

User Case Study 2: University College London Hospitals - Biomedical Research Centre

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- Born and raised in Pitesti, Romania



- 2010-2014: Studied MEng in Computer Science at Imperial College
- 2014: Joined the EPSRC CDT in Medical Imaging at UCL

- Daniel Ruckert from Imperial College recommended me to apply
- I liked the idea of working in a multi-disciplinary environment that combines:

computer science



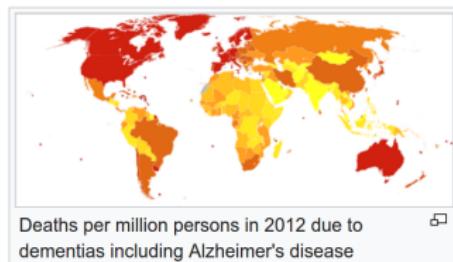
mathematics



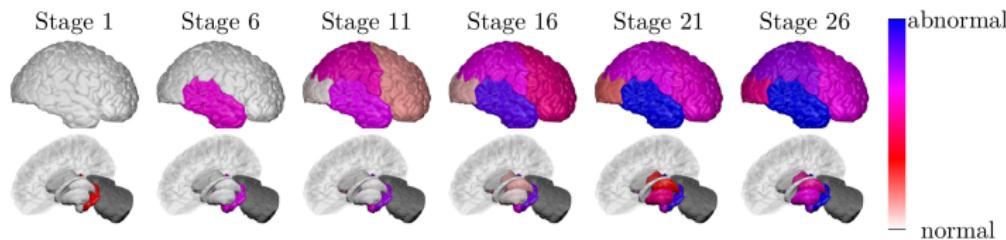
medicine



- Help solve some of the most devastating diseases worldwide



- 1 Study the progression of two diseases: typical Alzheimer's disease and Posterior Cortical Atrophy



- 2 Develop and improve disease progression models (DPMs)

$$p(X|S) = \prod_{j=1}^J \left[\sum_{k=0}^N p(k) \left(\prod_{i=1}^k p(x_{s(i),j} | E_{s(i)}) \prod_{i=k+1}^N p(x_{s(i),j} | \neg E_{s(i)}) \right) \right] \quad (1)$$

Motivation:

- Enables accurate patient staging and prognosis
- Helps development of potential drugs

- The usual cause of dementia (60-70% of cases)
- Symptoms: memory loss, problems with language, mood swings, loss of motivation
- Causes:

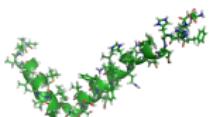
Genetics



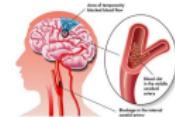
Neurofibrillary tangles



Amyloid-beta



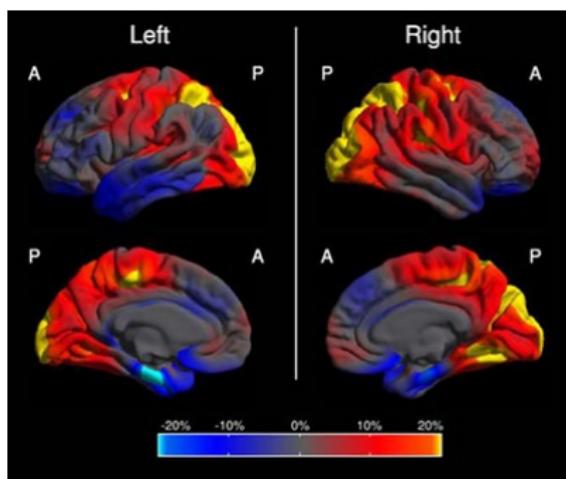
Vascular disease



- Risk factors: head injuries, depression, hypertension
- Treatments: none available that stop/slow cognitive decline

Posterior Cortical Atrophy (PCA):

- Atypical variant of AD that affects the posterior part of the brain
- Symptoms: predominantly vision deficits
- Very rare: only 5% of all AD cases



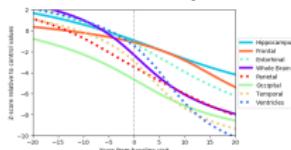
Key Contributions

1. Disease Progression Modelling of PCA and tAD (manuscript in preparation)

Event-based Model



Differential Eq. Model

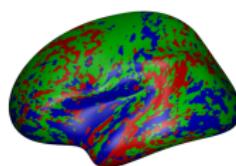


2. Performance Evaluation of DPMs

Model	Staging Consistency		Time-lapse	
	Hard	Soft	Hard	Soft
EBM - Standard	0.91 ± 0.16	0.71 ± 0.07	-	-
EBM - Sampling	0.96 ± 0.07	0.76 ± 0.10	-	-
EBM - EM	0.99 ± 0.01	0.72 ± 0.07	-	-
DEM - Standard	0.87 ± 0.10	0.88 ± 0.08	0.72 ± 0.91	0.67 ± 0.92
DEM - Optimised	0.87 ± 0.10	0.88 ± 0.08	0.74 ± 0.92	0.69 ± 0.92

3. Developed a Novel Disease Progression Model

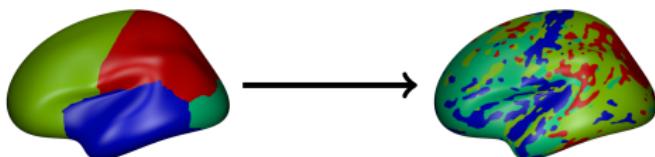
(Marinescu et al., IPMI, 2017)



4. TADPOLE competition

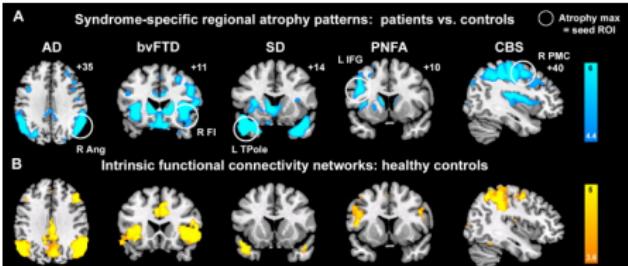


Aim: Increase the resolution of detectable atrophy patterns:



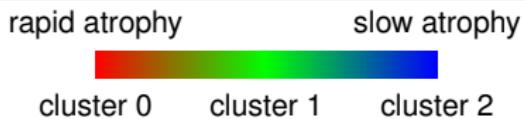
Motivation:

- 1 Atrophy patterns are not spatially connected (Seeley et al., Neuron, 2009)
- 2 Better biomarker prediction and disease staging

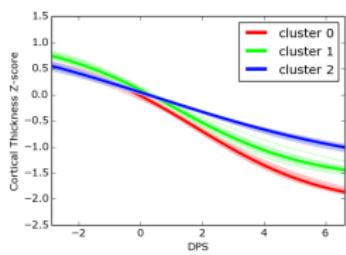
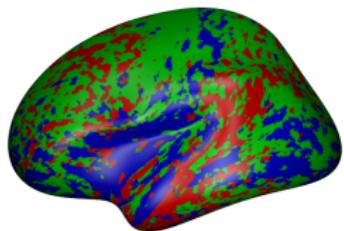


(a) Seeley et al., Neuron, 2009

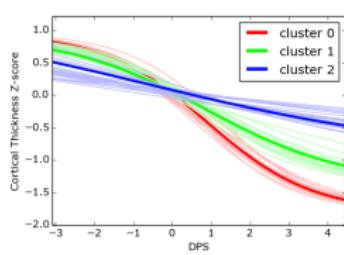
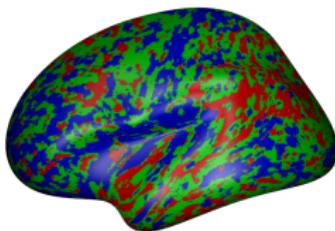
Vertexwise Model - ADNI and DRC Results



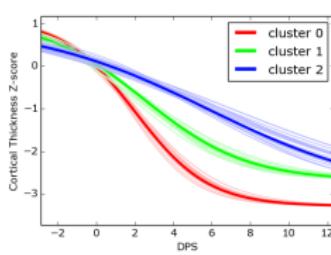
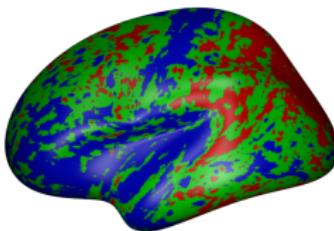
tAD - ADNI



tAD - DRC dataset



PCA - DRC dataset



Marinescu et al., IPMI, 2017

Conclusion: Model reveals spatially disconnected patterns of atrophy

Crucial to the success of my work were several aspects:

- Joint supervisors from distinct fields: computer science and neurology

Daniel
Alexander
(CMIC)



Sebastian
Crutch
(BRC)



- Multi-disciplinary collaboration: computational center (CMIC) + clinical center (DRC)
- Understanding of the clinical workflow through the miniMD
- Supportive research group



I would like to thank the EPSRC and NIHR BRC for funding me