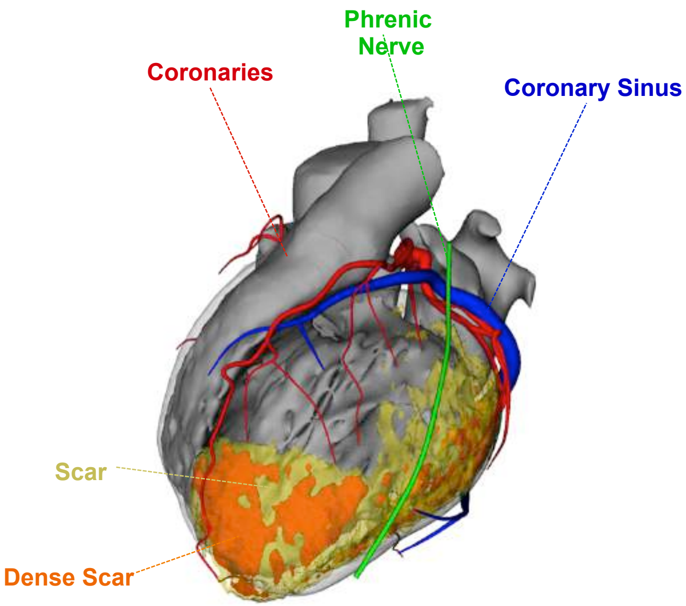
Normaux
Cardiomyopathies hypertrophiques
Cardiomyopathies dilatées
Infarctus du myocarde
Anomalies du ventricule droit

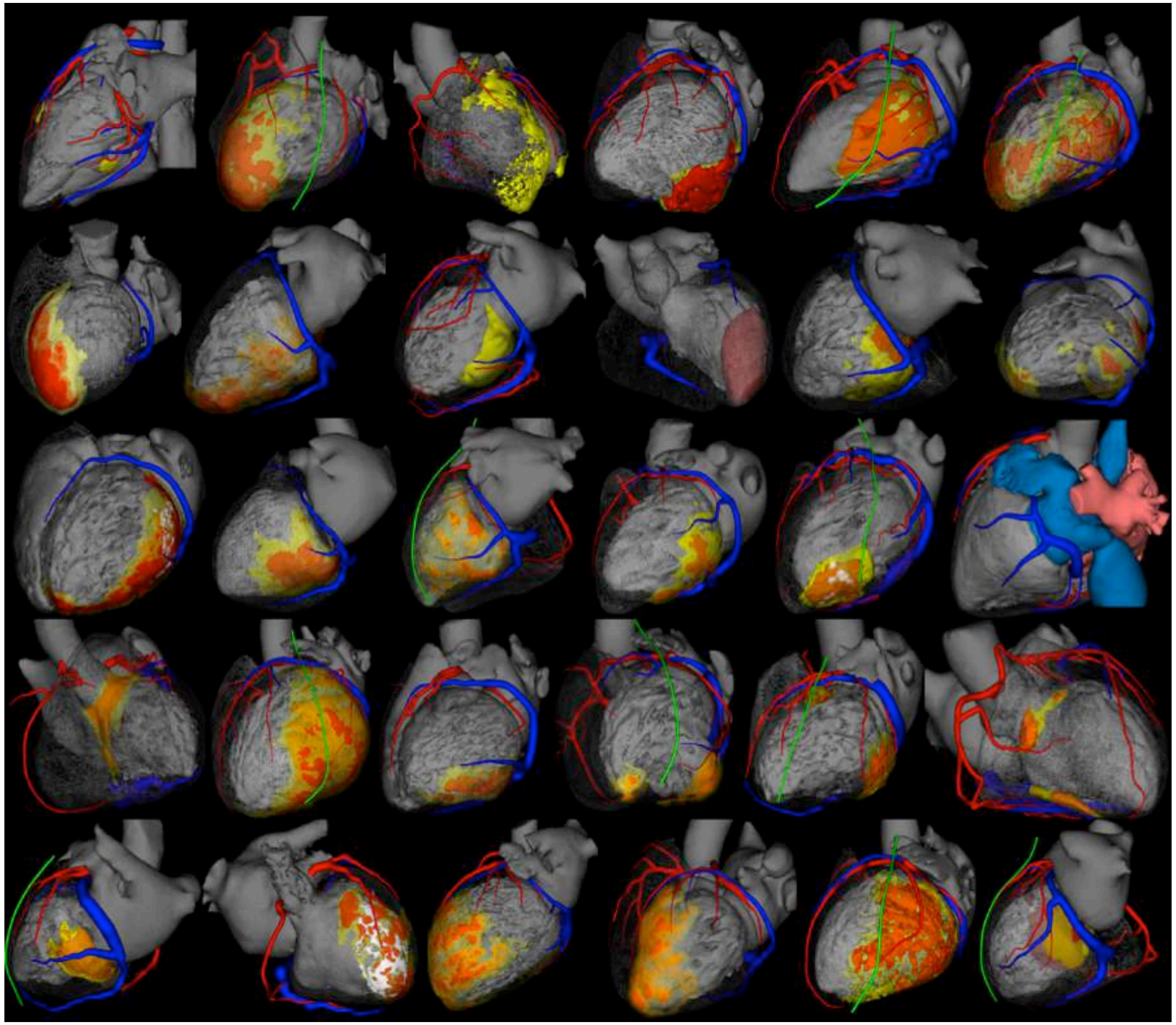
$$l(\omega,\gamma,\mathbf{F},\mathbf{M}) = -E_{z\sim q_\omega(\cdot|\mathbf{F},\mathbf{M})}\left[\log p_\gamma(\mathbf{F} \mid z,\mathbf{M})\right] + KL\left[q_\omega(z \mid \mathbf{F},\mathbf{M}) \parallel p(z)\right]$$

J Krebs, T Mansi, B Mailhé, N Ayache, H Delingette.
Learning Structured Deformations using Diffeomorphic Registration. ArXiv 2018.

Modèle anatomique



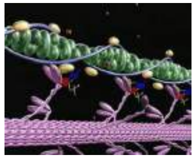




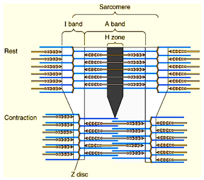
inHEART

Modèle biophysique

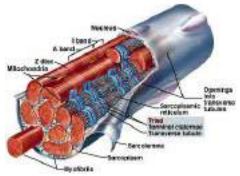
ATP



sarcomères

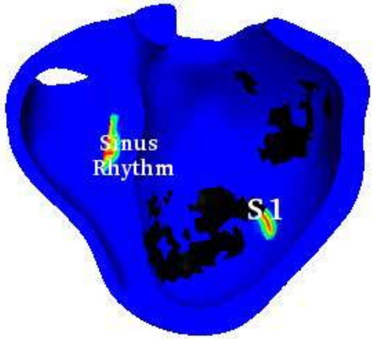


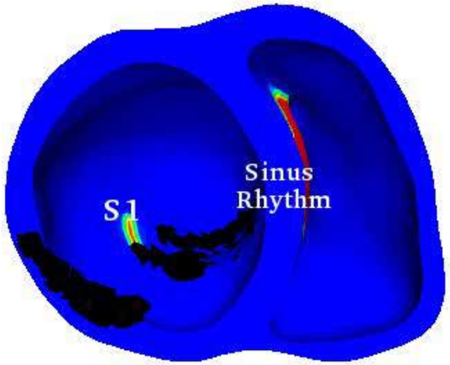
fibres



organe

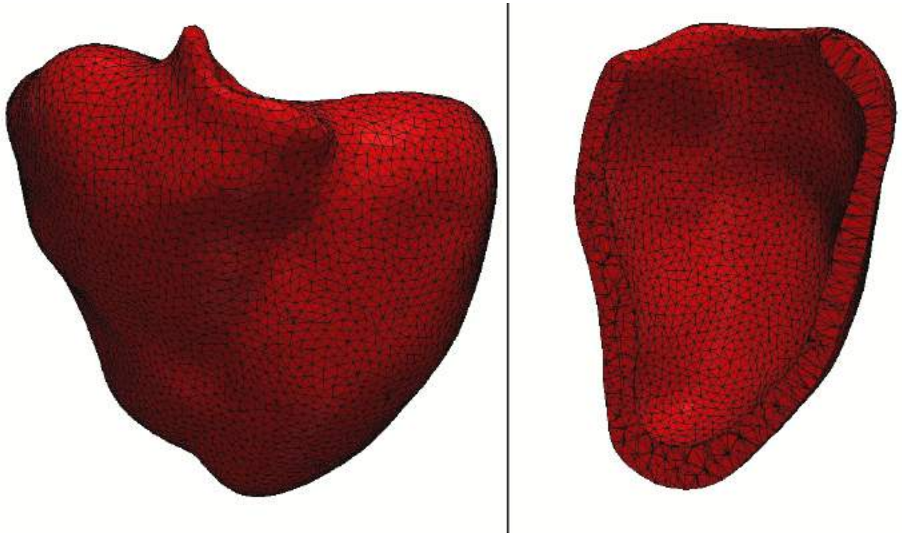
électrique





$$\left\{\begin{array}{lcl}\partial_t u & = & \mathrm{div}(d_{MS}\mathbf{M}\nabla u) + \dfrac{zu^2(1-u)}{\tau_{\mathrm{in}}} - \dfrac{u}{\tau_{\mathrm{out}}} + J_{\mathrm{stim}}(t) \\ \partial_t z & = & \left\{\begin{array}{ll}\dfrac{(1-z)}{\tau_{\mathrm{open}}} & if \quad u < u_{\mathrm{gate}} \\ \dfrac{-z}{\tau_{\mathrm{close}}} & if \quad u > u_{\mathrm{gate}}\end{array}\right.\end{array}\right.$$

mécanique



$$\rho \ddot{P} - \mathrm{div}(K_p\,\mathcal{E}_p + C_p\,\dot{\mathcal{E}}_p + \sigma_c + C_c\,\dot{\mathcal{E}}_c + K_c\xi_0) = 0$$

$$\partial_t K_c = K_0|u|_+ - (|\dot{\mathcal{E}}_c| + |u|)K_c$$

$$\partial_t \sigma_c = \sigma_0|u|_+ - (|\dot{\mathcal{E}}_c| + |u|)\sigma_c + K_c\dot{\mathcal{E}}_c$$

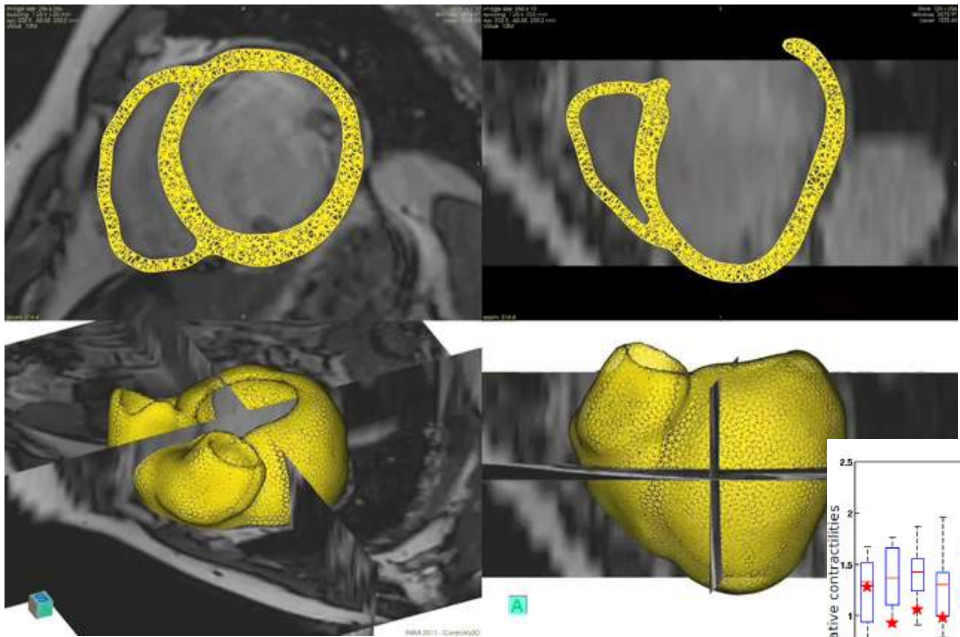
$$\sigma_c + C_c\,\dot{\mathcal{E}}_c + K_c\xi_0 = K_s(\mathcal{E}_p - \mathcal{E}_c)$$

K_c raideur
u potentiel d'action
ε_c déformation
σ_c contrainte

- Chen, Cabrera, Relan, ..Delingette, Ayache, Sermesant, Razavi: J. of Cardiovascular Electrophysiology, 2016.
- Marchesseau, Delingette, Sermesant, Ayache. Biomechanics and Modeling in Mechanobiology, 2012

Apprentissage

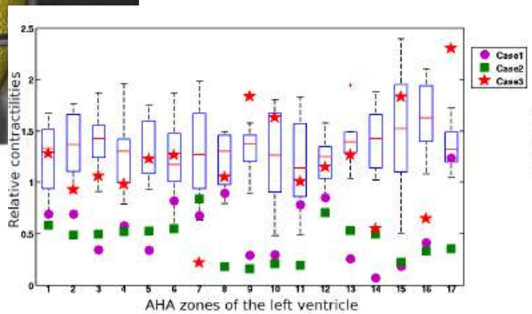
par filtrage optimal



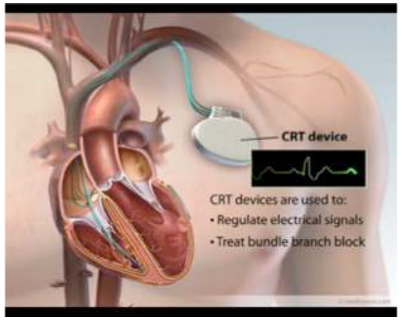
Insuffisance cardiaque

quantifier

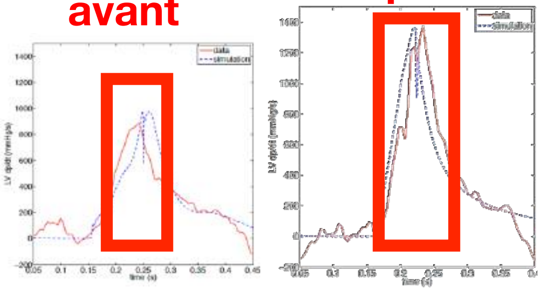
contractilité,
raideur,
taux relaxation,
taux contraction,
viscosité,
compressibilité,
résistance
périphérique, etc.



prédire



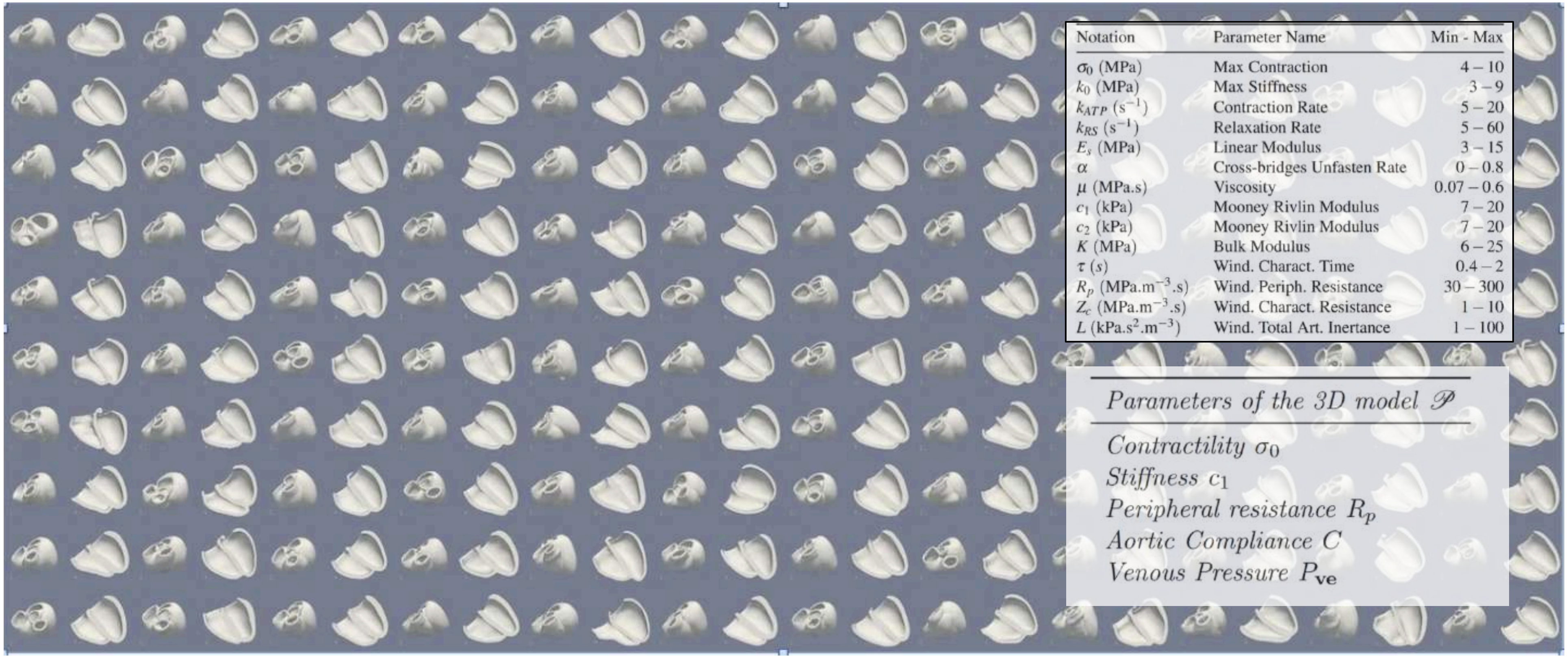
avant dP/dt **après**



Marchesseau, S., Delingette, H., Sermesant, M., Cabrera-Lozoya, R., Tobon-Gomez, C., Moireau, P., Figueras, R., Lekadir, K., Hernandez, A., Garreau, M. Donal, E., Leclercq, C., Duckett, S., Rhode, K., Rinaldi, C., Frangi, A., Razavi, R., Chapelle, D., and Ayache, N. *Personalization of a Cardiac Electromechanical Model using Reduced Order Unscented Kalman Filtering from Regional Volumes.* Medical Image Analysis 2013

120 cœurs personnalisés

Apprentissage par optimisation multi-fidélité et *a priori* statistique



Notation	Parameter Name	Min - Max
σ_0 (MPa)	Max Contraction	$4-10$
k_0 (MPa)	Max Stiffness	$3-9$
k_{ATP} (s^{-1})	Contraction Rate	$5-20$
k_{RS} (s^{-1})	Relaxation Rate	$5-60$
E_s (MPa)	Linear Modulus	$3-15$
α	Cross-bridges Unfasten Rate	$0-0.8$
μ (MPa.s)	Viscosity	$0.07-0.6$
c_1 (kPa)	Mooney Rivlin Modulus	$7-20$
c_2 (kPa)	Mooney Rivlin Modulus	$7-20$
K (MPa)	Bulk Modulus	$6-25$
τ (s)	Wind. Charact. Time	$0.4-2$
R_p ($MPa.m^{-3}.s$)	Wind. Periph. Resistance	$30-300$
Z_c ($MPa.m^{-3}.s$)	Wind. Charact. Resistance	$1-10$
L ($kPa.s^2.m^{-3}$)	Wind. Total Art. Inertance	$1-100$

Parameters of the 3D model $\mathscr{P}$
Contractility σ_0
Stiffness c_1
Peripheral resistance R_p
Aortic Compliance C
Venous Pressure P_{ve}

R Molléro, X Pennec, H Delingette, A Garny, N Ayache, M Sermesant. *Multifidelity-CMA for efficient personalisation of 3D cardiac electromechanical models*. Biomechanics and Modeling in Mechanobiology, 2017.

Atlas intelligent du futur

Nouvelle séquence

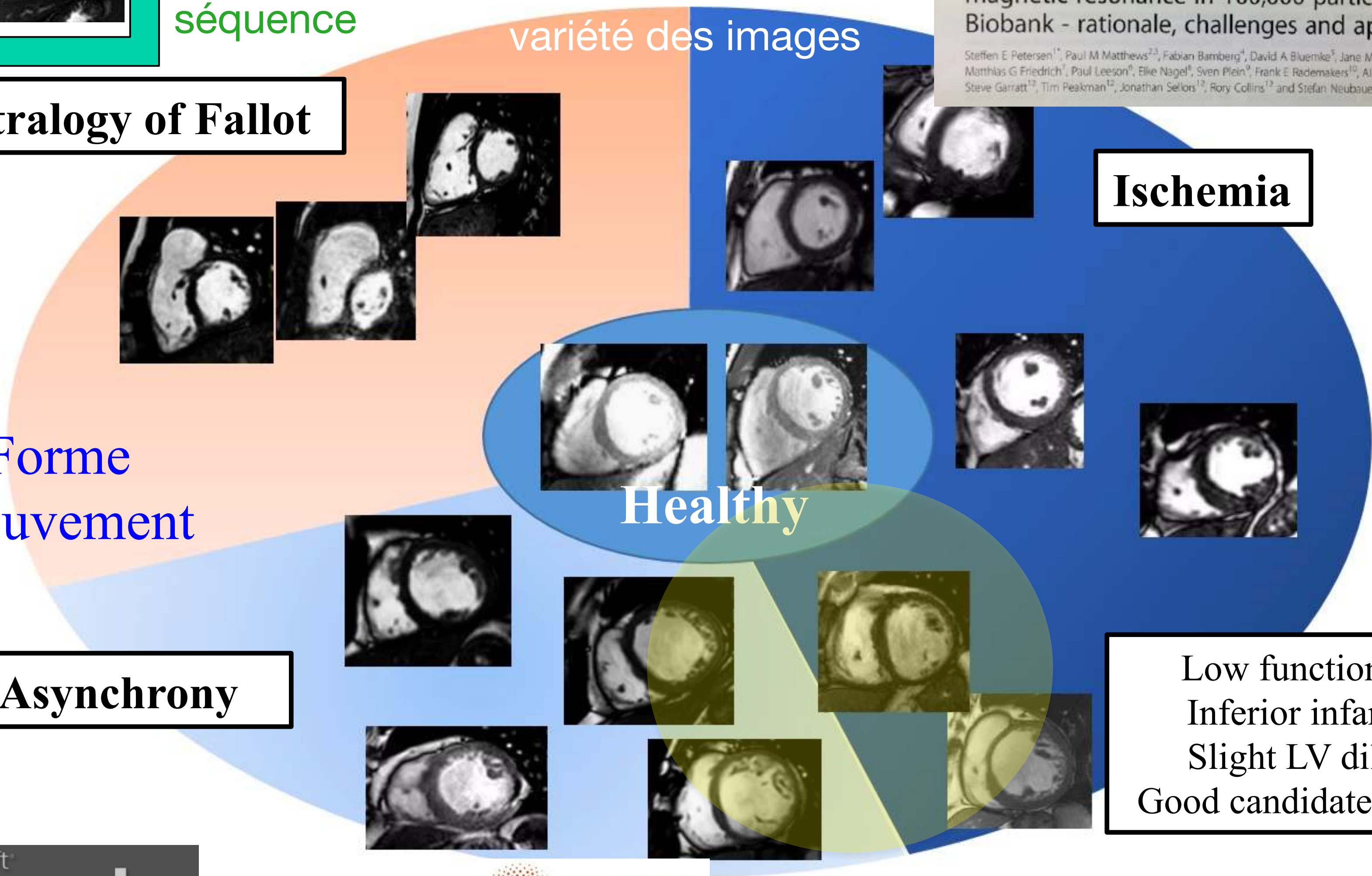
Petersen et al. Journal of Cardiovascular Magnetic Resonance 2013, 15:46
http://www.jcmr-online.com/content/15/1/46

Journal of Cardiovascular Magnetic Resonance

REVIEW — Open Access

Imaging in population science: cardiovascular magnetic resonance in 100,000 participants of UK Biobank - rationale, challenges and approaches

Steffen E Petersen[1*], Paul M Matthews[2,3], Fabian Bamberg[4], David A Bluemke[5], Jane M Francis[6], Matthias G Friedrich[7], Paul Leeson[6], Eike Nagel[8], Sven Plein[9], Frank E Rademakers[10], Alistair A Young[11], Steve Garratt[12], Tim Peakman[12], Jonathan Sellors[12], Rory Collins[12] and Stefan Neubauer[6]



Low function (EF)
Inferior infarction
Slight LV dilation
Good candidate for CRT

Margeta et al. 2015
Le Folgoc et al .2017

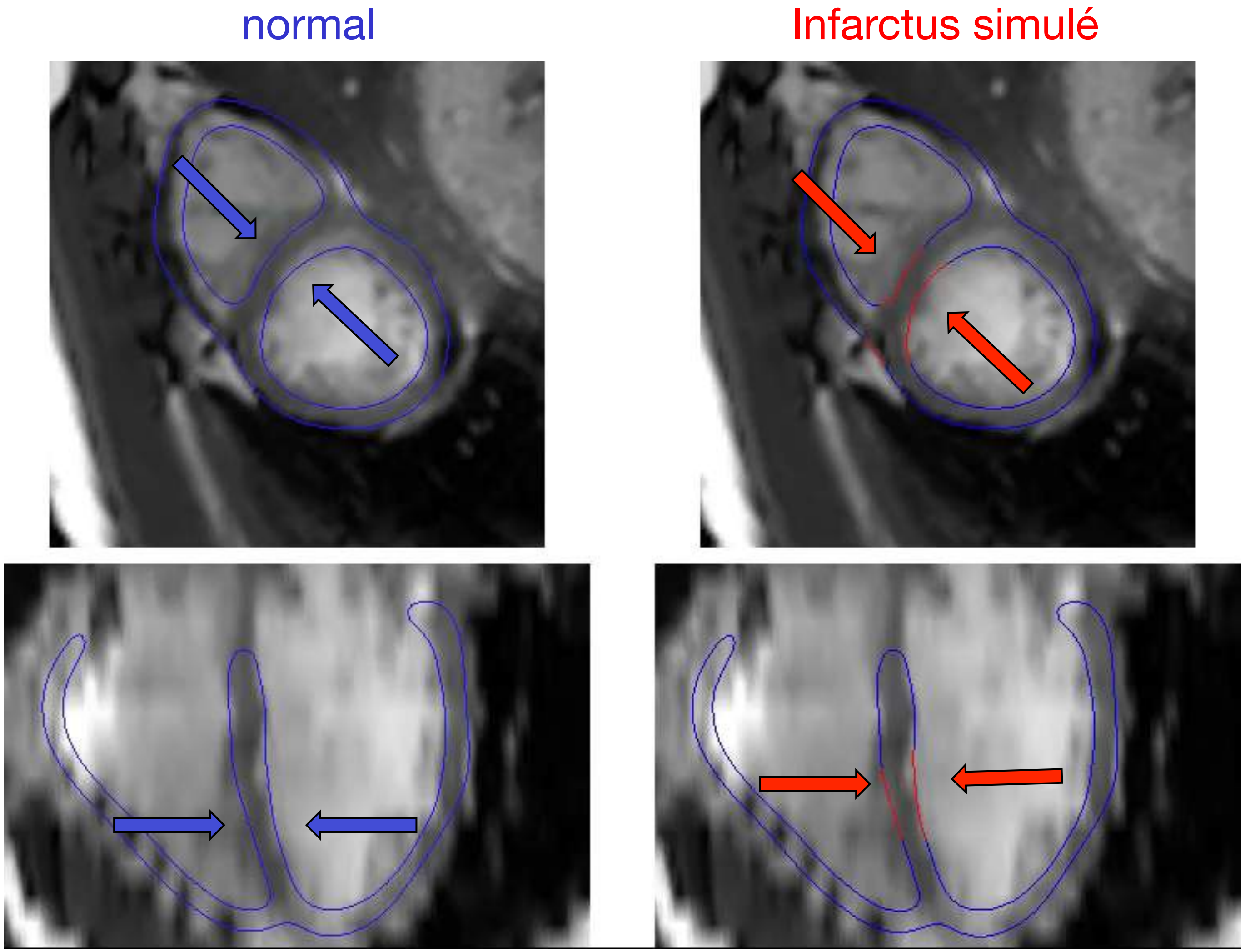
Microsoft Research Cambridge

erc MedYMA

Inria informatiques mathématiques

Augmenter les données

erc MedYMA

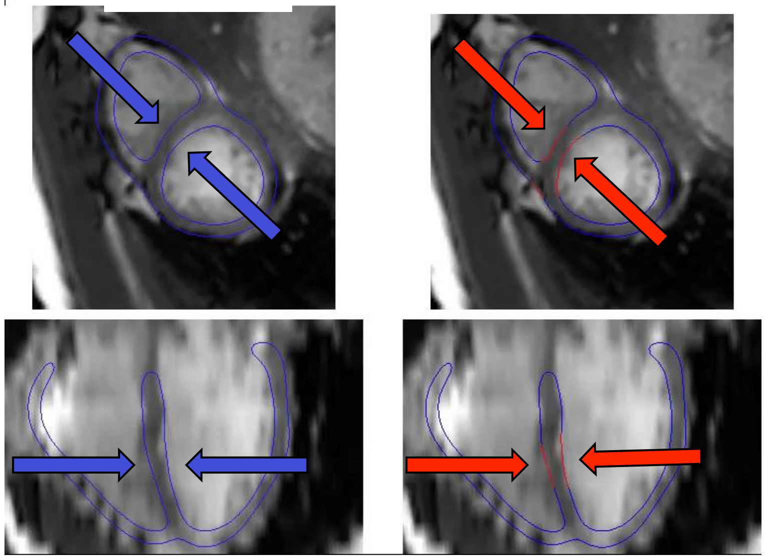


- N Duchateau, M. Sermesant, H Delingette, N Ayache. IEEE Tr. on Medical Imaging, 2018.

Apprendre infarctus par la simulation

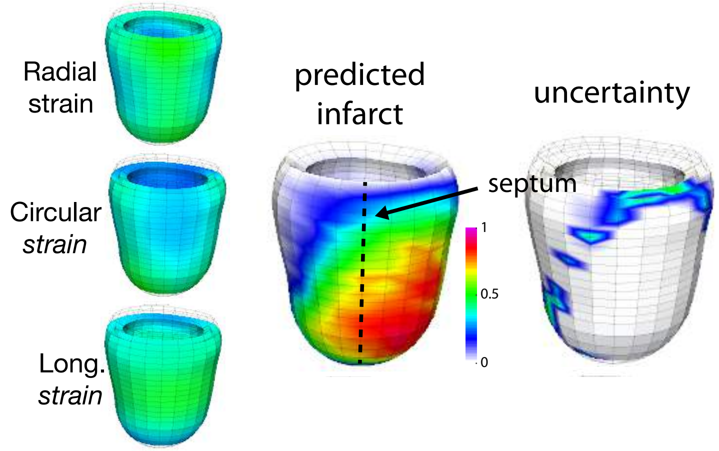
- 15 séquences normales
- 450 séquences simulées infarctus : localisation, étendue, gravité variables

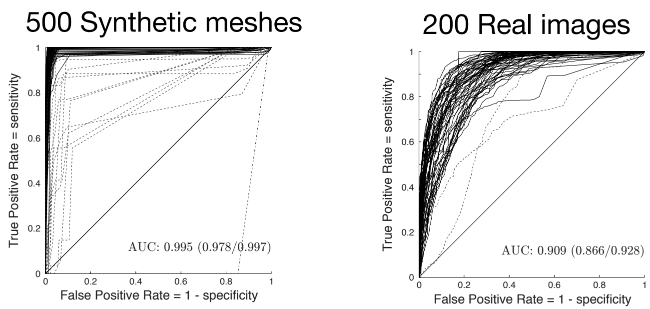
normal | Infarctus simulé



- détection & localisation infarctus

Régression sur les déformations, espace réduit

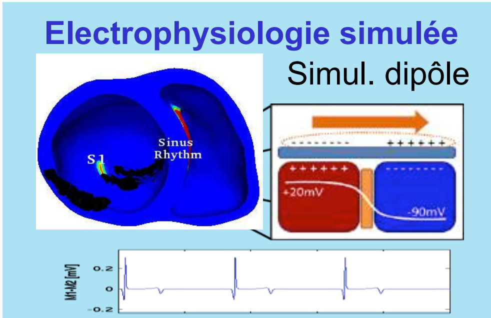




- N Duchateau, M. Sermesant, H Delingette, N Ayache. IEEE Tr. on Medical Imaging, 2018.
- N Duchateau, P Allain, E Saloux, M Sermesant IEEE Tr. on Med Imaging, 2016

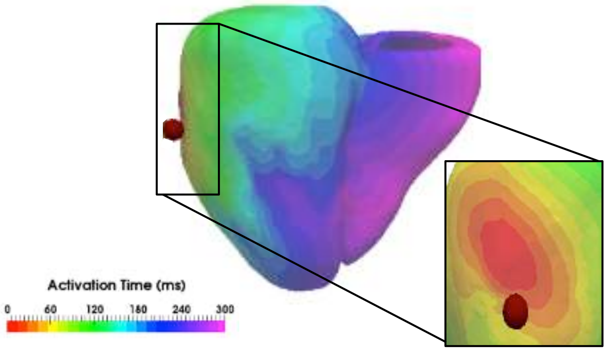
Apprendre l'électrophysiologie par la simulation

- Personnaliser électrophysiologie



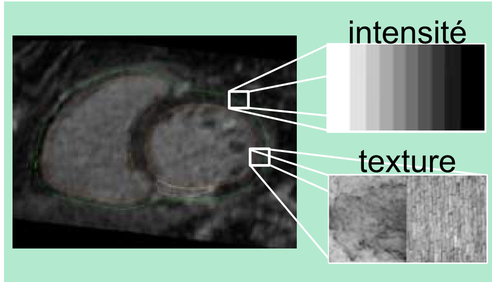
- régression bayésienne parcimonieuse

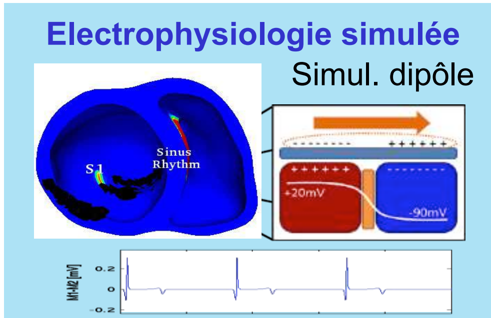
Point de départ + vitesse de conduction



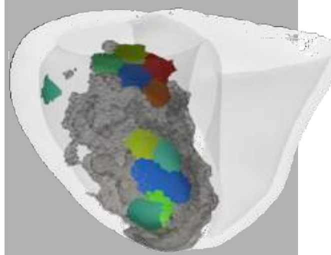
- Prédire anomalies de conduction
- Forêts aléatoires :

texture + simulation EP





LAVAs: Local Abnormal Ventricular Activation



Cibles ablation

S Giffard-Roisin, Jackson, Fovargue, Lee, Delingette, Razavi, Ayache, Sermesant, IEEE TBME 2017 + 2018

R Cabrera-Lozoya, B Berte, H Cochet, P Jaïs, N Ayache, M Sermesant. IEEE TBME 2016 + 2018

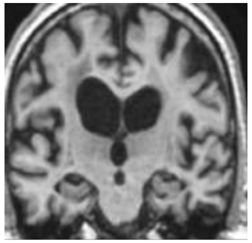
Pour finir

- Vers des données « holistiques »
  - Images & signaux
  - Biologie, génétique, métabolomique, etc.
  - Comportement, style de vie, etc.

Bases de données : ADNI, Enigma, UK Biobank, Insight, etc.

Neuropsychiatrie numérique

Prise en charge
de patients avec une
maladie neuropsychiatrique

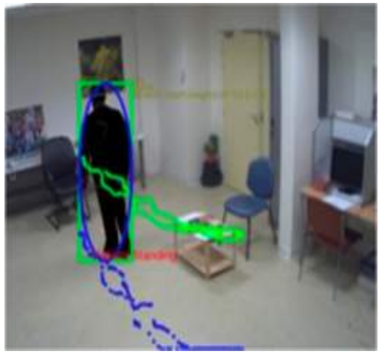


baseline

Images

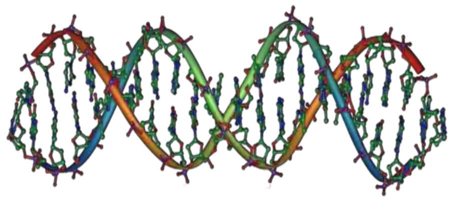
MNC^3

Idex UCA^{Jedi}
Inria, UNS,
CHU, IPMC,
CoBTeK



Mouvement/activité

Science
des
données

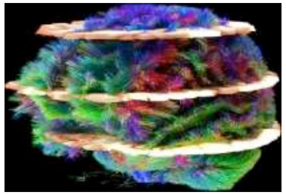


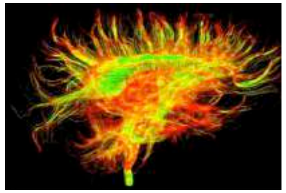
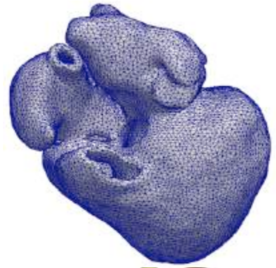
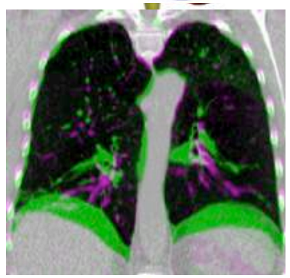
Biologie/génomique

L. Antelmi, C. Abi-Nader, V. Manera, P. Robert, N. Ayache, M Lorenzi. A method for statistical learning in large databases of heterogeneous imaging, cognitive and behavioural data: proof of concept. Epiclin 2018.

Patient numérique et IA

www.journals.elsevier.com/medical-image-analysis

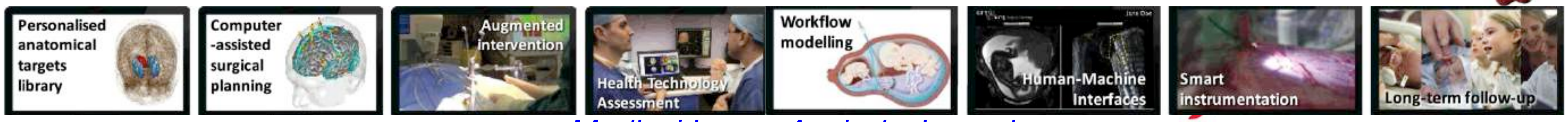




De nouveaux outils informatiques au service d'une médecine

plus personnalisée
plus précise
plus prédictive
plus préventive

Pour mieux soigner le patient réel



Medical Image Analysis Journal
20th anniversary special issue (free access)

Patient numérique et IA

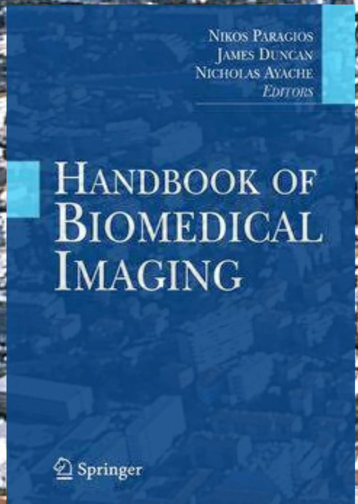
De nouveaux outils informatiques
pour **assister** le médecin,
pas pour le **remplacer** :

compassion
compréhension
créativité
esprit critique
conscience professionnelle

Intelligence naturelle

Philosophie magazine 04/18

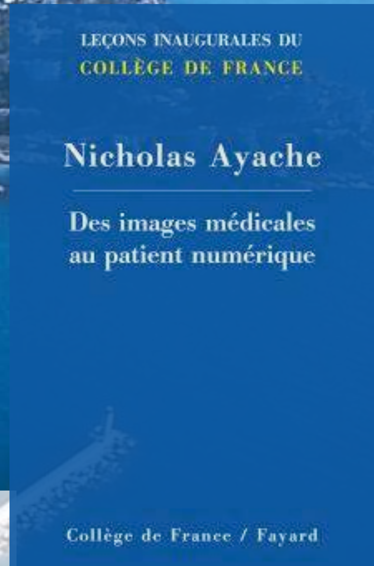
Remerciements



Equipe Inria Epione

Collaborateurs et partenaires

- Académiques
- Cliniques
- Industriels



Medical Image Analysis Journal

20th anniversary special issue (free access)

erc MedYMA

Inria informatiques mathématiques

COLLÈGE DE FRANCE 1530

team.inria.fr/Epione/

www.college-de-france.fr

complément

Ophtalmologie

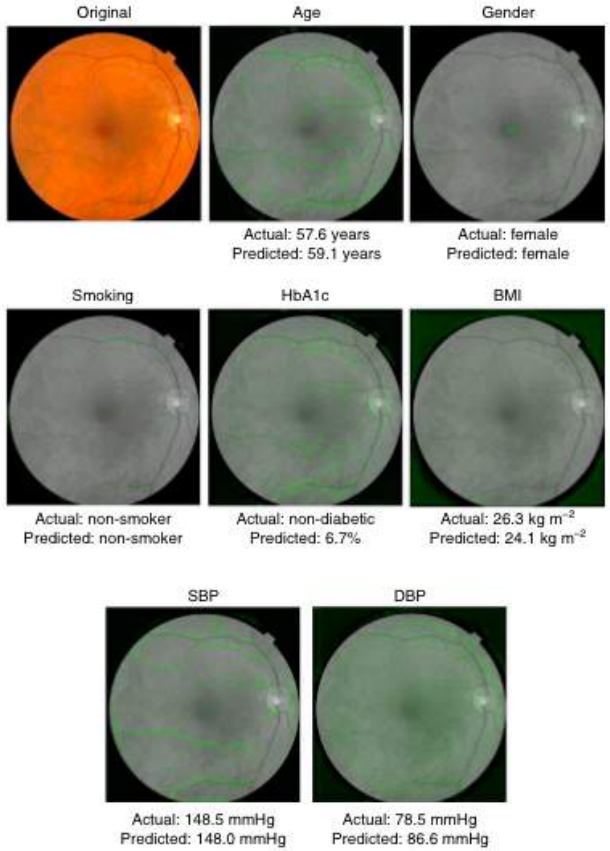
Fév. 2018

ARTICLES
https://doi.org/10.1038/s41551-018-0195-0

nature biomedical engineering

Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning

- Apprentissage : ~300 000 patients



Déc. 2016

JAMA | Original Investigation | INNOVATIONS IN HEALTH CARE DELIVERY

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

- Apprentissage : ~130 000 patients

IDx-DR
FDA Approved
April 2018

Imagerie & génétique
Maladie d'Alzheimer

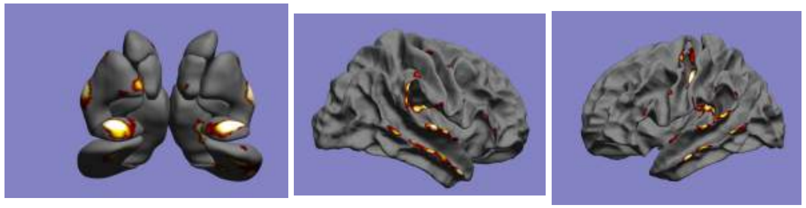
UCL

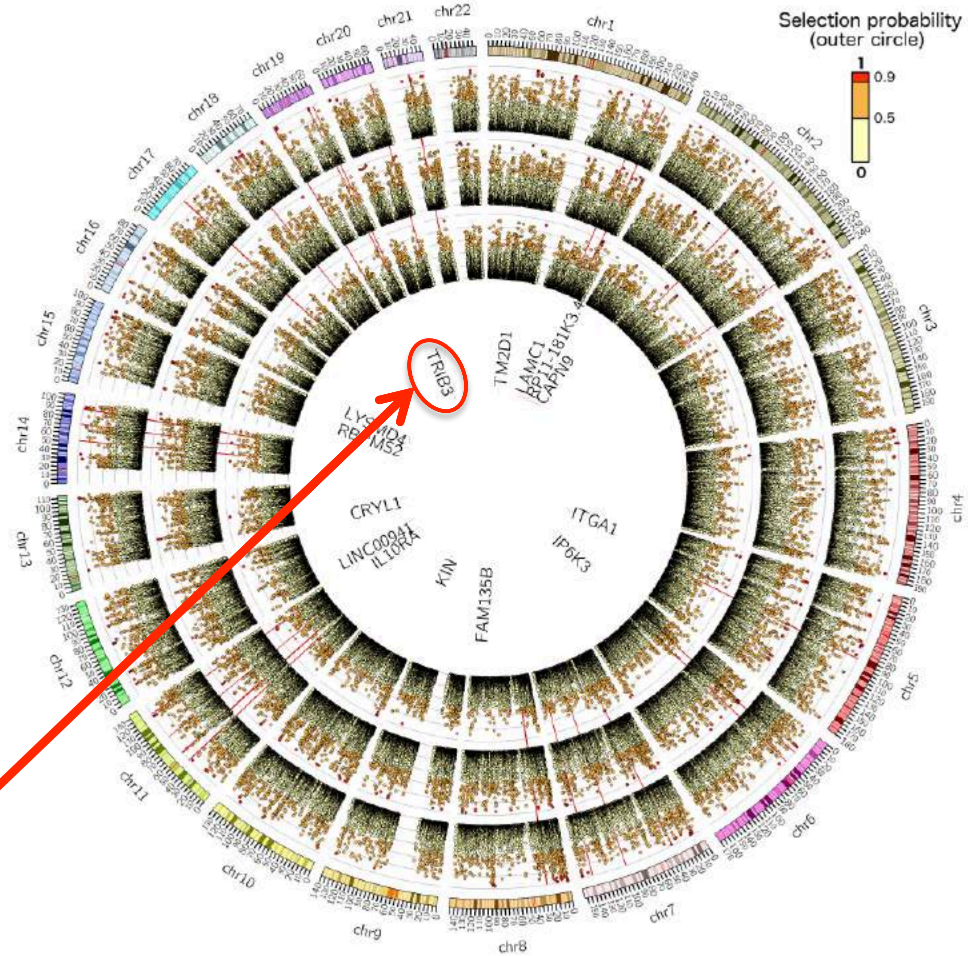
Analyser covariance (PLS) :

600 patients

Phénotypes IRM :~10^5 mesures
atrophie matière grise

Génotypes SNPs: ~10^6 mesures
polymorphismes nucléotidiques





Phénotype

Hippocampes, Amygdales Cortex cingulaire, enthorinal, temporal

Génotype

TRIB3 + APOE, TOMM40,... : Neurodégénérescence Maladie d'Alzheimer

M Lorenzi,…,PM Thompson, S Ourselin. *Susceptibility of brain atrophy to TRIB3 in Alzheimer's disease, evidence from functional prioritization in imaging genetics.* PNAS 2018.