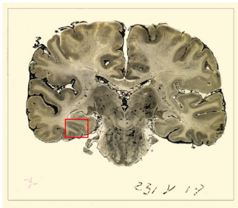
IMAGE Registration in Biology
G. Malandain

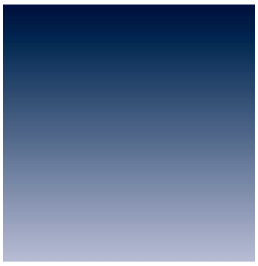
Cerebral microcirculation

confocal microscopy

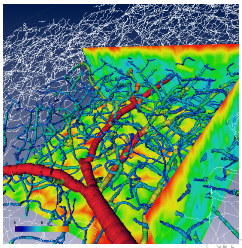


- MicroVisu3D project
  - INSERM U455 (Toulouse)
  - INRIA : C. Fouard
  - IMFT (Toulouse)
  - INDEED et TGS
- Duvernoy's material [Duvernoy, Selon, Vannson, BRB, 1981]
  - Human brain
  - Indian ink injection
  - Thin slices
  - Optical microscope observation

Image mosaicing

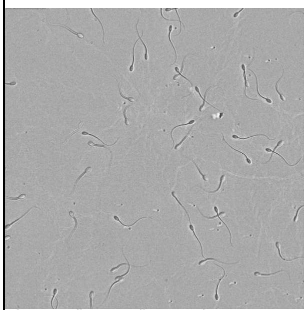


- Object of interest: vessels
- positioning error accumulation lead to disconnections
- positioning correction via (pairwise) image registration

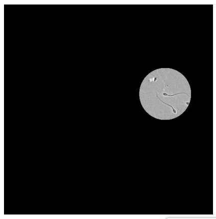


- Fouard et al., IEEE Trans Med Imaging, 25(10), 2006.
- Cassot et al., Microcirculation,13(1), 2006

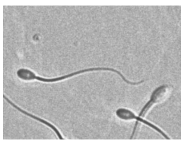
Object tracking

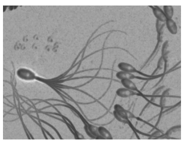


Sperm Motility Analysis:
INRA,INRIA, IMFT



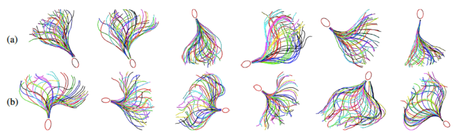
Object tracking



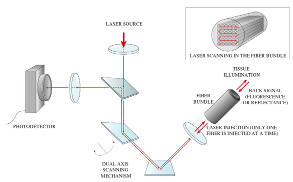


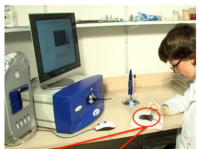
Head motion:
- speed
- orientation
- frequency

Flagellum
- angular sector
- frequency

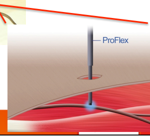


Imaging Regenerative Peripheral Axons in Live Mice





Fibered confocal microscopy, Mauna Kea Technologies



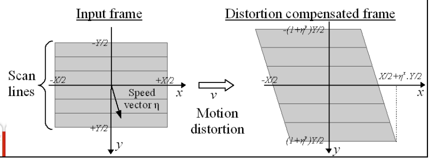
Thy1-YFP adult male mice: expression of YFP in the whole peripheral nervous system
- I. Charvet, P. Meda, CMU, Geneva,Switzerland
- L. Stoppini, Biocell Interface, Geneva

Mosaic

Motion Artifacts

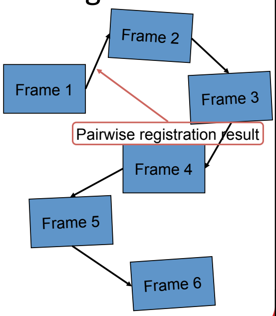
Scanning distortions similar to slit-scan camera effects

Known speed
⇒ Motion
artifacts
compensation



Consistent Global Alignment

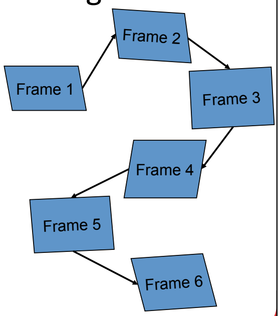
- Initialization
  - Consecutive pairwise registration
  - Compose registration results



T. Vercauteren et al. Med Image Anal. 10:5, 2006

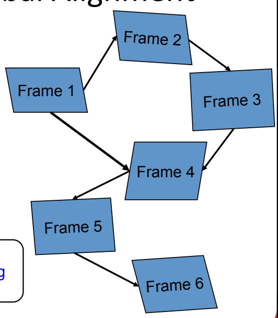
Consistent Global Alignment

- Initialization
  - Consecutive pairwise registration
  - Compose registration results
  - Motion estimation and distortion compensation



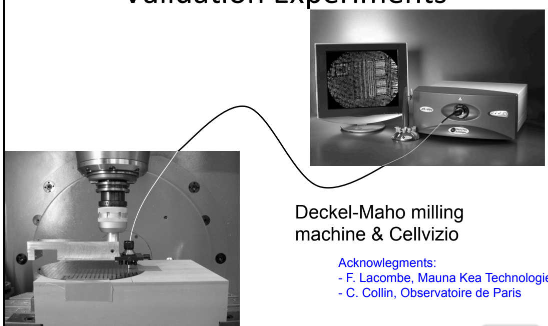
Consistent Global Alignment

- Initialization
  - Consecutive pairwise registration
  - Compose registration results
  - Motion estimation and distortion compensation
- From local registration to global alignment
  - Add *most informative* pairwise registration



Most constraining pair of overlapping frames

Validation Experiments

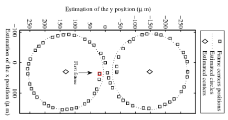


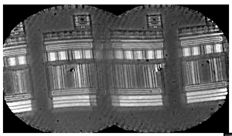
Deckel-Maho milling machine & Cellvizio

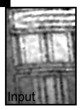
Acknowlegments:
- F. Lacombe, Mauna Kea Technologies
- C. Collin, Observatoire de Paris

Validation: Initial vs Final Results

Initial recursive mosaic

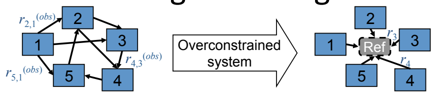






Mosaic

Global Alignment Algorithm

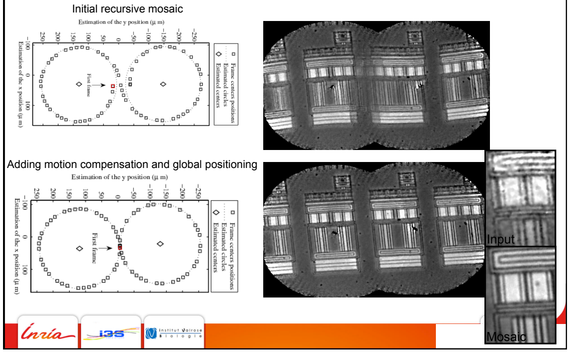


- System
  - $r_{j,i}^{(obs)}$: Pairwise registration results
  - r_i: Global frame-to-reference transformations
  - Ideally: $r_{j,i}^{(obs)} = r_j^{(-1)} \circ r_i$
- Registration errors ⇒ Least square approach
- Lie group structure
  - Cost function: $\Sigma_{(i,j)} \text{dist}(r_{j,i}^{(obs)}, r_j^{(-1)} \circ r_i)^2$
  - $\text{dist}(r, s) = \text{dist}(r^{(-1)} \circ s, Id) = \| \log_{Id}(r^{(-1)} \circ s) \|$
  - Optimization routine with intrinsic update rule

Validation: Initial vs Final Results

Initial recursive mosaic

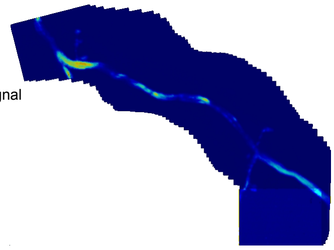
Adding motion compensation and global positioning



Final mosaic

High deformations
- Interaction probe/material

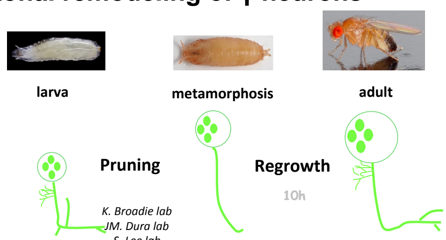
Noisy and temporal varying signal
- Reconstruction
- Segmentation



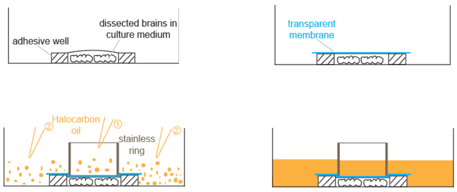
Motion compensation in two-photon microscopy temporal series

Caroline Medioni, Florence Besse (IBV)
Xavier Descombes Grégoire Malandain (INRIA)

Biological context: Axonal remodeling of γ neurons

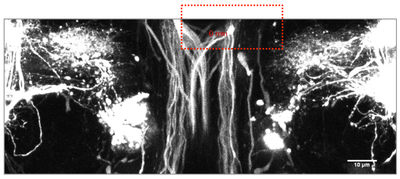


2-photon imaging: regrowth of γ neuron axons

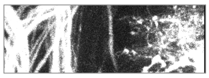


"Live-imaging of axonal transport in Drosophila pupal brains"
Medioni et al., April 2015, Nature Protocols

2-photon imaging: regrowth of γ neuron axons

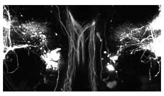


γ axons stained with GFP



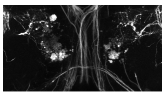
γ axon regrowth has been followed in real time for more than 10h

2-photon imaging: regrowth of γ neuron axons



MIP view of timepoint #1

…



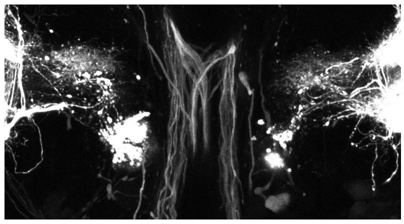
MIP view of timepoint #170

Time series of 3D volumes,

- 1012 x 548 pixels of 0.13 µm,
- 16 slices of thickness of 0.8 µm,
- 170 time points with step of 5 min (more than 14 hours of imaging)

Visual inspection demonstrate a 3D displacement (in plane motion as well as along z)

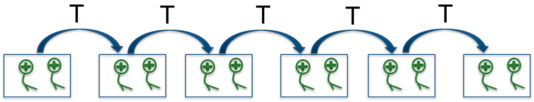
2-photon imaging: regrowth of γ neuron axons



MIP view

Drift correction: to compensate for a global motion (relative motion of imaged material w.r.t. acquisition device) while preserving local differences

Introduction



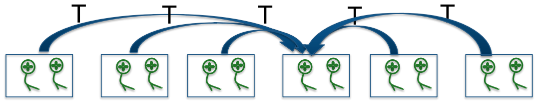
Naive solution #1

- Transformations T between I(t) and I(t+dt)
- Pairwise transformations w.r.t. a reference are computed by compounding transformations

Pros:

- deals with "small" transformations

Introduction



Naive solution #2

- Transformations T between I(t) and a reference

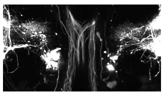
Pros:

- Does not require transformation compounding

Cons

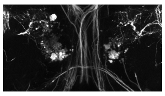
- Possible bias w.r.t. the reference
- Has to deal with (possibly) large transformations

Example



MIP view of timepoint #1

…

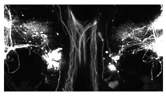


MIP view of timepoint #170

Solution #1 (co-registration of successive volumes)

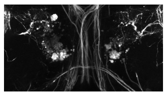
- able to recover the in-plane motion
- unable to recover the z motion (too small w.r.t. the slice thickness)

Example



MIP view of timepoint #1

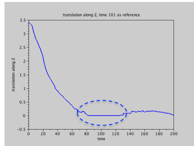
…



MIP view of timepoint #170

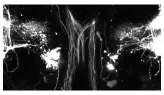
Solution #2 (registration w.r.t. a reference)

- able to recover the z motion
- except near the reference



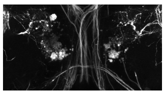
z translation component

Example



MIP view of timepoint #1

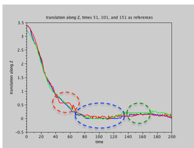
…



MIP view of timepoint #170

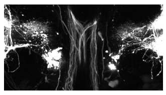
Solution #2 (registration w.r.t. a reference)

- able to recover the z motion
- except near the reference
- different references:
  same behavior



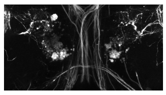
z translation component

Example



MIP view of timepoint #1

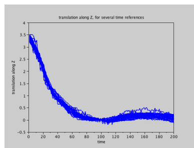
…



MIP view of timepoint #170

Solution #2 (registration w.r.t. a reference)

- able to recover the z motion
- except near the reference
- different references:
  same behavior



z translation component

Proposed solution

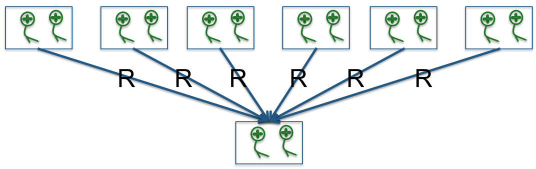
Multiple transformations strategy

- image stitching
- mosaicking with endomicroscopy
  [Vercauteren, Media, 2006]
- super-resolution microscopy
  [Wang, Opt Express, 2014]

Idea:

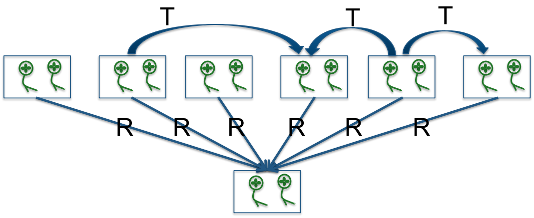
- compute all/several transformations $T_{i \leftarrow j}$ from image I_j to image I_i
- use redundancy for a better estimation

Problem definition



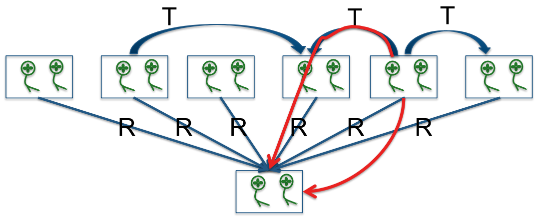
- Problem: to find the optimal transformations $\hat{R}_i$ where $R_i = T_{i \leftarrow ref}$ denotes the transformation from a reference to image I_i

Problem definition



- Observations: transformations $T_{i \leftarrow j}$ from image I_j to image I_i

Problem definition



$$R_i = T_{i \leftarrow j} \circ R_j$$

Problem definition

- Problem: to find the optimal transformations $\hat{R}_i$ where $R_i = T_{i \leftarrow ref}$ denotes the transformation from a reference to image I_i
- Observations: transformations $T_{i \leftarrow j}$ from image I_j to image I_i
- $R_i = T_{i \leftarrow j} \circ R_j$
- Least squares formulation

$$\left\{\hat{R}_i\right\} = \arg\min_{\{R_i\}} \sum_{i,j} \left\| R_i - T_{i \leftarrow j} \circ R_j \right\|^2 \text{ with } R_i = T_{i \leftarrow ref}$$

Problem resolution

- No close form solution for the general problem (except for translations)
- Iterative solution

Given initial values $R_1^{(0)}, \ldots, R_n^{(0)}$
loop
for i=1…n **do**
$R_i^{(t+1)} = mean\left(\left\{T_{i \leftarrow j} \circ R_j^{(t)}\right\}_{(j)}\right)$
done
$t \leftarrow t+1$
endloop

Problem resolution

$$R_i^{(t+1)} = mean\left(\left\{T_{i \leftarrow j} \circ R_j^{(t)}\right\}_{(j)}\right)$$

Requires to compute average of transformations:
- translations: straightforward
- rotations [Hartley, IJCV, 2012]
- affine transformations: straightforward
- non-linear transformations (deformations) [Vercauteren, Media, 2006]

Again, iterative method
- if outliers, robust estimation (least trimmed squares)

We want to compensate for global motion and growth: affine transformation

Implementation details / questions

How many $T_{i \leftarrow j}$?
- *j* every 5 images: $j \in \{1, 6, \ldots\}$
- *i* in interval of length 2N+1, centred at *j*
  $i \in \{j-N, j-N+1, \ldots, j-1, j+1, \ldots, j+N\}$

How many iterations?
Enforce regularity of $\hat{R}_i$?
- low pass filtering of transformations

Robust estimation of transformation means?

Assessment
- visual assessment
- quantitative assessment

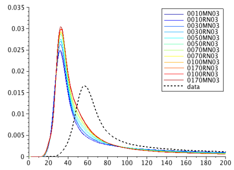
Quantitative assessment

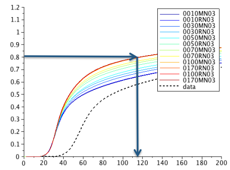
If the drift compensation is successful, the value of a point M does not vary over time

- Study of standard deviation of $I_i \circ \hat{R}_i(M)$ over *i*

quality measure = the s.d. associated to a centile (say 0.8) of the s.d. cumulated distribution

Quantitative assessment


Histogram

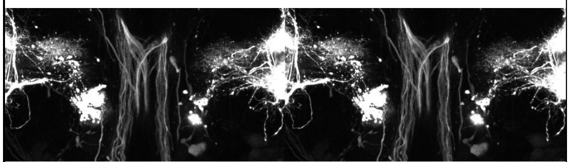

Cumulative histogram

Less blur (over time) implies smaller standard deviations values: use a centile (say 0.8) of the cumulative histogram as quality measure.

Some trends

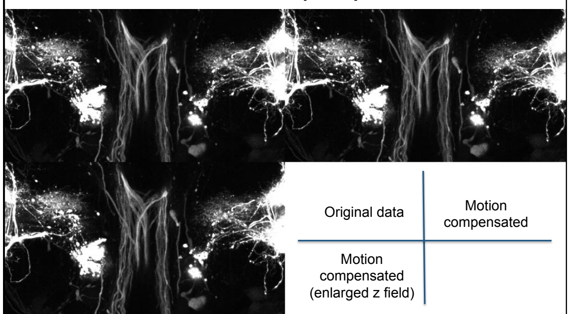
- The more observations (i.e. $T_{i \leftarrow j}$), the better
- The more iterations (of the optimization procedure), the better (20 is enough)
- Robust estimation yields a little bit better results (you won't visually notice the difference)
- Transformation smoothing deteriorates a little bit the results (you won't visually notice the difference)

Visual assessment (MIP)



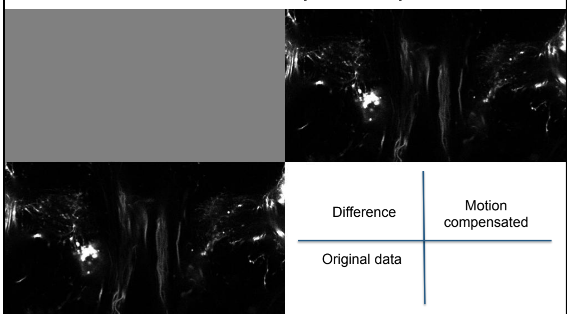
Original data	Motion compensated

Visual assessment (MIP)



Original data	Motion compensated
Motion compensated (enlarged z field)	

Visual assessment (section)



Difference	Motion compensated
Original data	

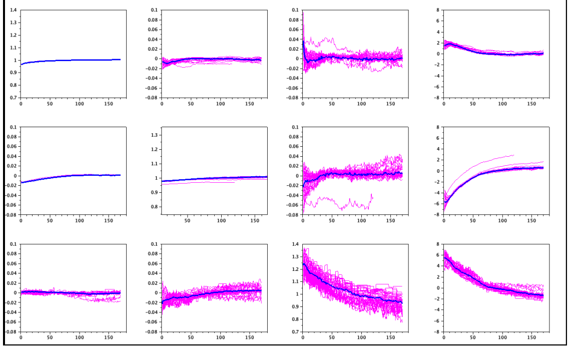
Affine transformation

Affine transformation in homogeneous coordinates

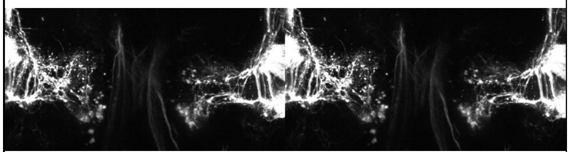
$$\begin{pmatrix} x' \\ y' \\ z' \\ 1 \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} & a_{13} & t_x \\ a_{21} & a_{22} & a_{23} & t_y \\ a_{31} & a_{32} & a_{33} & t_z \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}$$

Scaling factors Shearing factors Translation

Estimated affine transformation

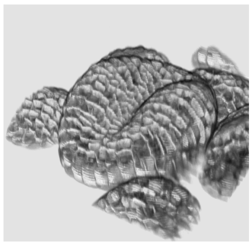


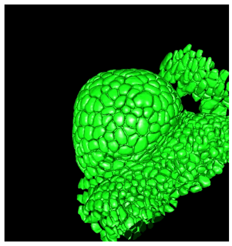
Visual assessment (MIP)



Original data | Motion compensated

Development in plants



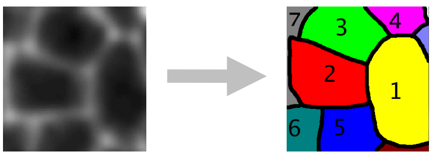


From confocal images to a fancy movie

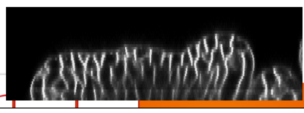
Fernandez et al., *Nature Methods*, 7(7), 2010

Development in plants

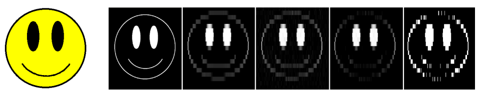
Cell segmentation: watershed, …



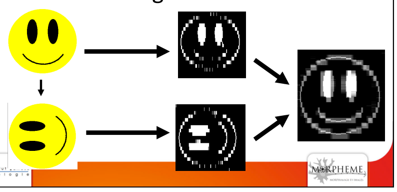
but …



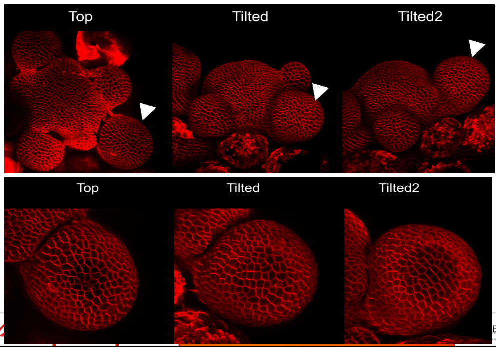
Multi-angles imaging



- principle: take several images and fuse them



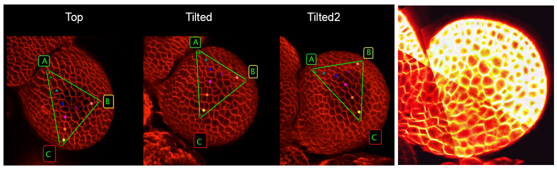
Multi-angles imaging



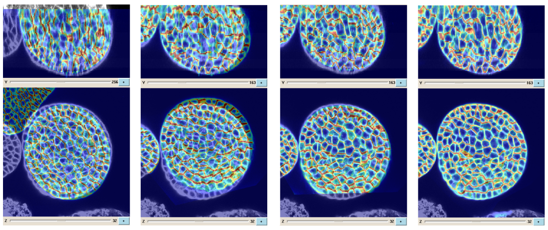
Multi-angles imaging

Successive registration

1. Manual (point pairing) rigid registration
2. Automated rigid registration
3. Automated deformable registration



Multi-angles imaging



Before matching | manual matching | automated rigid matching | automated non-linear matching

Multi-angles imaging

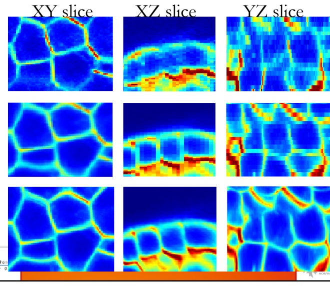
1. Image averaging: improve SNR
2. Reconstruction with a smaller slice thickness

XY slice | XZ slice | YZ slice

Original image

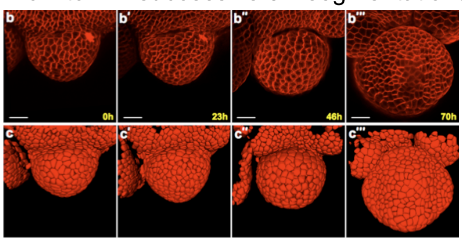
Fusion at same slice thickness

Fusion at smaller slice thickness



Development in plants

- How to link successive 3D segmentations?



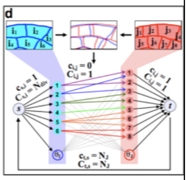
Development in plants

- How to link successive 3D segmentations ?
- Changes to handle:
- geometrical: deformations
- topological: cell division
- solution: alternate between

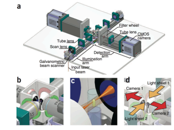
1. cell lineage tracking (topology)
2. deformation estimation (geometry)

Development in plants

1. (partial) pairing estimation: graph-based approach
2. deformation estimation: non-linear registration with pairings as prior



Embryogenesis in ascidian



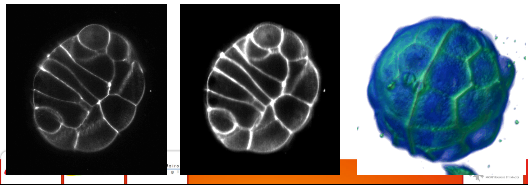
Krzic et al. (2012), *Nature Methods*, 9(7):730-733.

SPIM acquisition:

- 2 x 2 images per time point

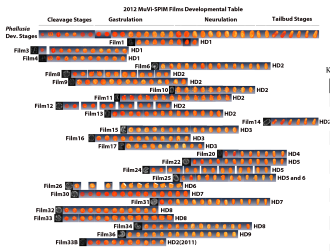
1. fusion at each time point
2. registration of successive time points

P. Lemaire U.-M. Fiuza (CRBM), L. Guignard, C. Godin (Virtual Plants, INRIA), L. Hufnagel, U. Krzic (EMBL – Heidelberg)

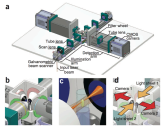


Embryogenesis in ascidian

A certain number of acquisition :



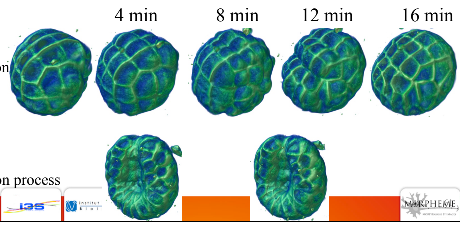
Acquired by U.-M. Fiuza at the Hufnagel lab EMBL


Krzic et al. (2012), *Nature Methods*, 9(7):730-733.

	Phallusia mammillata
# Acquisition	90 – 180
Time between 2 acquisitions	1 or 2 minutes
# Time laps	2h to 3h
Resolution	1200 x 1200 x 200
Bit depth	16 bits
# channels	1
Single image size	~ 520 Mo
# Angles	4
Full view size	~ 2 Go
Full film size	From ~ 180 Go to 360 Go
# film planned	~ 50
Total size	From 5 To to 20 To

Morphogenetic milestones as 4D landmarks

- *Phallusia m.* :
  - Stereotypical development
  - Punctual and local deformation such as cell division or the invagination process

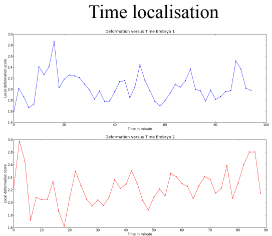


Morphogenetic milestones as 4D landmarks

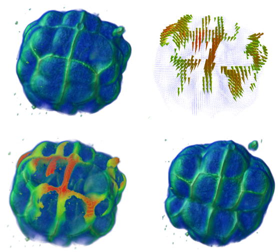
- Computation of non-linear registration between t and t+∂t
- Norm of the vector fields
- localization in time
  - Moment of high local deformation
  - Top 10% over lowest 90%
- localization in space
  - Largest connected component of the top 10%

Morphogenetic milestones as 4D landmarks

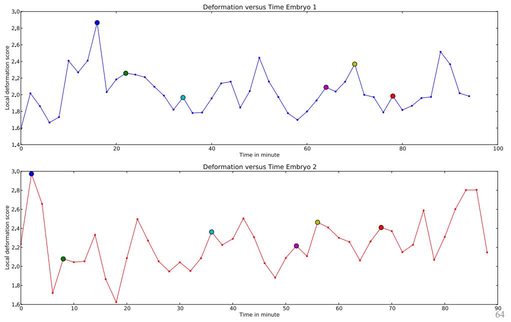
Time localisation



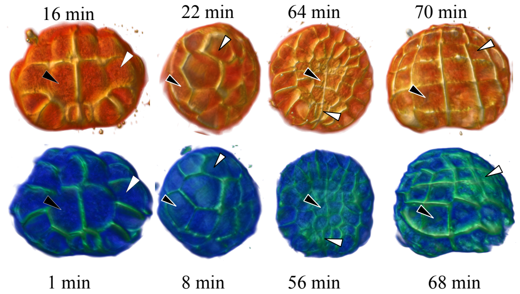
Spatial localisation



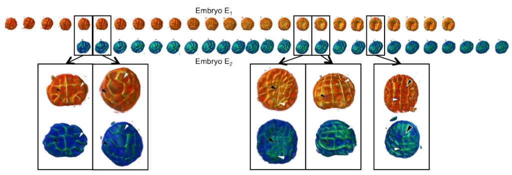
Morphogenetic milestones as 4D landmarks: registration in time



Morphogenetic milestones as 4D landmarks: registration in space



Morphogenetic milestones as 4D landmarks: 4D registration



L. Guignard et al., ISBI 2014