## Histological validation and reconstruction

Juan Eugenio Iglesias
ERC Senior Research Fellow University College London

MS Workshop@UCL, January 31 ${ }^{\text {th }} 2018$


## Probabilistic atlases combining in vivo and ex vivo MRI

Each has its own advantages

- In vivo:
- Complete FOV.
- Faster to label.
- Negligible geometric distortions.
- Ex vivo:
- Higher resolution and / or contrast (no motion, dedicated coils).
- Enables more detailed delineations
${ }^{-}$We have a framework to combine both!



## 1 JCl

## Example: atlas of hippocampal subfields



Alveus


Parasubiculum
Presubiculum
Subiculum CA1
CA23
CA4
GC-DG
HATA
Fimbria
Molecular Layer
Hippo. fissure
Hippo. tail

## Example: atlas of hippocampal subfields

Represented as sparse, adaptive, tetrahedral mesh

(Iglesias et al., Neuroimage, 2015)

## However, ex vivo is MRI not always enough

 Some boundaries are only visible in histology

## Histology reconstruction: Blockface photos

Block-face photographs to assist reconstruction


## Example: Thalamic atlas

Block-face to MRI registration (rigid = easy!)


## $1 \mathrm{ICl}_{1}$

## Thalamic atlas

## Resampled MRI to histology



## Thalamic atlas

Reconstructing segmentations with "smart" interpolation (Gaussian mixture model + Markov random field)


## Atlas construction and image segmentation

 In vivo segmentations to learn surrounding structures

## Thalamic atlas

Comparison with Krauth, Morel, et al. (also based on histology)


(Iglesias et al., SfN 2017, OHBM 2017)

## How about the 2D inter-modality registration?

 Synthesis and multimodal registration

Iglesias et al., MICCAI, 2013.

## How about the 2D inter-modality registration?

Synthesis and multimodality registration

## Synthesis:

- Can improve multimodality registration
- Requires aligned training data



## Multimodality-registration:

- Aligns (multimodality) data


## $\mathrm{I}_{\mathrm{Cl}}^{1}$

## Histology reconstruction

Probabilistic model


INTENSITY WARPING

NONLINEAR \&
INTENSITY WARPING


## Uncertainty in registration (BigBrain)



## Uncertainty in registration (Allen)



## Quantitative evaluation of registration Simulated deformations on ADNI T1-T2 data (2D)

${ }^{-} 1 \mathrm{~mm}$ isotropic T1, $0.4 \times 0.4 \times 2.0 \mathrm{~mm}$ T2 (coronal, resampled to 1 mm )

- 1000 randomly selected coronal planes.
- Diffeomorphic random deformations, recovered with control points + Bsplines





## Example on synthetic data

## T1-T2 MRI with known correspondence



T2 (floating)

## Example on synthetic data

## T1-T2 MRI with known correspondence



T1 (reference)

## Example on synthetic data <br> T1-T2 MRI with known correspondence



Real T2

## Example on synthetic data T1-T2 MRI with known correspondence



Synthetic T2

## Example on synthetic data

## T1-T2 MRI with known correspondence



T1 (reference)

## Example on synthetic data

## T1-T2 MRI with known correspondence



Registered with MI
(spacing: 6 mm )

## Joint registration / synthesis T1-T2 MRI with known correspondence



Registered with synthesis
(spacing: 6 mm )

# Joint registration / synthesis T1-T2 MRI with known correspondence 



Synthetic T2

## Allen atlas

Publicly available at brain-map.org

- 106 coronal slices (histology) with manual segmentation of 806 structures
- Whole hemisphere microtome, but major cracks present on many sections.
${ }^{-}$Manually placed $\sim 200$ landmarks.
- Problems:
${ }^{-}$No blockface images available.
- Pixel dimensions are wrong for many sections.
- Section thickness not consistent.
- Spacing between coronal slices very uneven.


## Qualitative evaluation of registration (Allen)



## $\mathrm{IJCl}_{1}$

## Qualitative evaluation of registration (Allen)



## Qualitative evaluation of registration (Allen)



## Extensions

## And open questions

- Integration of multiple blocks (jigsaw puzzle) into probabilistic model.
- Make model robust when no blockface images and/or landmarks are given.
- Exploring smarter ways of interpolating segmentations*
- Smoothness priors in probabilistic model to make reconstructions visually more pleasant in orthogonal view.
- How do bridge (large) resolution gaps in Bayesian segmentation? Forward model is simple, but inference is complex (especially in multimodal).


## Acknowledgements: funding agencies

## Eugenio's salary:

- EU Horizon 2020, ERC Starting Grant No 677697 ("BUNGEE-TOOLS").
- EU's Horizon 2020 research and innovation programme, under the Marie Sklodowska-Curie grant agreement No 654911 (project THALAMODEL").


## Other

National Center for Research Resources (P41-RR14075, and the NCRR BIRN Morphometric Project BIRN002, U24 RR021382), the National Institute for Biomedical Imaging and Bioengineering (R01EB013565, R01EB006758), the National Institute on Aging (AG022381, 5R01AG008122-22), the National Center for Alternative Medicine (RC1 AT005728-01), the National Institute for Neurological Disorders and Stroke (R01 NS052585-01, 1R21NS072652-01, 1R01NS070963), and was made possible by the resources provided by Shared Instrumentation Grants 1S10RR023401, 1S10RR019307, and 1S10RR023043. Additional support was provided by The Autism \& Dyslexia Project funded by the Ellison Medical Foundation, by the NIH Blueprint for Neuroscience Research (5U01-MH093765), which is part of the multi-institutional Human Connectome Project, the Academy of Finland (133611), and the Finnish Funding Agency for Technology and Innovation (ComBrain). The collection and sharing of the MRI data used in the evaluation was funded by the ADNI (National Institutes of Health Grant U01 AG024904). Gipuzkoako Foru Aldundia (Fellows Gipuzkoa Program), MINECO’s "Plan Estatal de Investigación".

## Acknowledgements: people

Jean Augustinack (MGH/Harvard)
Koen Van Leemput (MGH/Harvard)
Bruce Fischl (MGH/Harvard/MIT)
Khoa Nguyen (MGH/Harvard)
Zeynep Saygin (MIT)
Dorit Kliemann (MIT)
Karla Miller (Oxford)
Mert Sabuncu (Cornell)
Ricardo Insausti (UCLM)
Cesar Caballero (BCBL)

Kepa Paz-Alonso (BCBL)
Garikoitz Lerma-Usabiaga (BCBL)
New Fei Ho (Singapore)
Sebastien Ourselin (UCL)
Marc Modat (UCL)
Marzia Scelsi (UCL)
David Thomas (UCL)
Loic Peter (UCL)
Martina Bocchetta (UCL)
Martin Reuter (DZNE)
$\qquad$ , whom I often forget to mention

## Thank you for your attention!

Questions?

