FRAMEWORK FOR NEUROSPHERE GROWTH MODELLING UNDER PHASE CONTRAST MICROSCOPE

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Mars, 10th 2014

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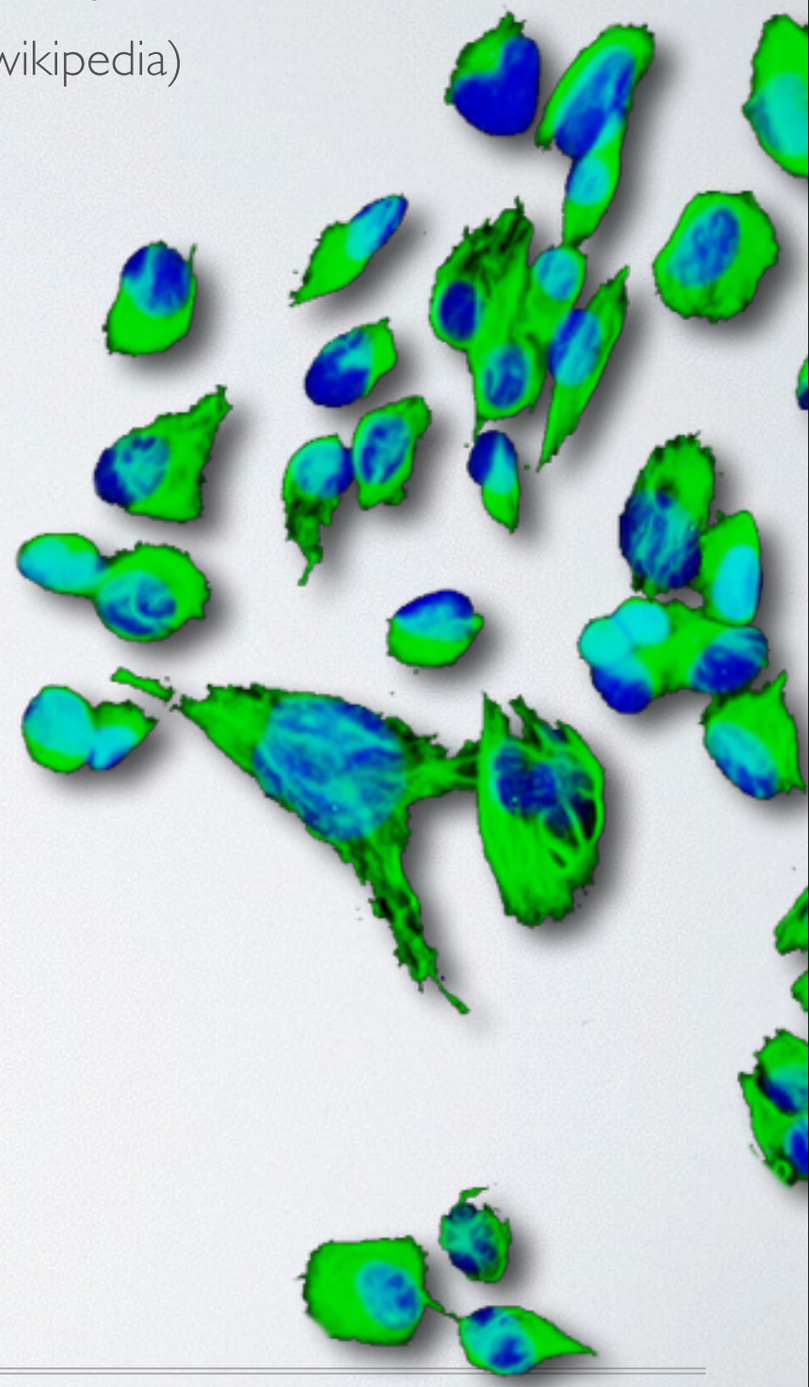
NEURAL STEM CELL

- "Undifferentiated biological cell with the following properties: self-renewal, multi-potency, and tissue (re)generation" (wikipedia)



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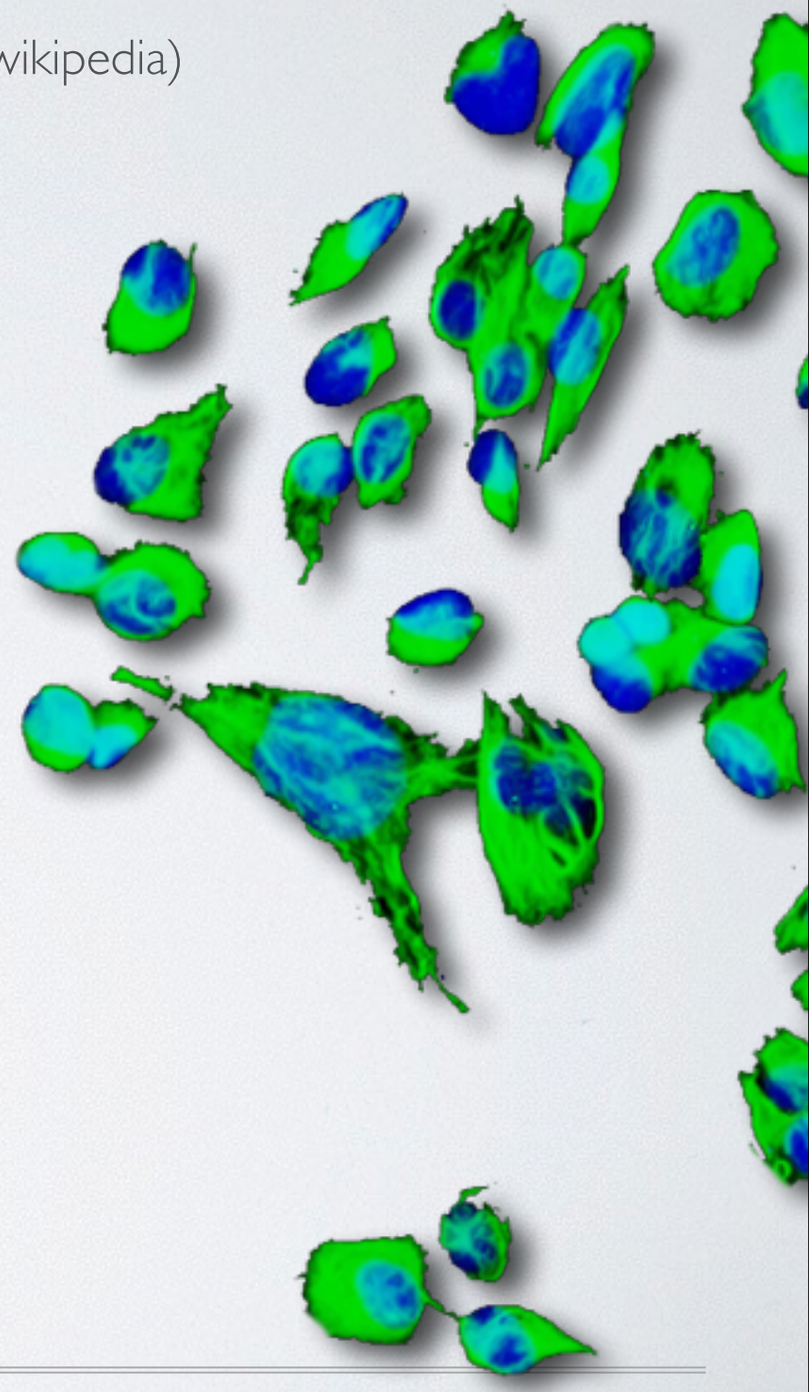

- Neural stem cell history:
  - first described in 1989 (Temple, 89)
  - first isolated in 1992 (Reynolds and Weiss, 92)

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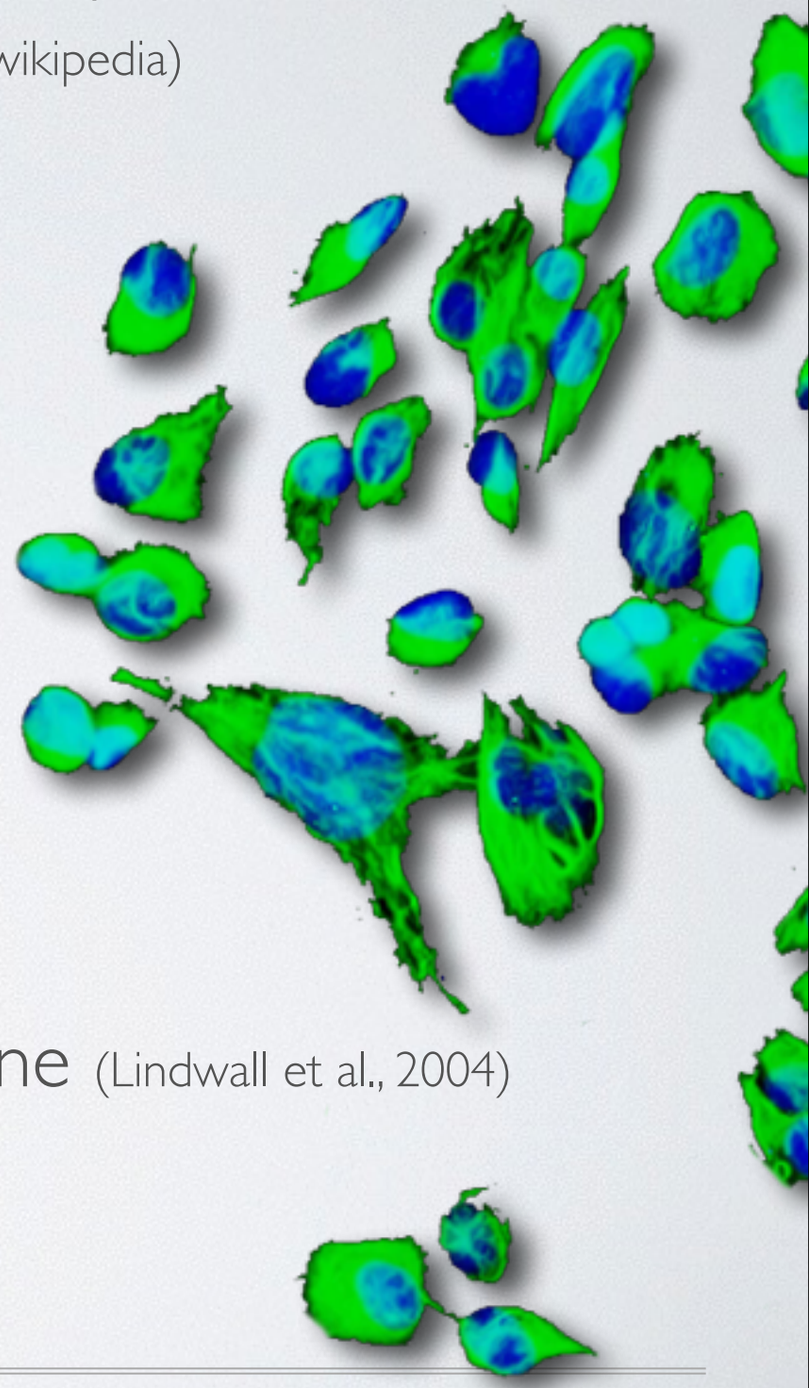
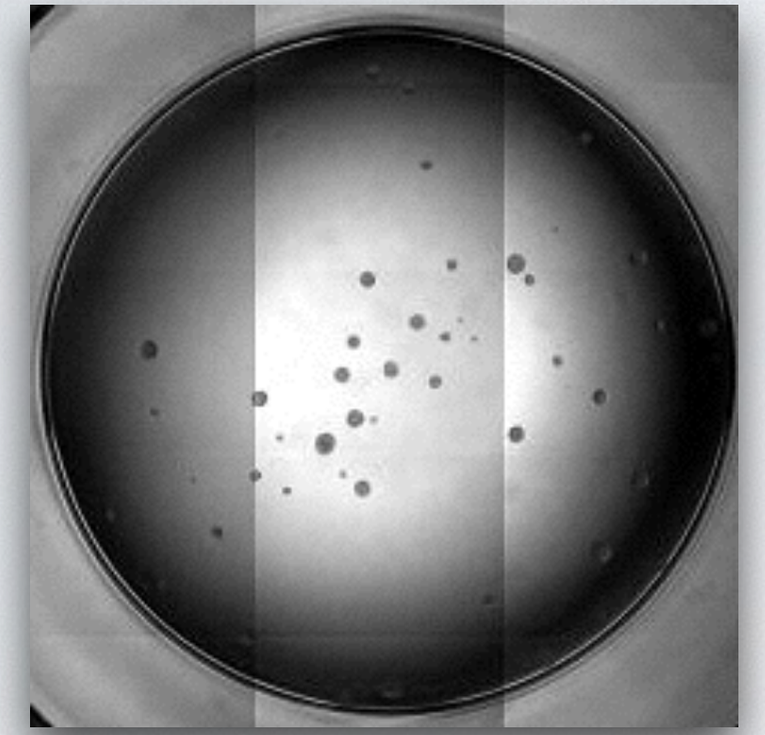


- Neural stem cell history:
  - first described in 1989 (Temple, 89)
  - first isolated in 1992 (Reynolds and Weiss, 92)

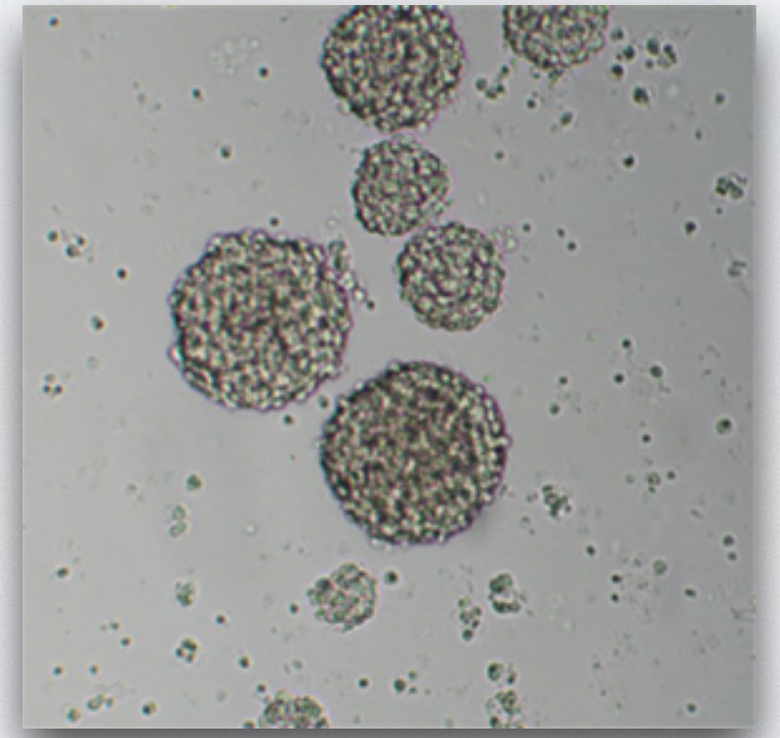
- Clinical application of NSC for regenerative medicine (Lindwall et al., 2004)

NEURAL STEM CELL

- Free-floating spherical cluster of neural stem cells and progenitor stem cells

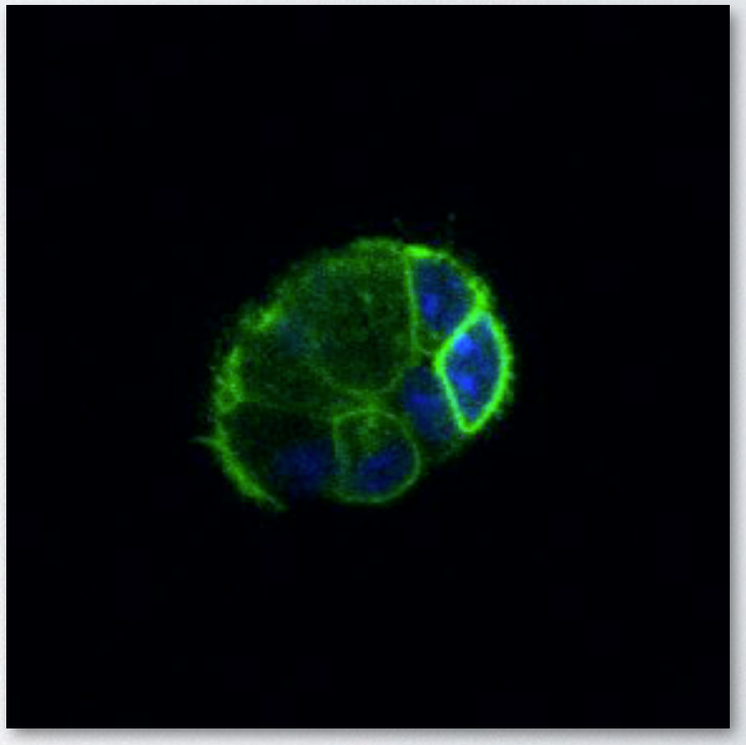


x4



x6

confocal



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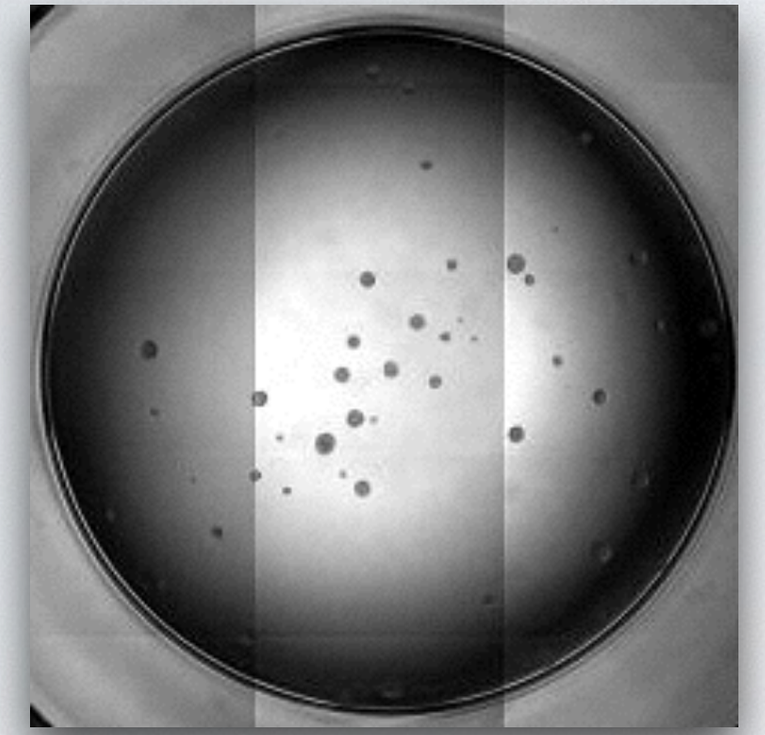

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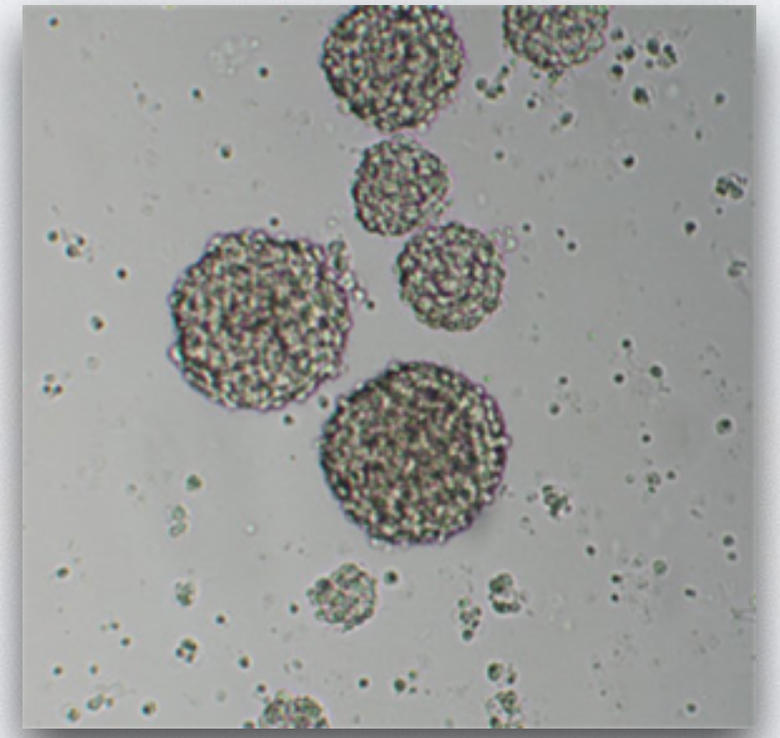

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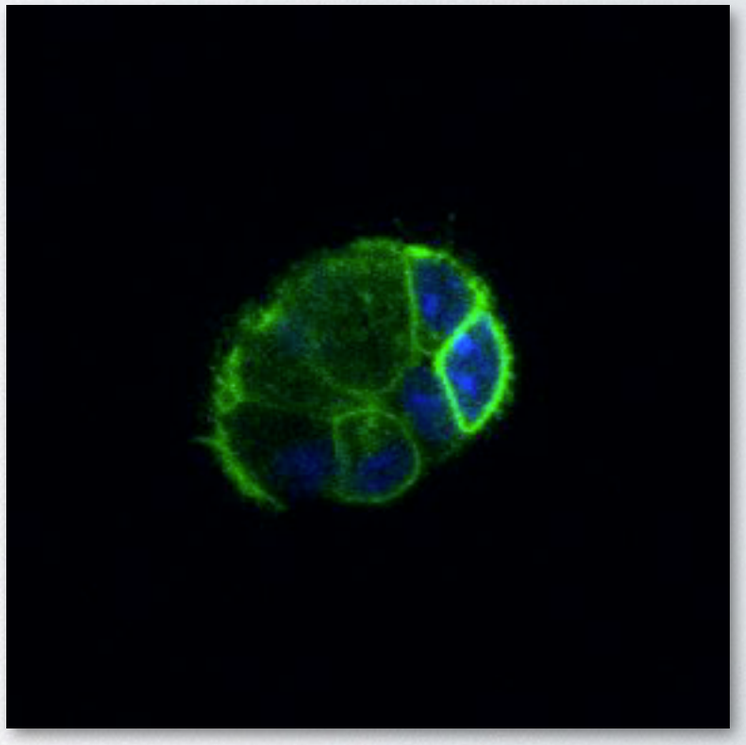

NEURAL STEM CELL

- Neurosphere Formation Assay (Reynolds and Weiss, 92)

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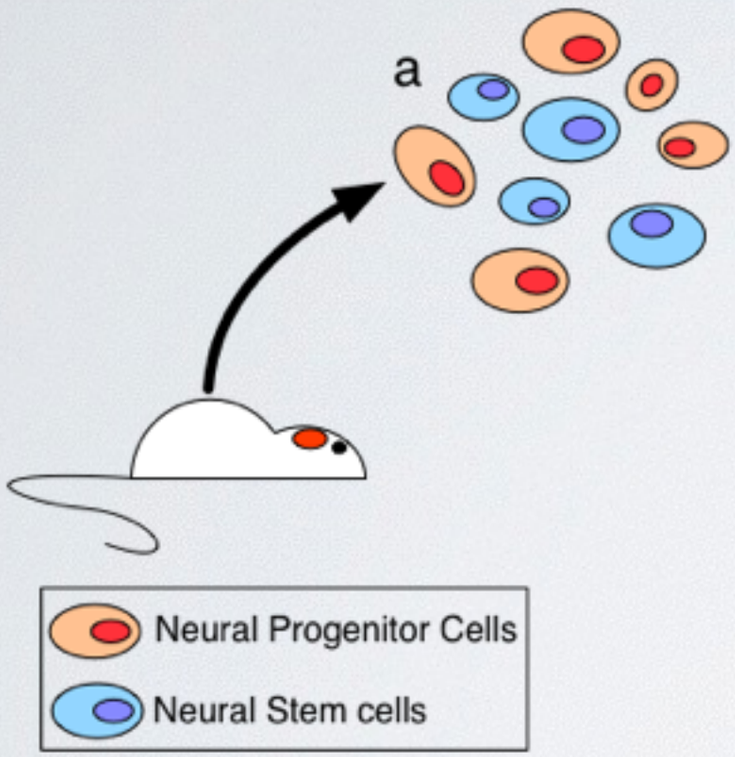

a - cell extraction from mouse brain

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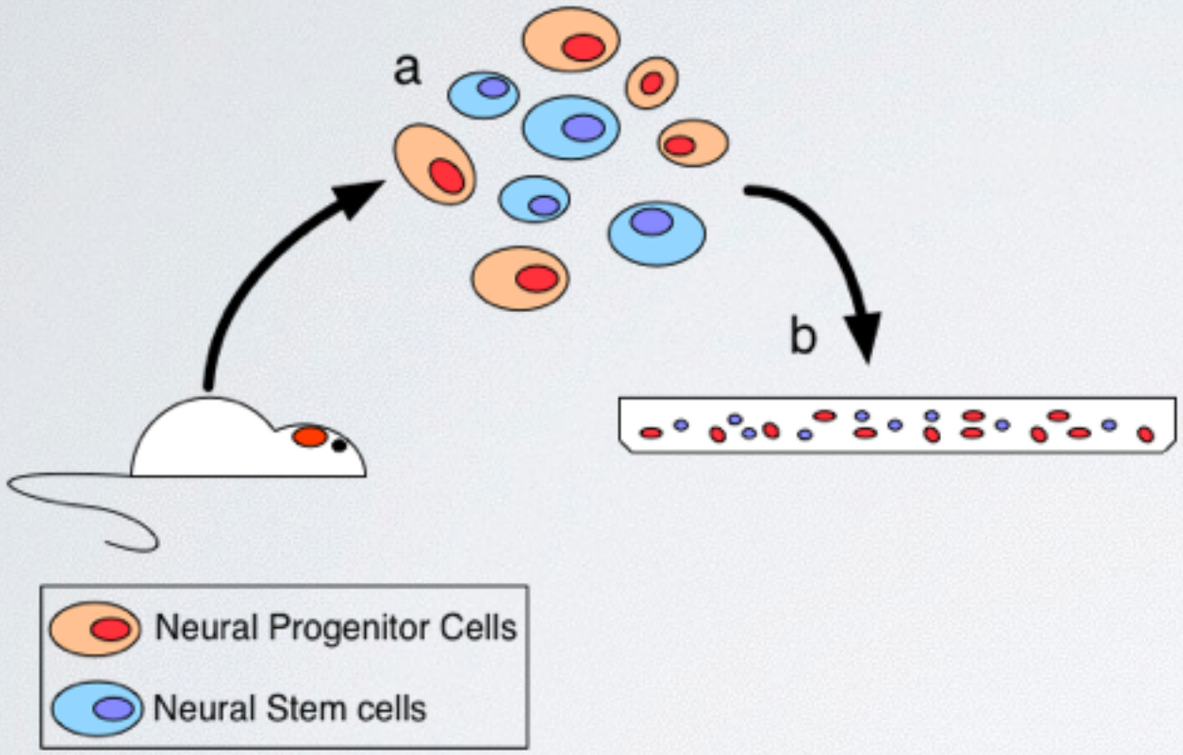

b - floating culture in serum-free solution with growth factor

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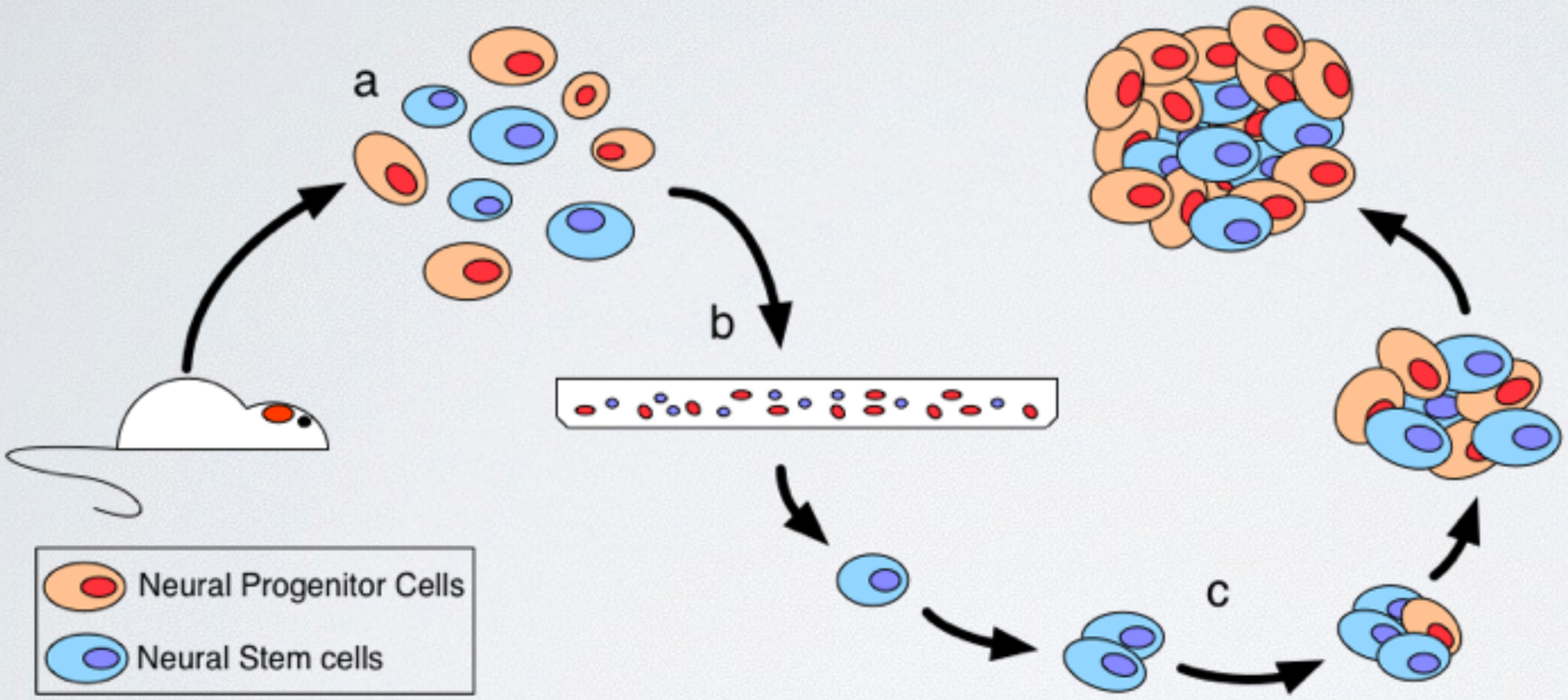

c - cell proliferation under incubation conditions (controlled T°, CO_2, *etc.*)

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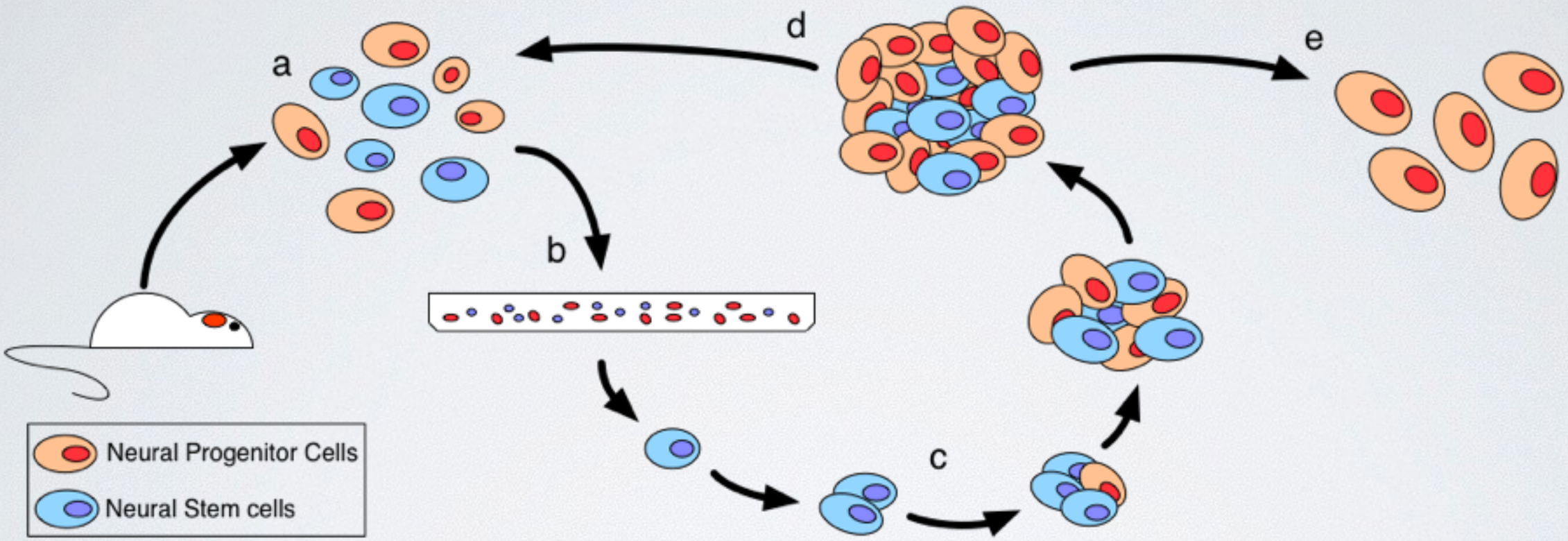

d - new generation from cultured cells
e - introduction of differentiation factor into the culture

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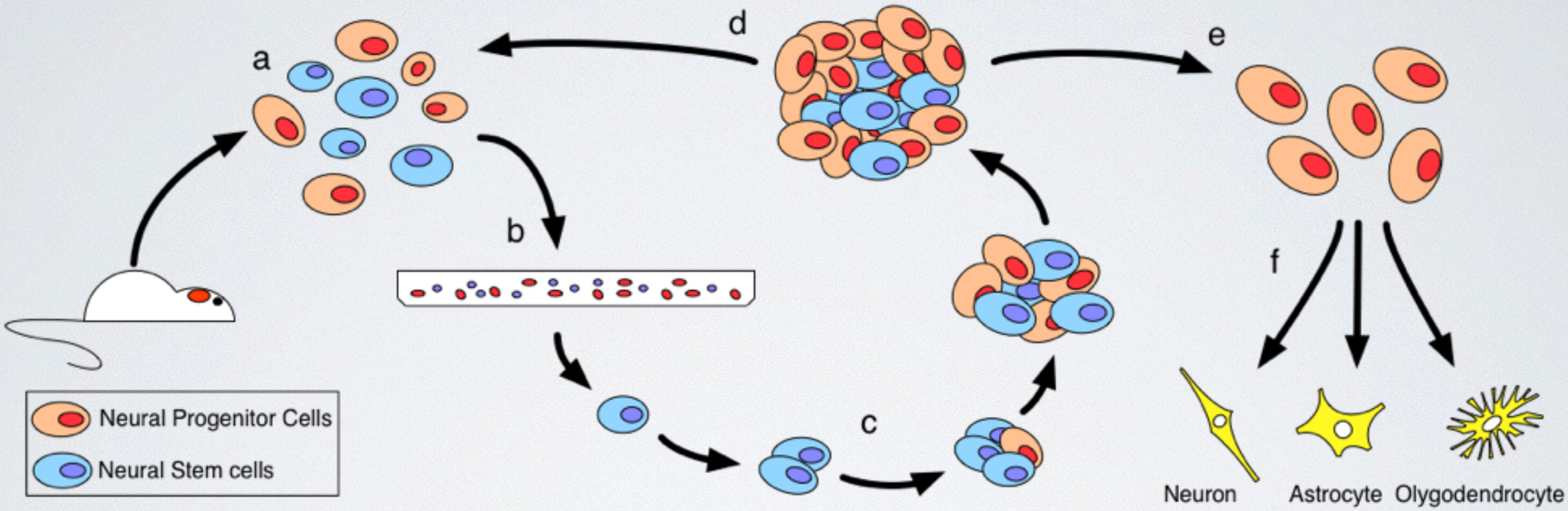
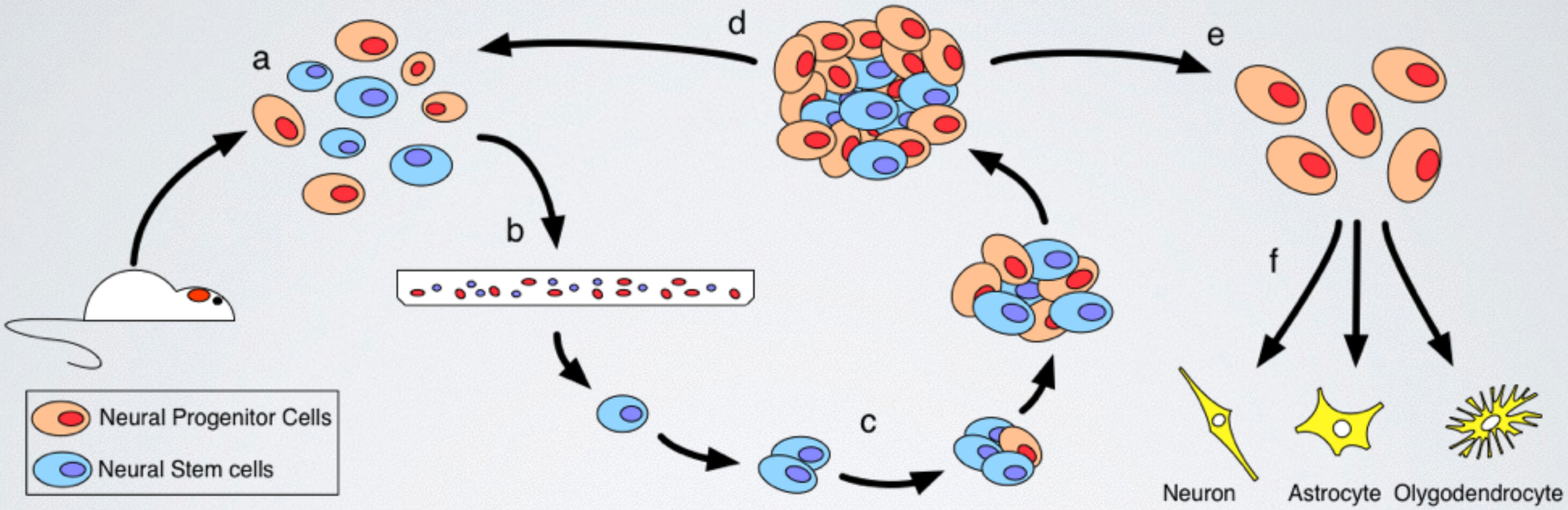


f - differentiation of the cells into specialised brain cells

NEURAL STEM CELL



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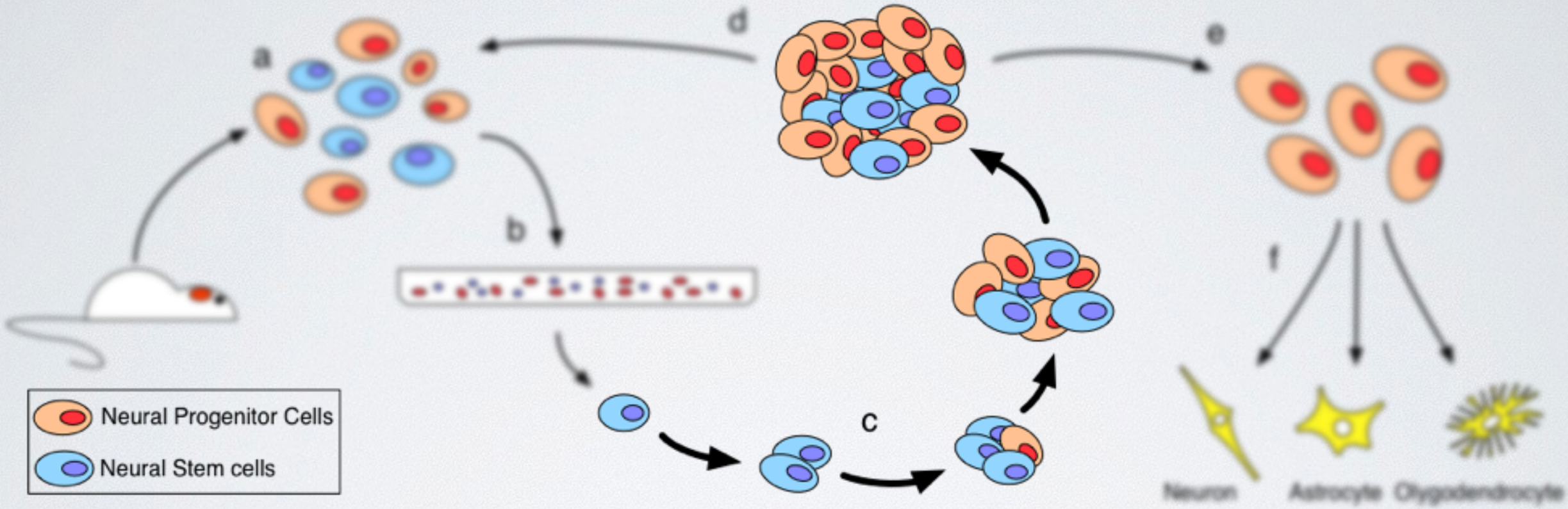

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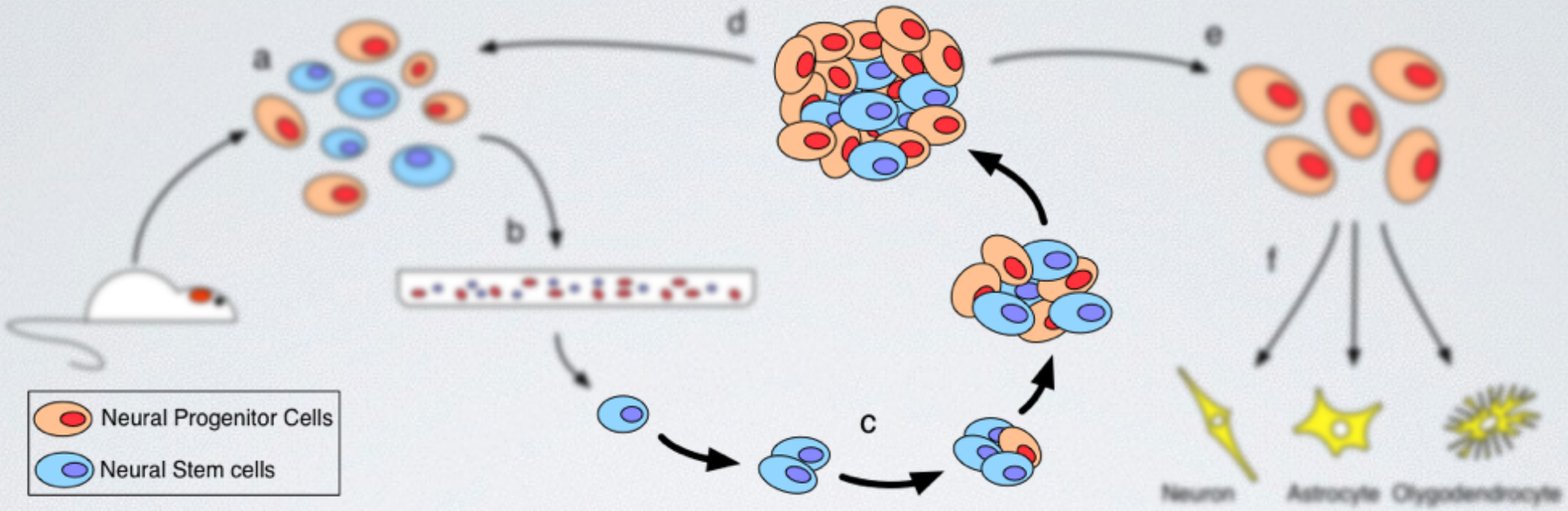

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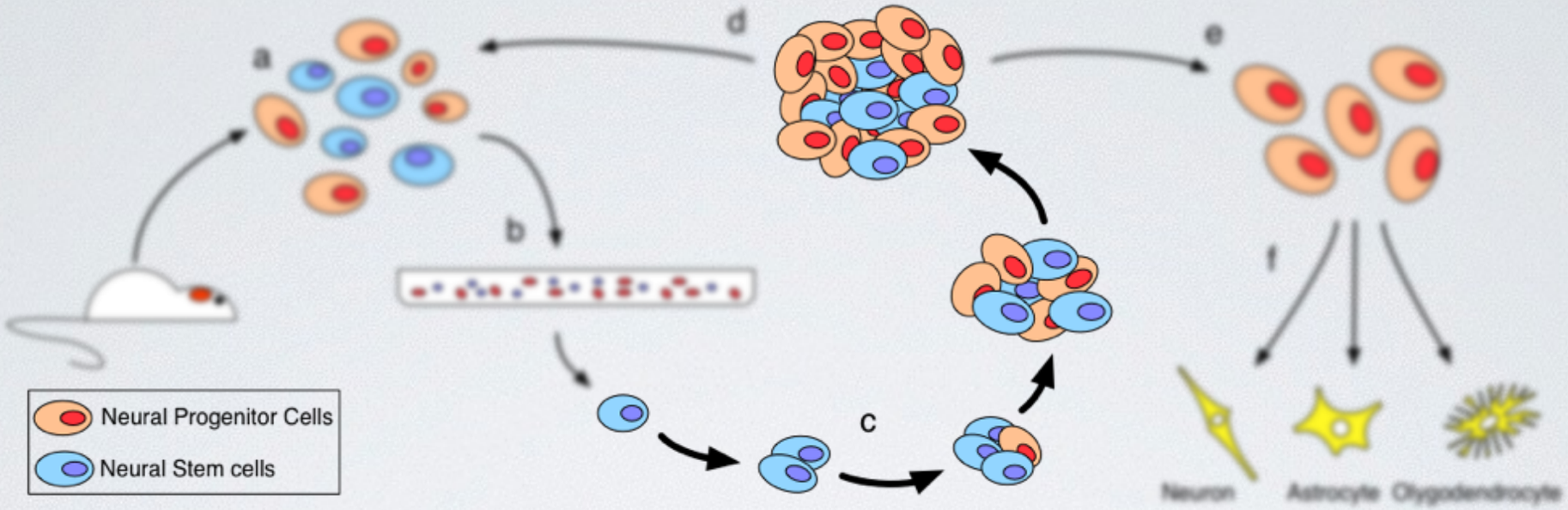
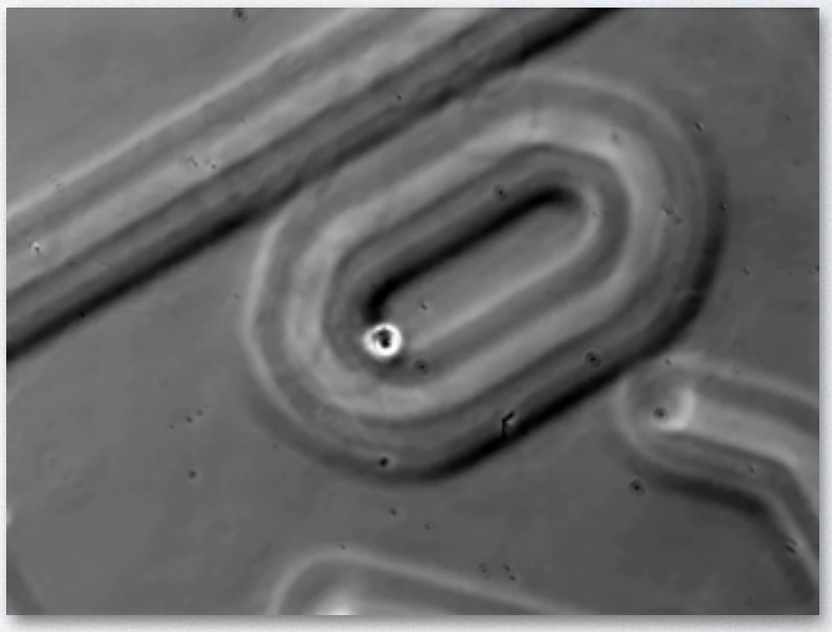


7 days observation at x4

5 days observation at x10



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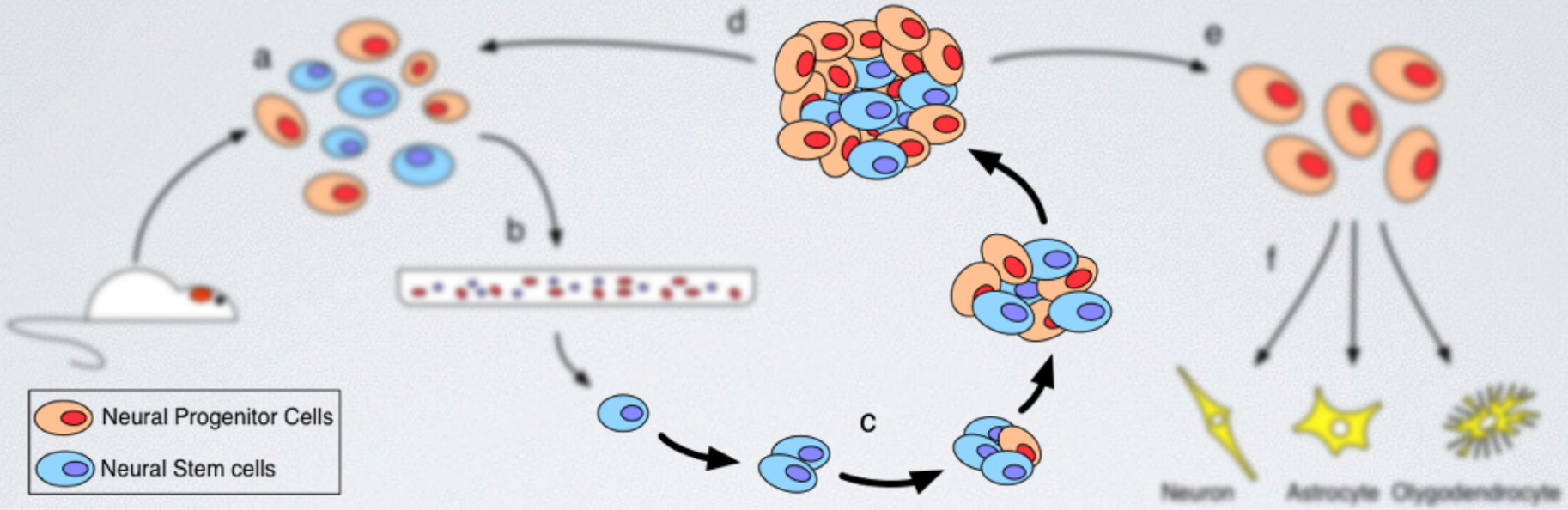

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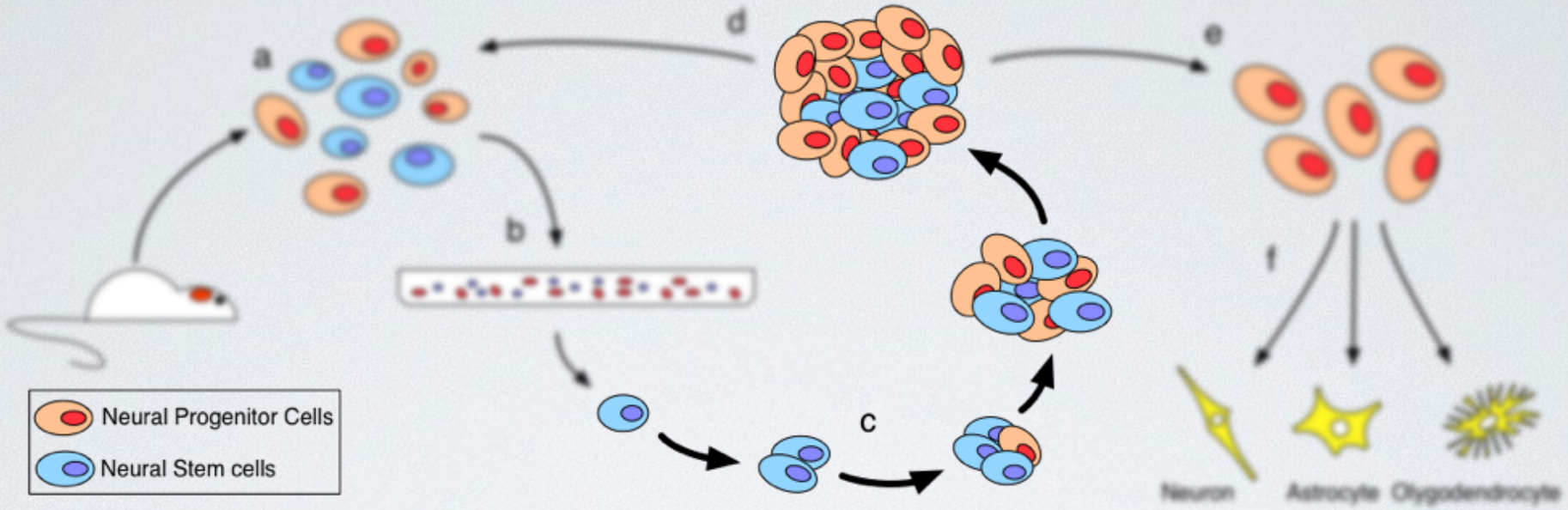

- Enhanced monitoring of the proliferation sequence of the NFA

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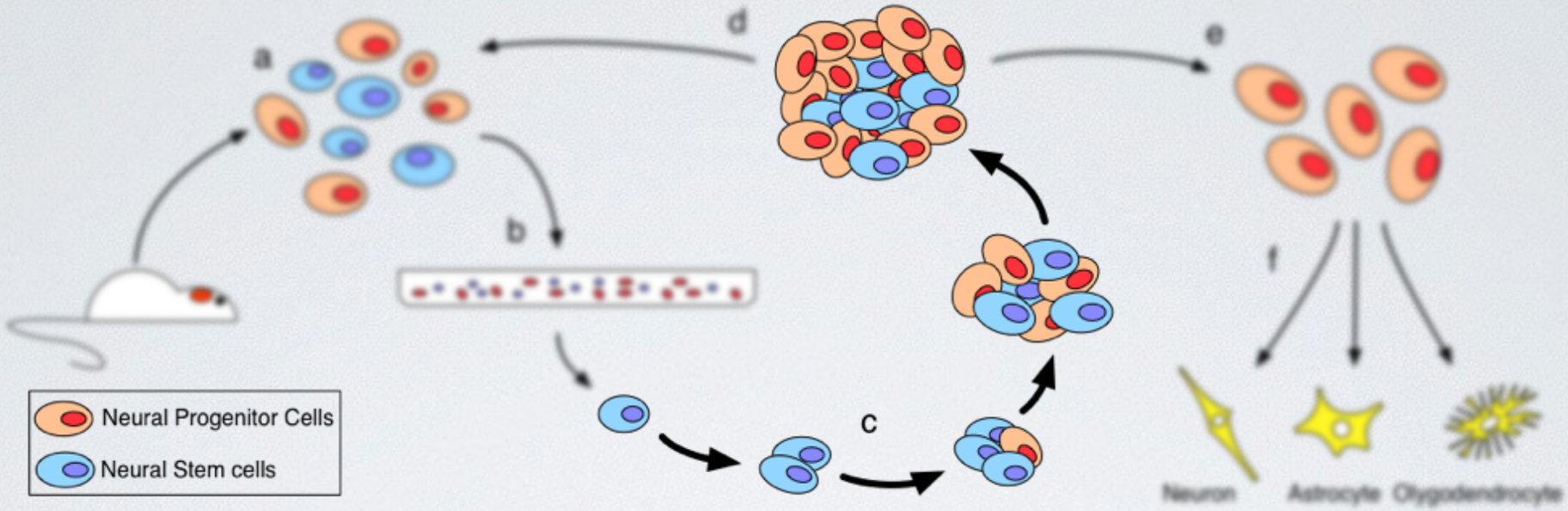

- Enhanced monitoring of the proliferation sequence of the NFA
- Gather possible relevant data on cells configuration in the sphere

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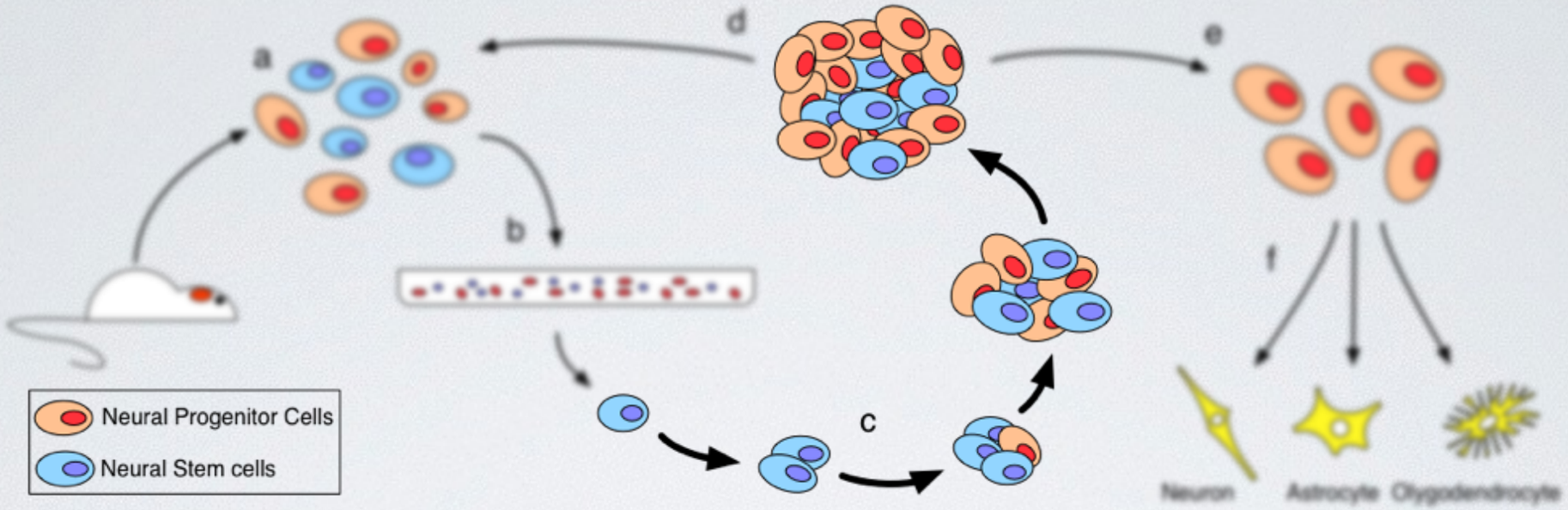
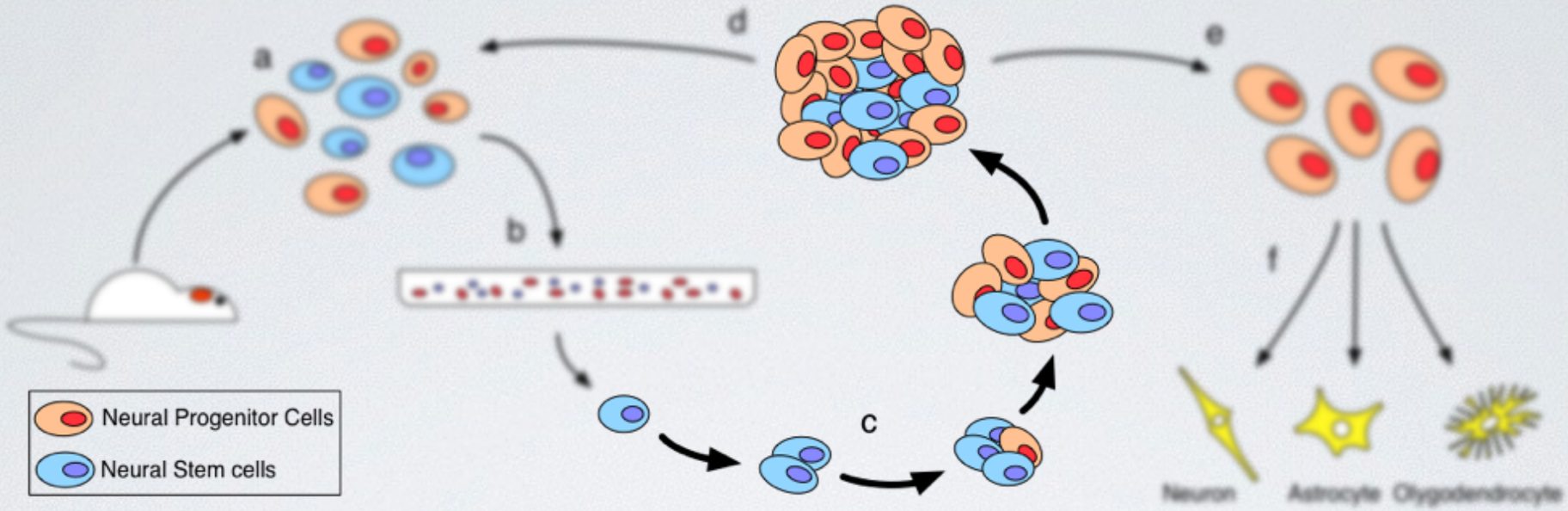


- Enhanced monitoring of the proliferation sequence of the NFA
- Gather possible relevant data on cells configuration in the sphere
- Enhanced observation of drug effects over cells proliferation

NEURAL STEM CELL



Improve **knowledge** and **control** on neural stem cell for clinical application

FRAMEWORK

- Determine cells configuration over time of the neurosphere growth

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- Limitations of the experiments

  - phase contrast microscopy
  - no bio-marker
  - low temporal resolution (15 $^{min}/_{img}$)
  - dimensional difference between 3-D culture and 2-D modality

FRAMEWORK

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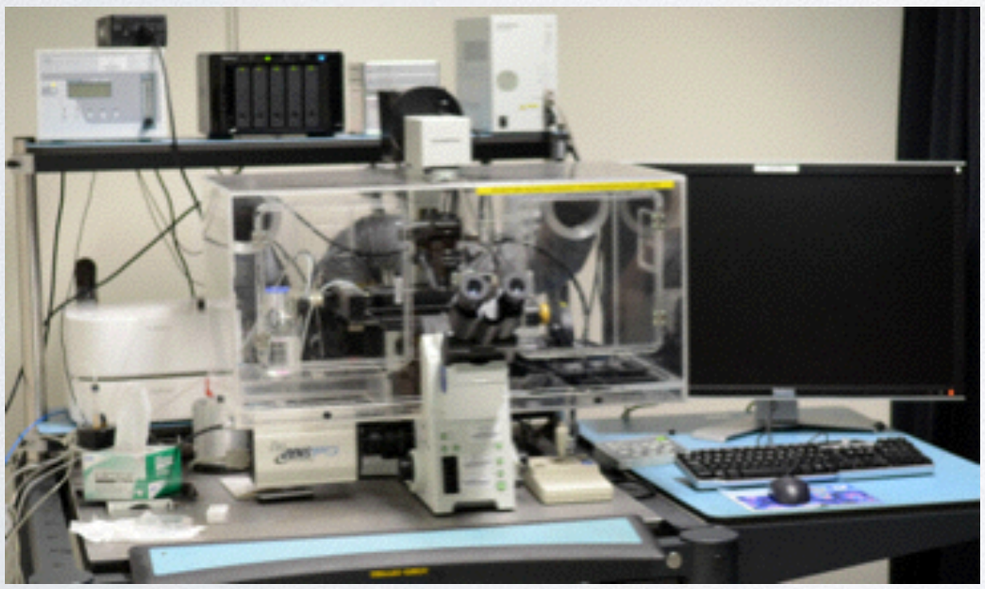
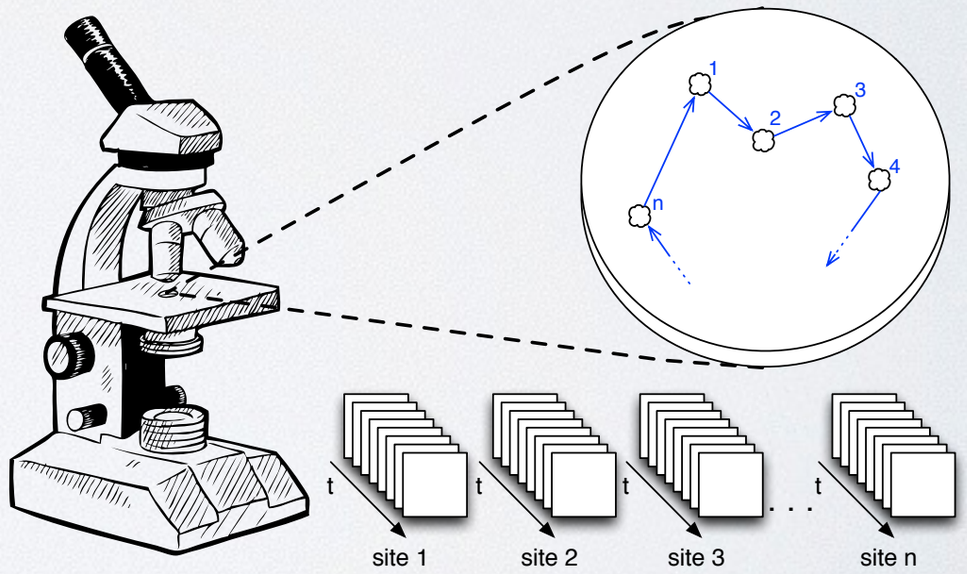
Microscope Image





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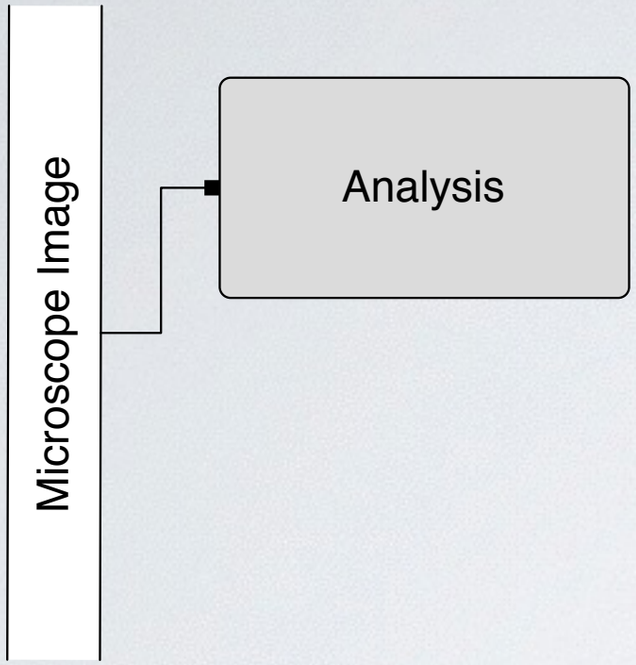
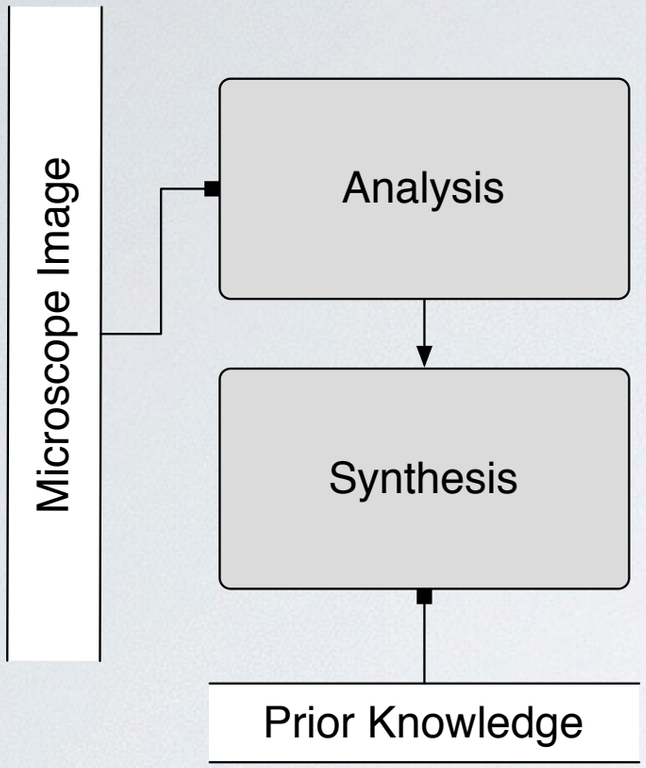


Analysis Module: Extraction of relevant information from image

- neurosphere detection
- image restoration
- cell detection

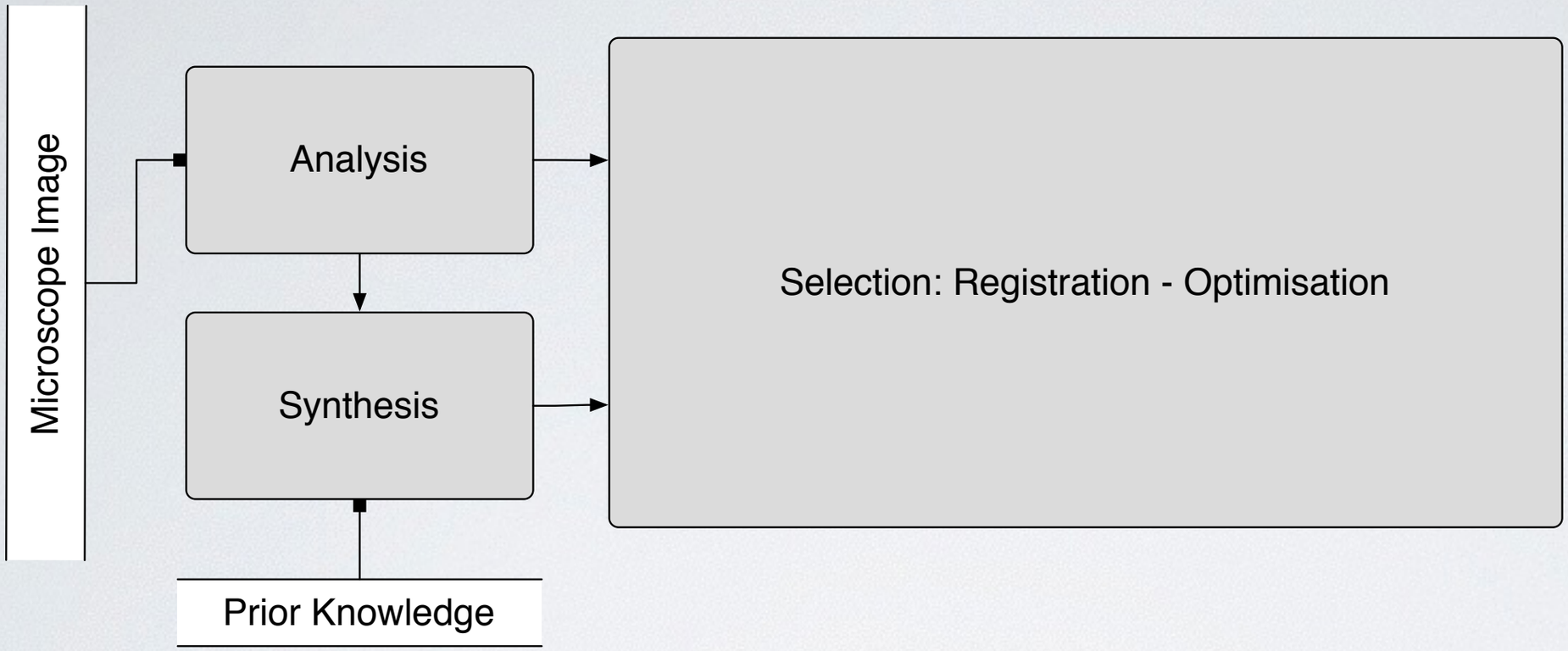
FRAMEWORK



Synthesis Module: Generation of multiple possible cell configuration

- prior knowledge
- information from analysis module

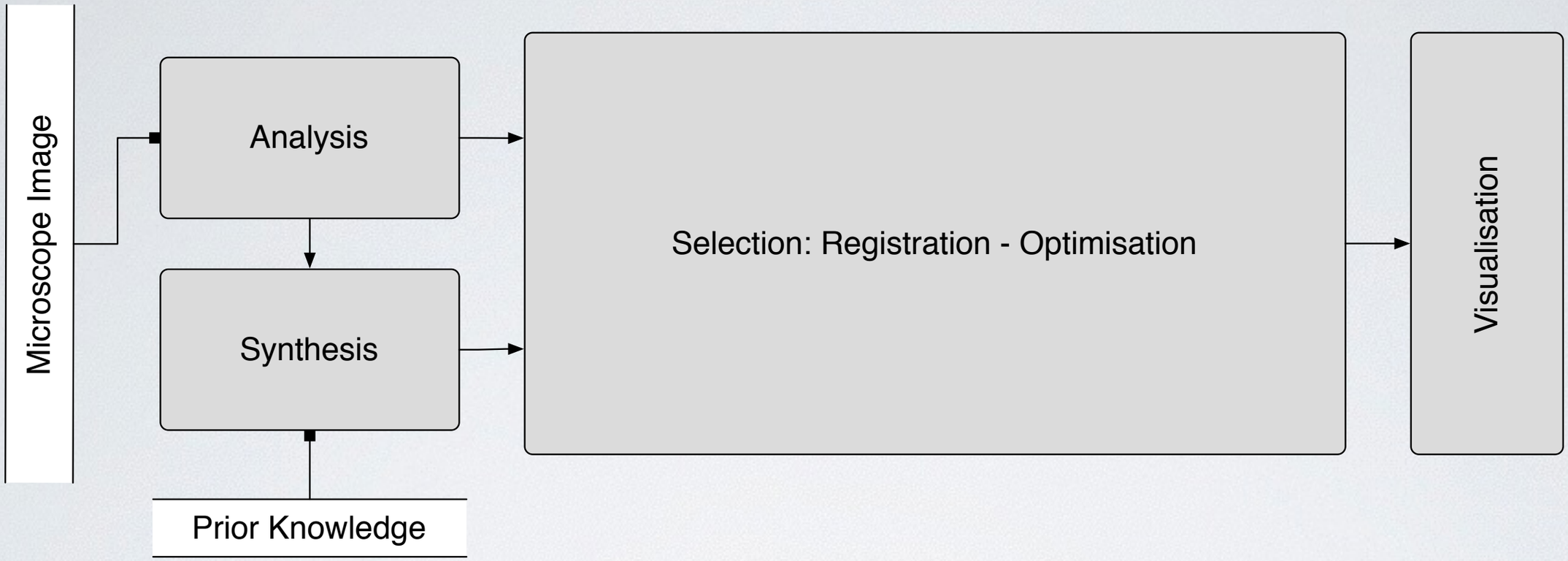
FRAMEWORK



Selection Module: Rate and rank all the models based on the image

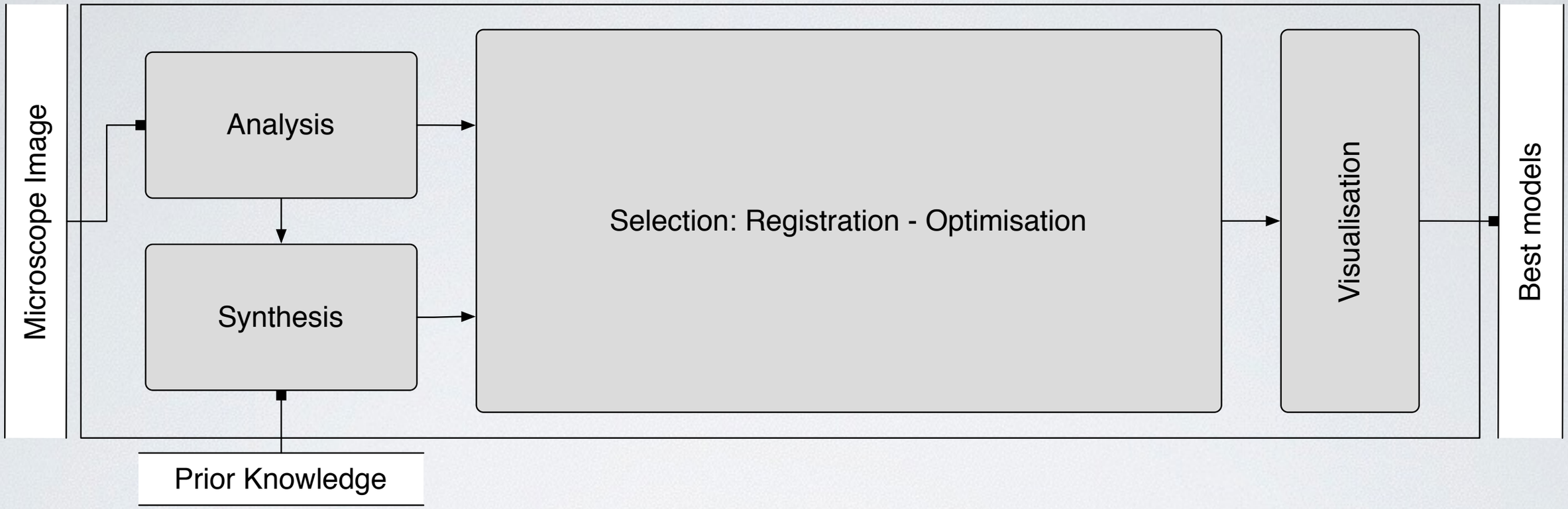
- 3-D to 2-D registration

FRAMEWORK



Visualisation: Merging of both model and image

FRAMEWORK


Microscope Image
Analysis
Synthesis
Prior Knowledge
Selection: Registration - Optimisation
Visualisation
Best models

CONTENT

- Introduction
- Analysis Module
- Generation Module
- Selection Module
- Results and Visualisation
- Conclusion

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ANALYSIS MODULE

- Analyse and extract information from the microscope image

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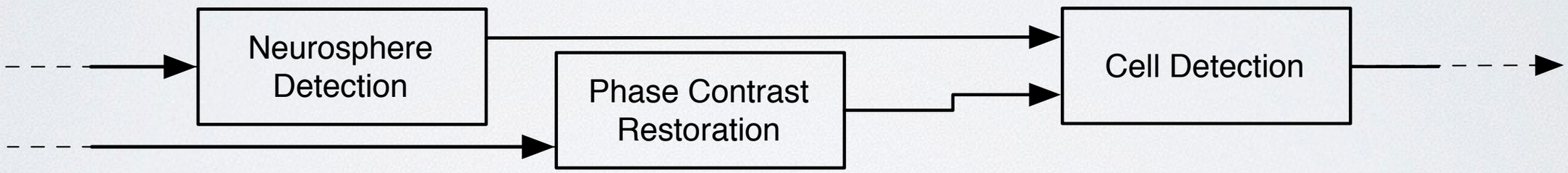
- Three processes pipeline



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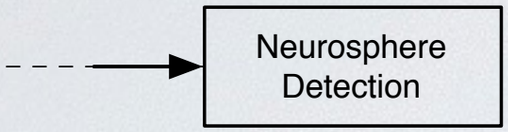

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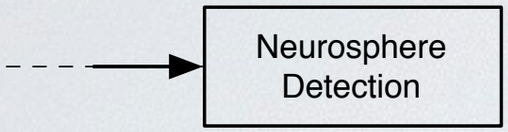

- Temporal detection using Σ-Δ filter (Manzanera and Richefeu, 07)

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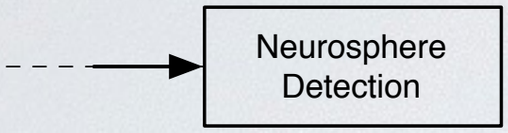

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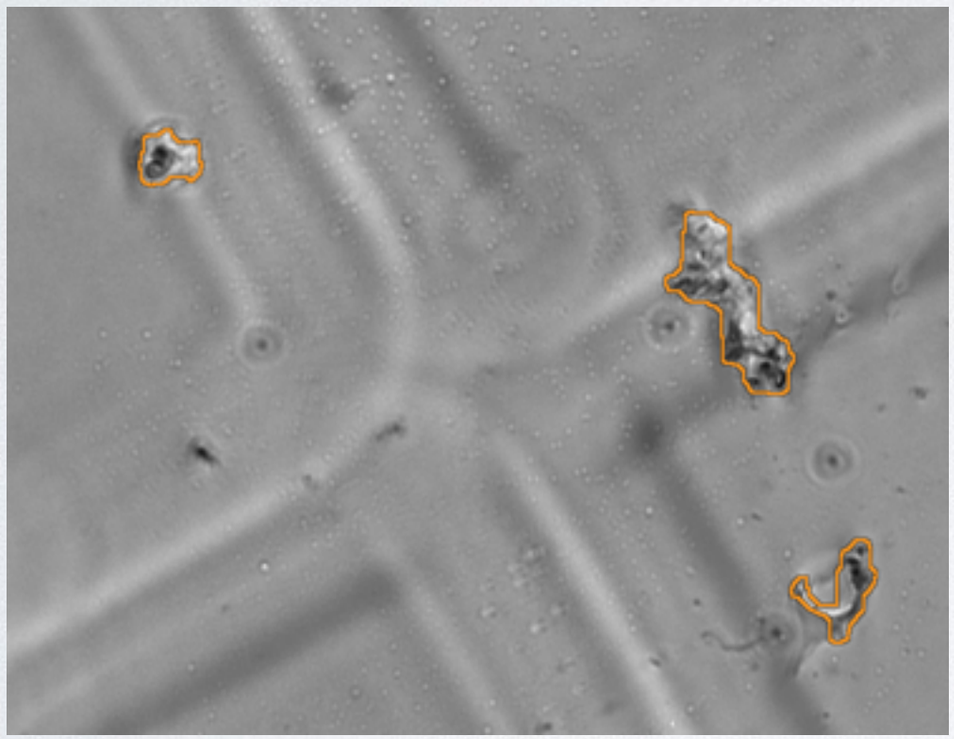

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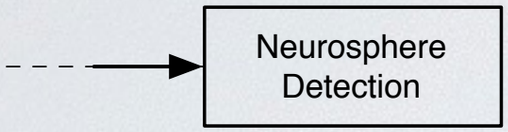

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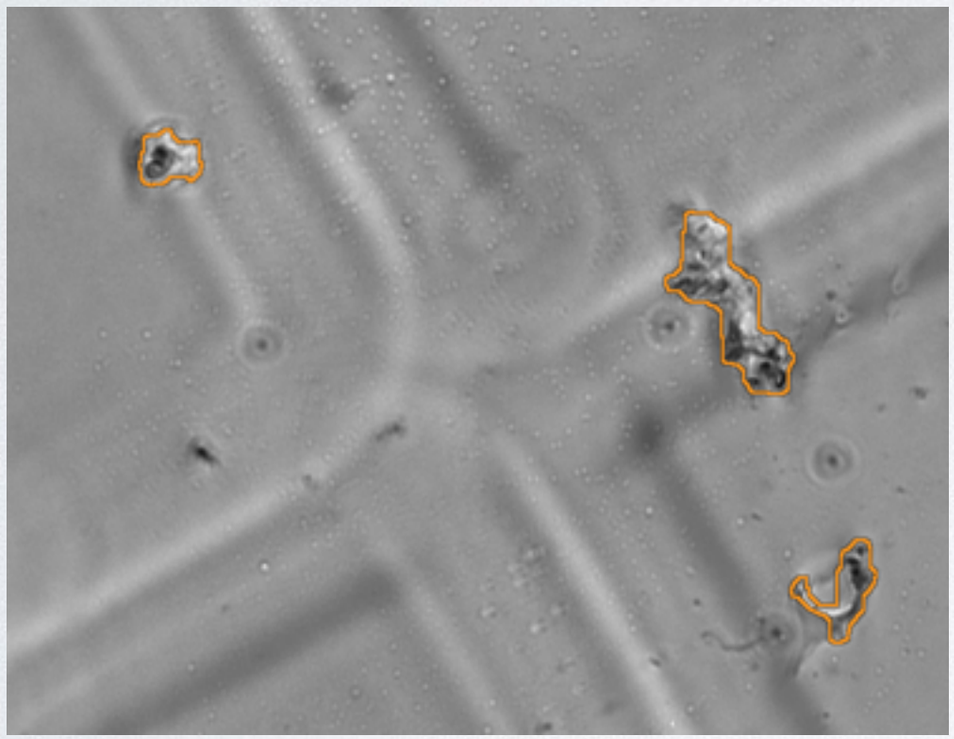

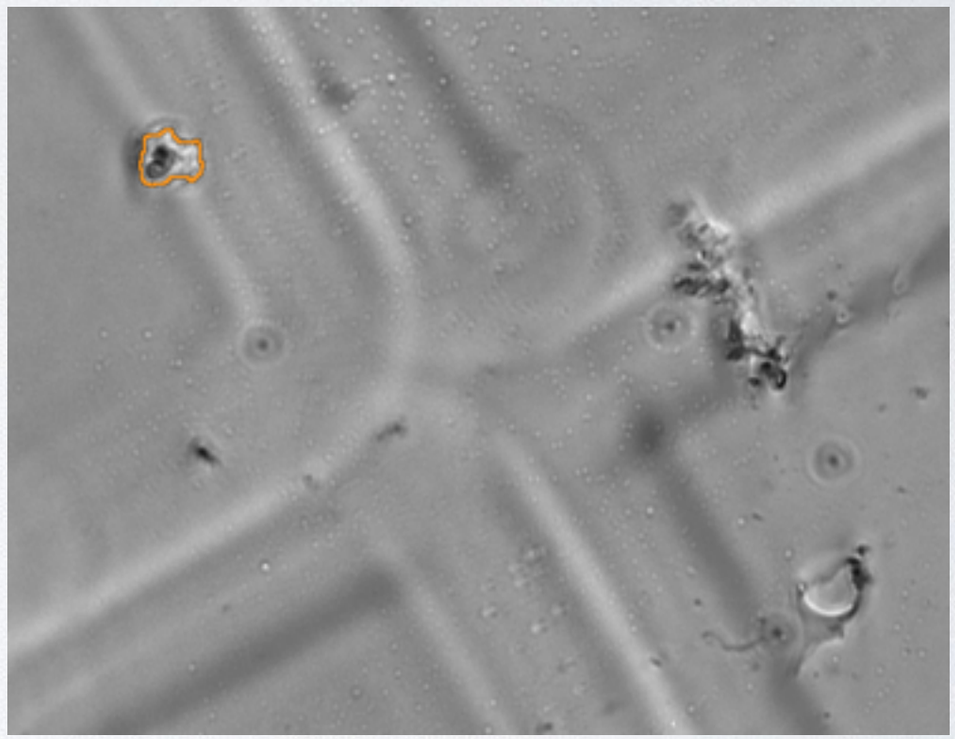

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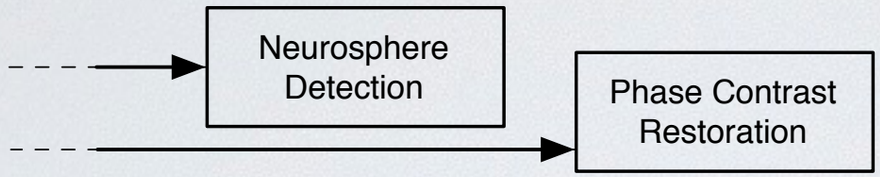

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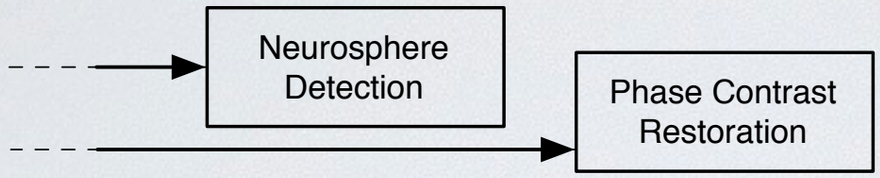

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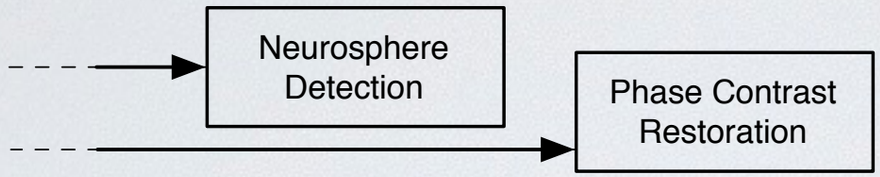

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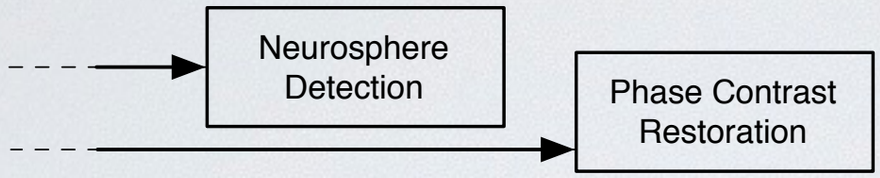
$$g(x) = || \; l_s(x) - l_d(x) \; ||^2$$

$$l_s(x) = i\theta_p A e^{i\beta}$$

$$l_d(x) = i\theta_c A e^{i(\beta - f(x))} + (i\theta_p - 1)\theta_c A e^{i(\beta - f(x))} \times airy(r)$$

ANALYSIS MODULE



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$$g(x) \propto (\delta(r) - airy(r)) * f(x) + C$$

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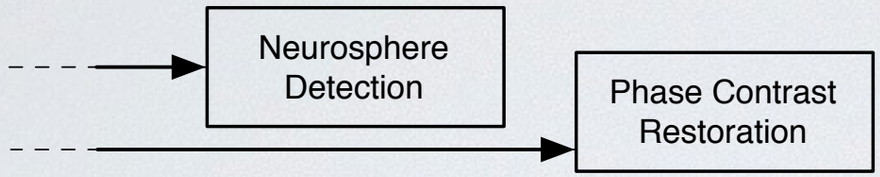

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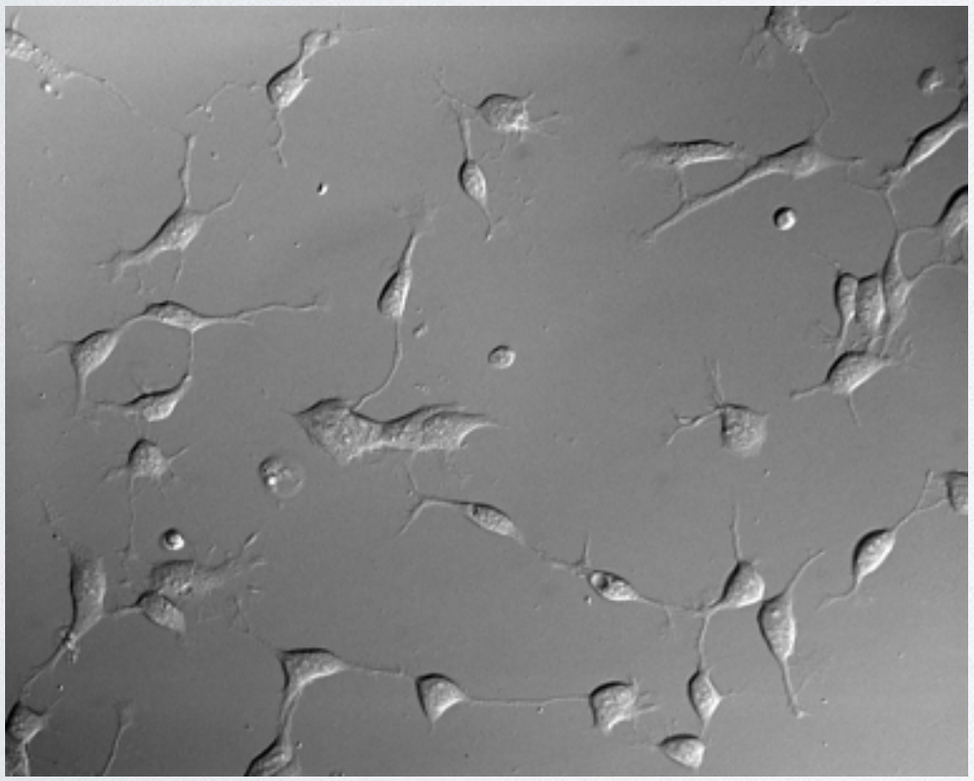

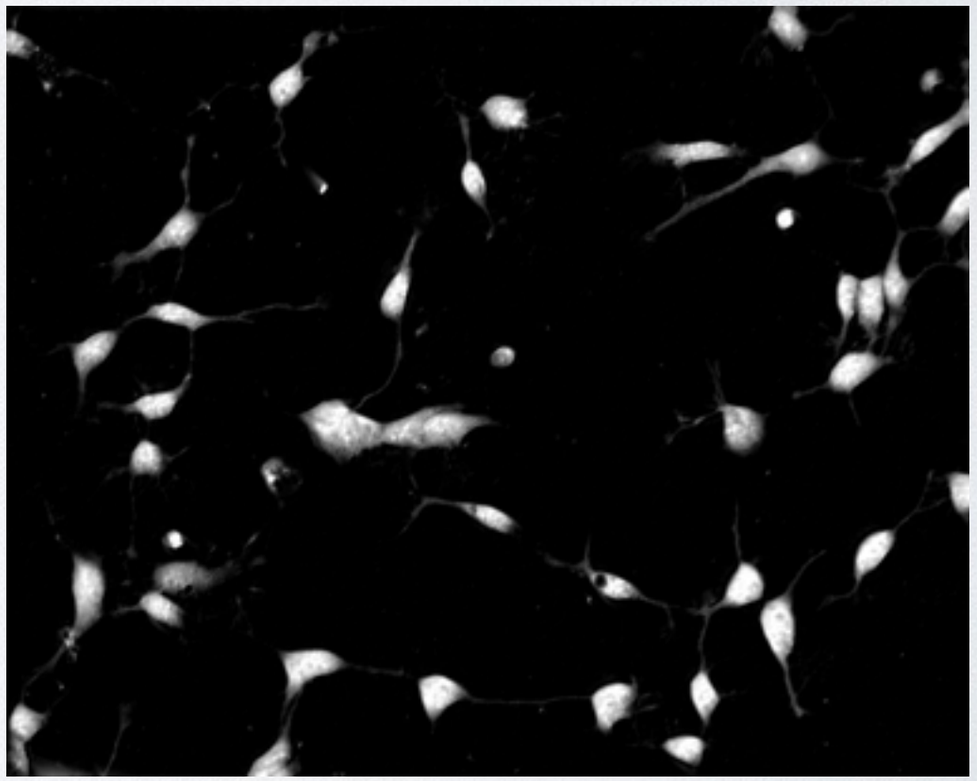

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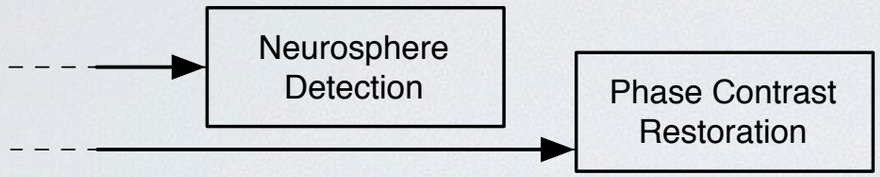

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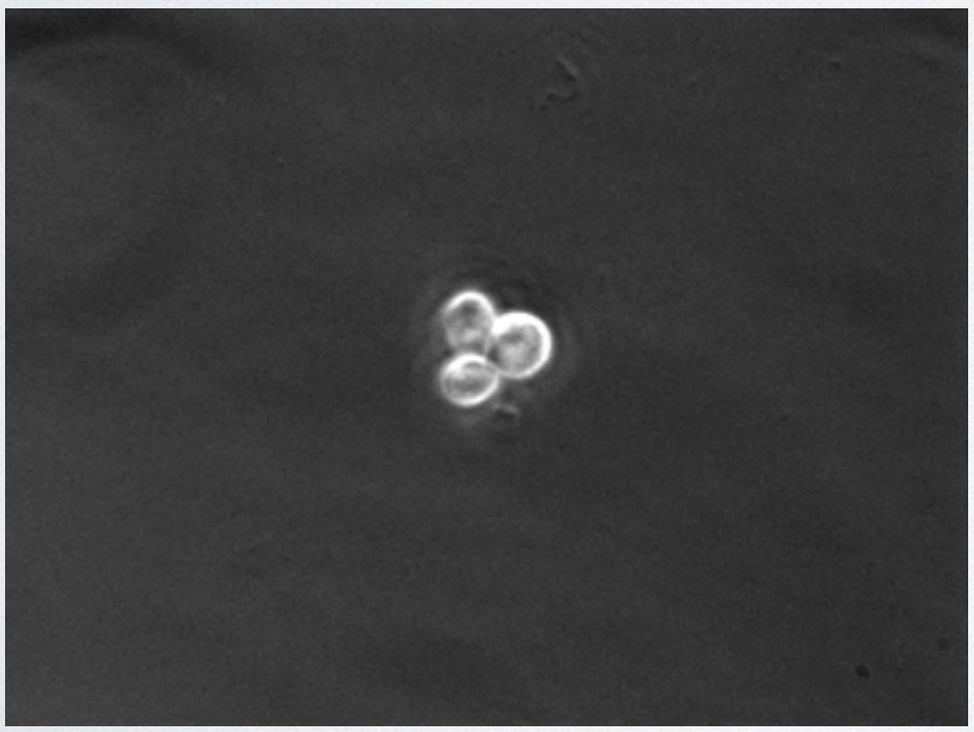

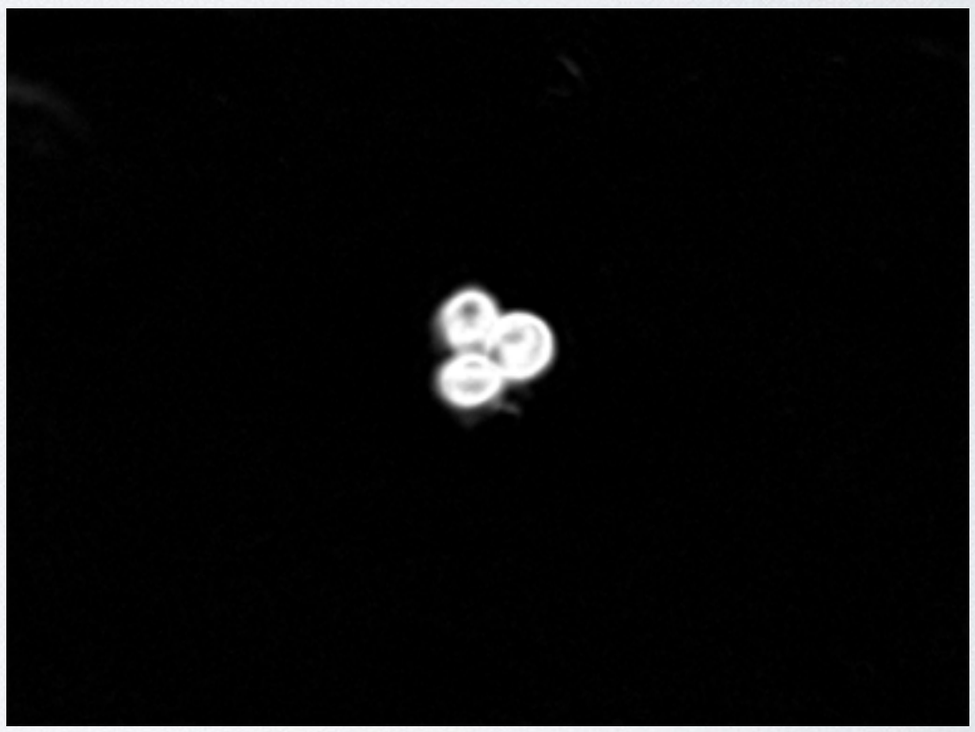

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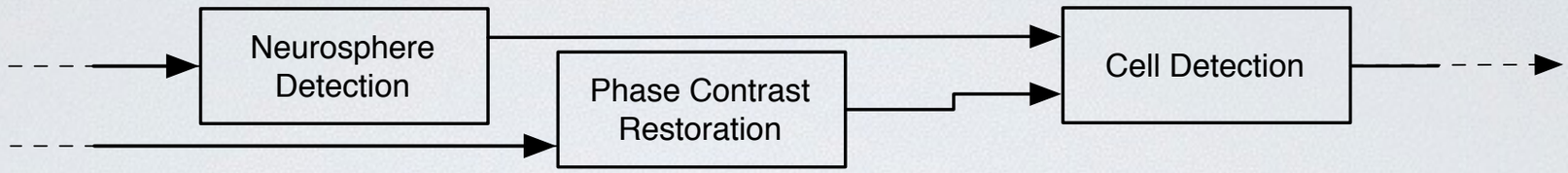
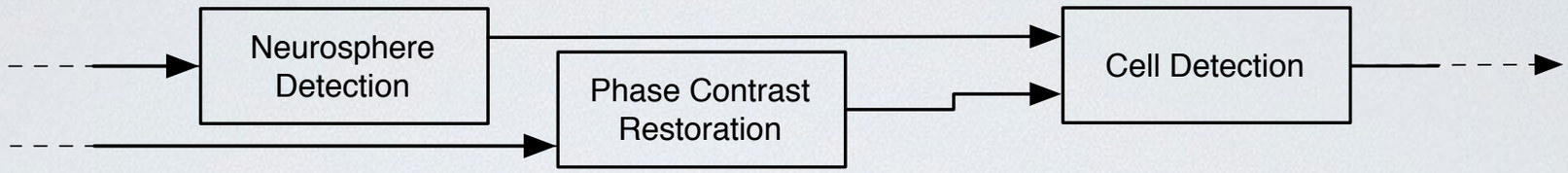
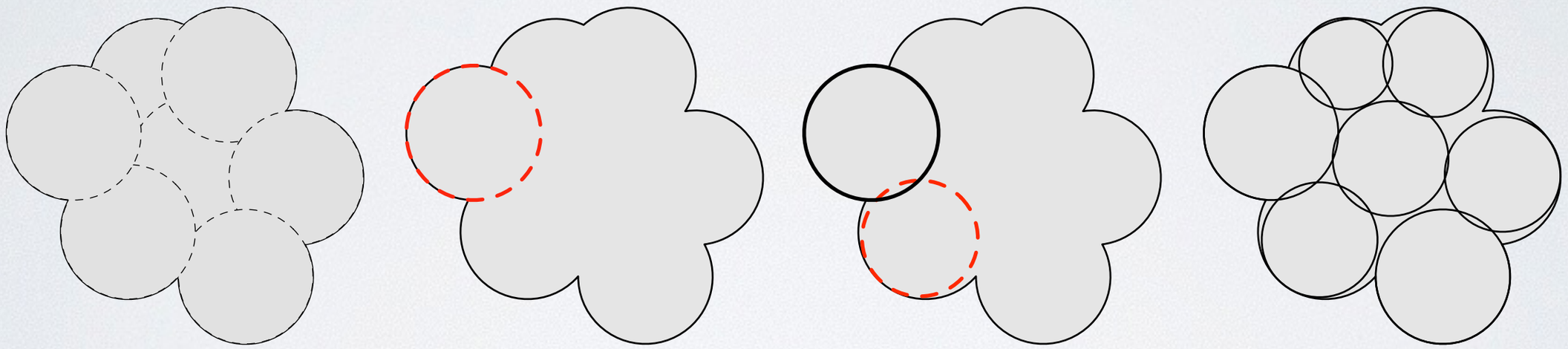


- Detection using circle fitting process

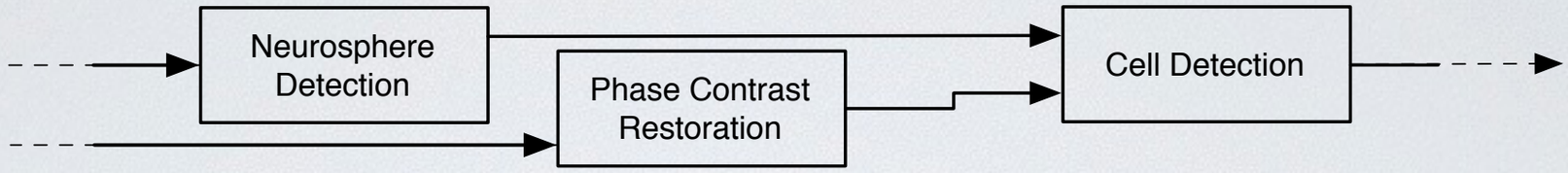
ANALYSIS MODULE



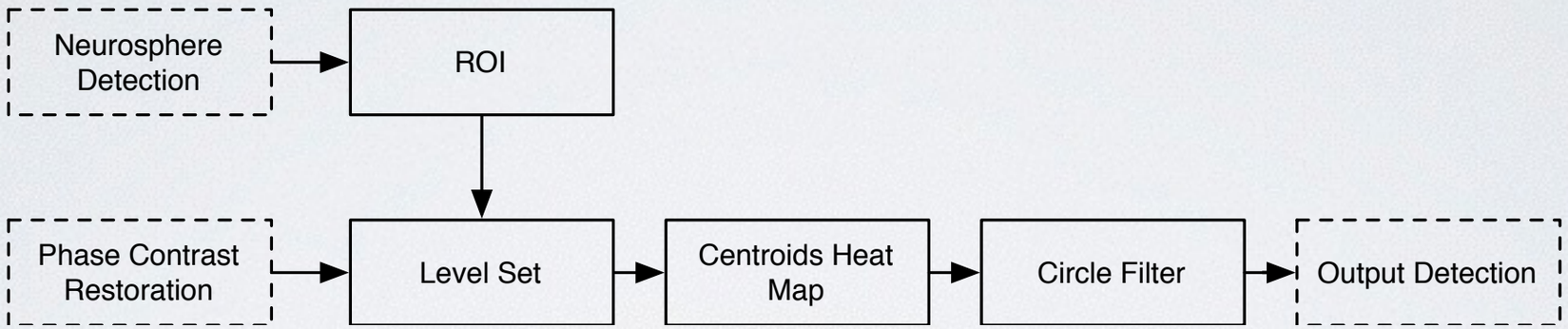
- Detection using circle fitting process



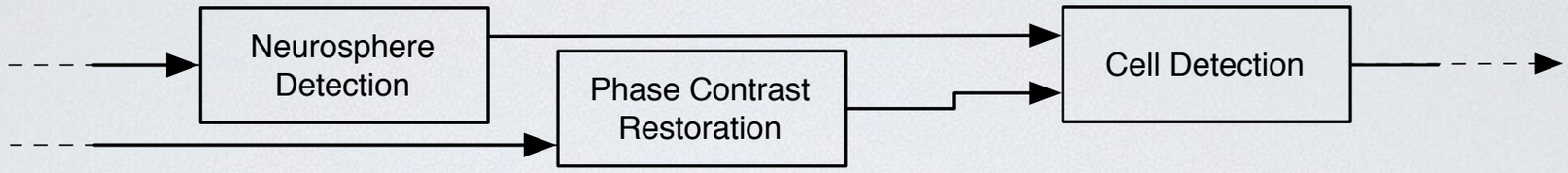
ANALYSIS MODULE



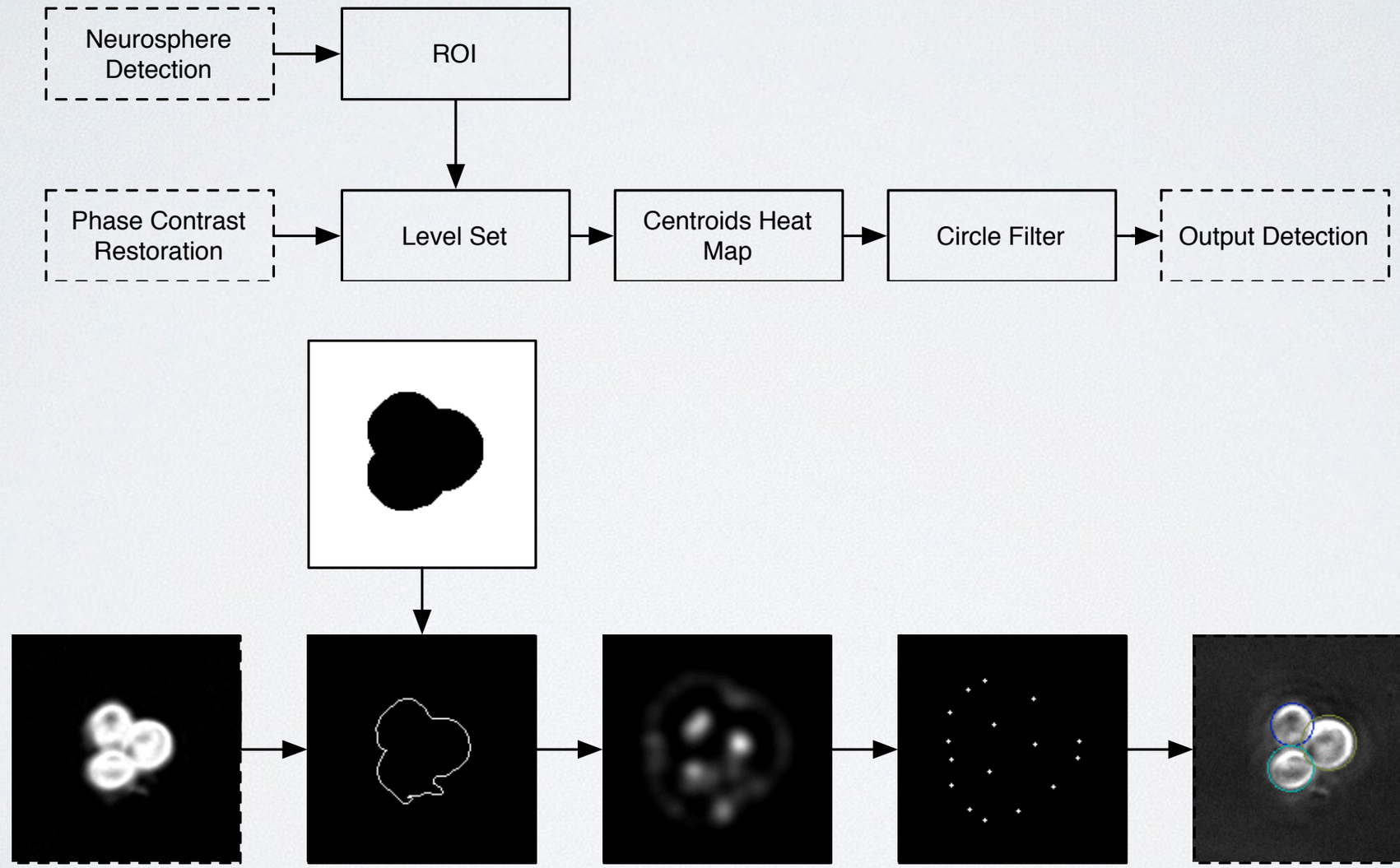
- Detection using circle fitting process



ANALYSIS MODULE

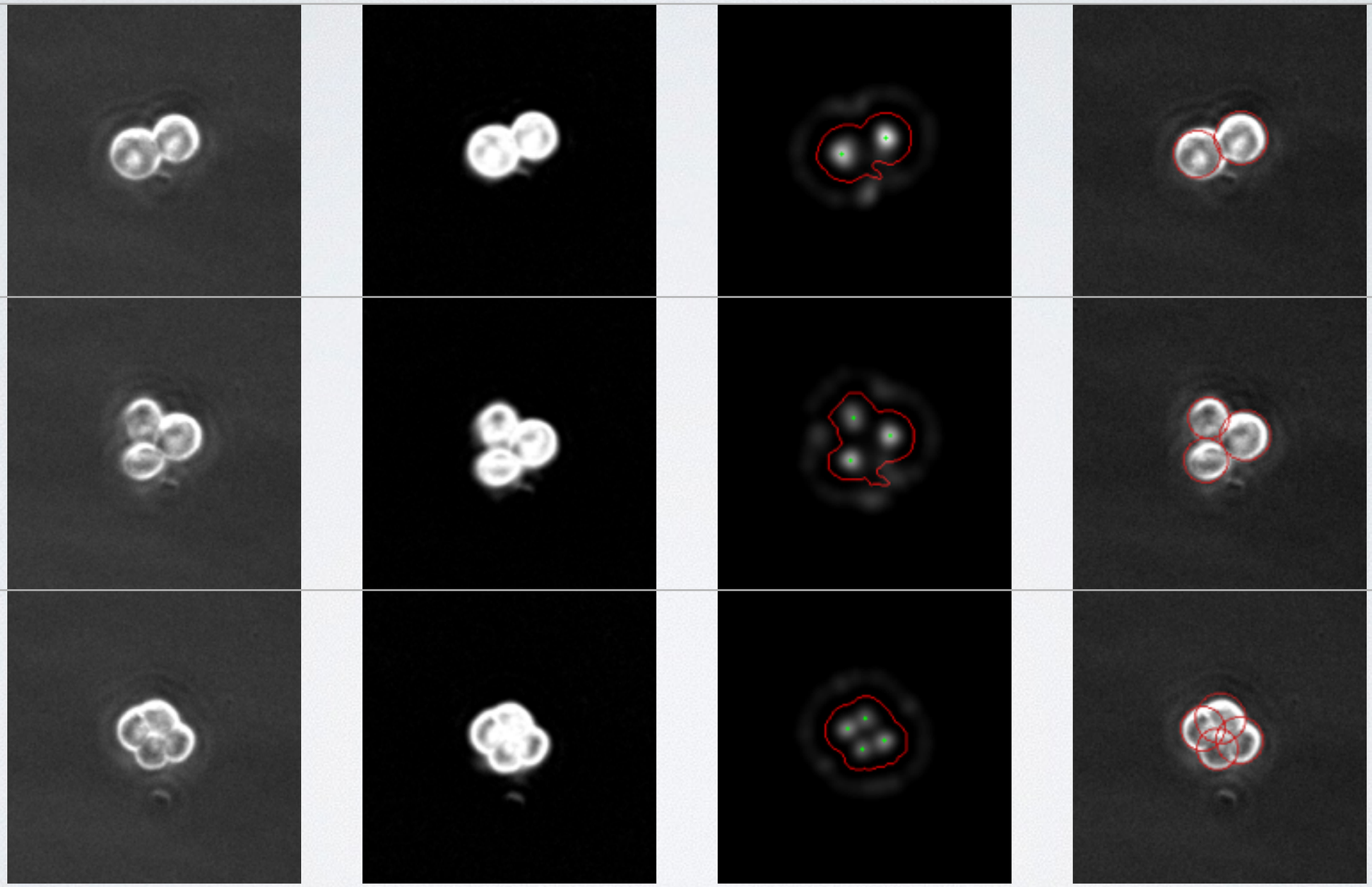


- Detection using circle fitting process



ANALYSIS MODULE

raw restored process results



ANALYSIS MODULE

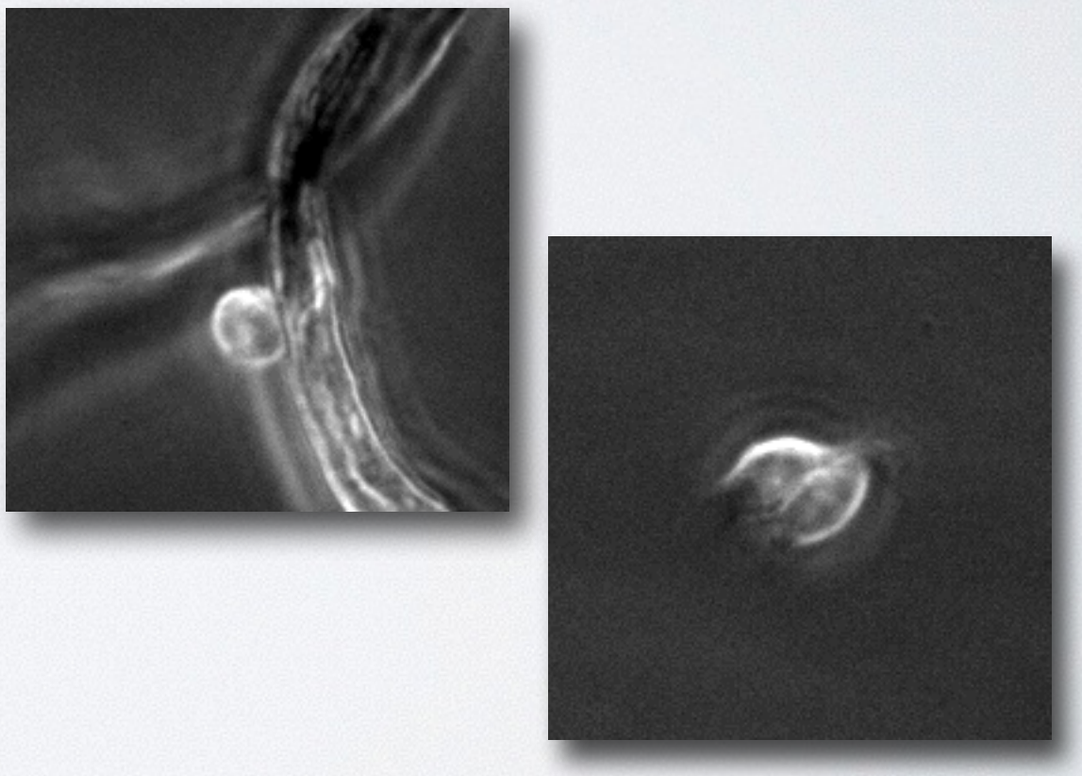
Precision	Recall	F-score
0.874	0.898	0.886

- 19 time lapse sequences from 130 to 300 images

ANALYSIS MODULE

Precision	Recall	F-score
0.874	0.898	0.886

- 19 time lapse sequences from 130 to 300 images
- Process limits
  - dust
  - large cell deformation



CONTENT

- Introduction
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SYNTHESIS MODULE

- Generates a set of possible cells configurations using
  - analysis module
  - prior knowledge

SYNTHESIS MODULE

- Generates a set of possible cells configurations using
  - analysis module
  - prior knowledge

- Two generation processes
  - evolution algorithm
  - primal / dual mesh

SYNTHESIS MODULE

PRIOR KNOWLEDGE

- Three major knowledge

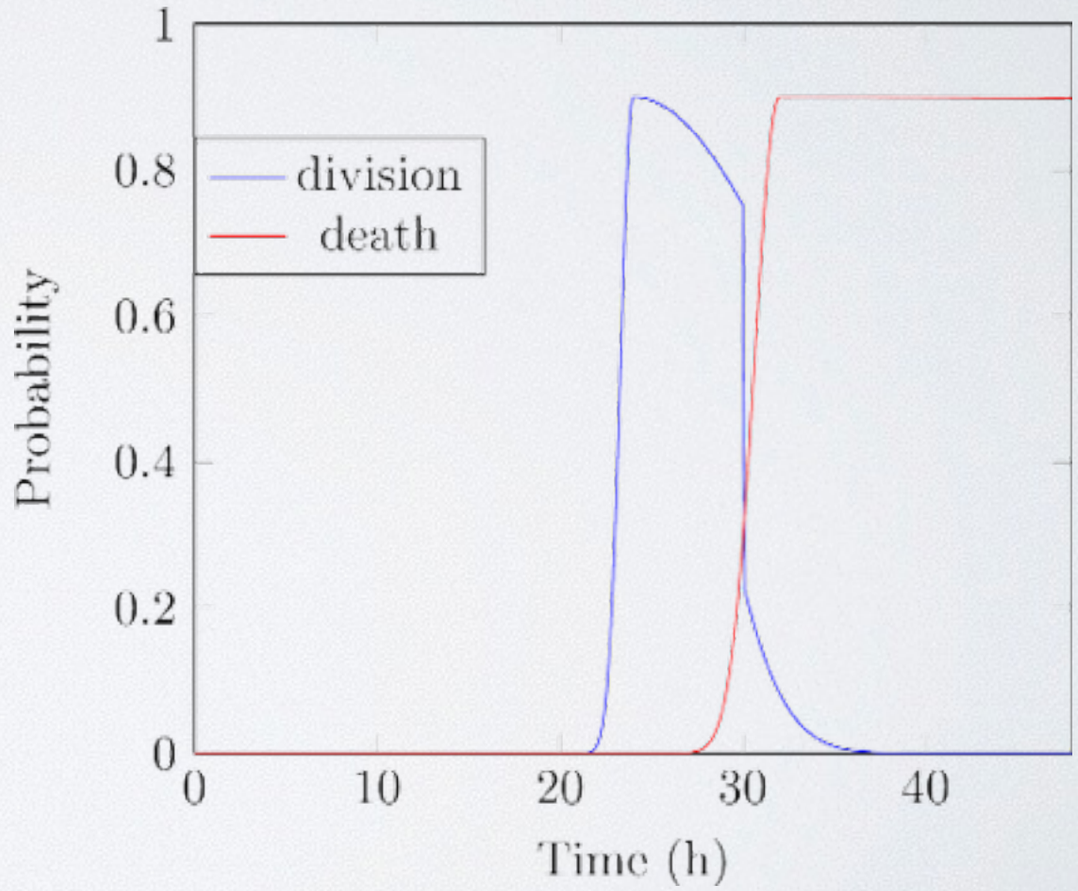
SYNTHESIS MODULE

PRIOR KNOWLEDGE

- Three major knowledge

  - proliferation speed

cell **division** speed

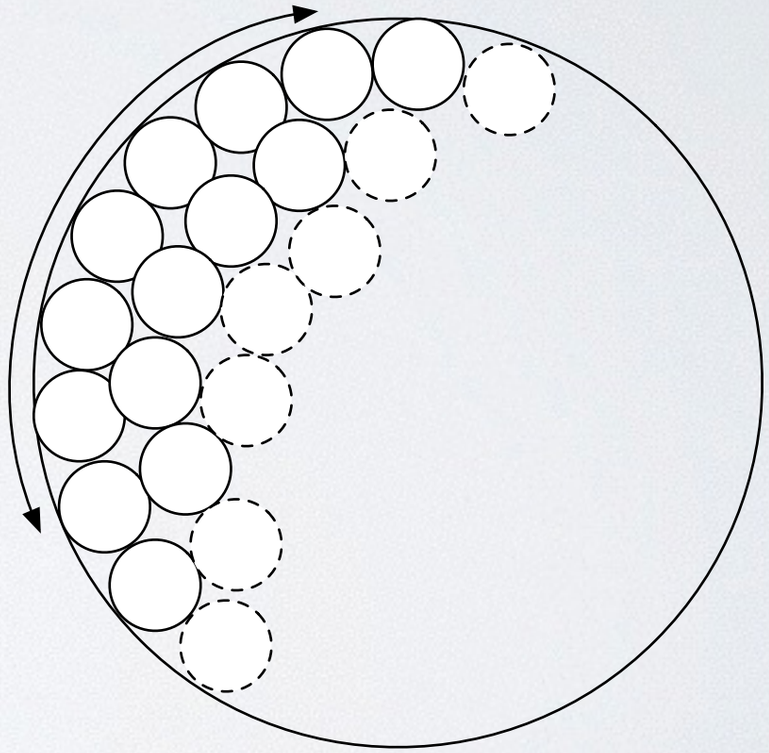


SYNTHESIS MODULE

PRIOR KNOWLEDGE

- Three major knowledge
  - proliferation speed
  - structural constrains

minimal **distance** between cells
maximal **compression** of a cell



SYNTHESIS MODULE

PRIOR KNOWLEDGE

- Three major knowledge
  - proliferation speed
  - structural constrains
  - visual appearance

phase contrast **intensity**

SYNTHESIS MODULE

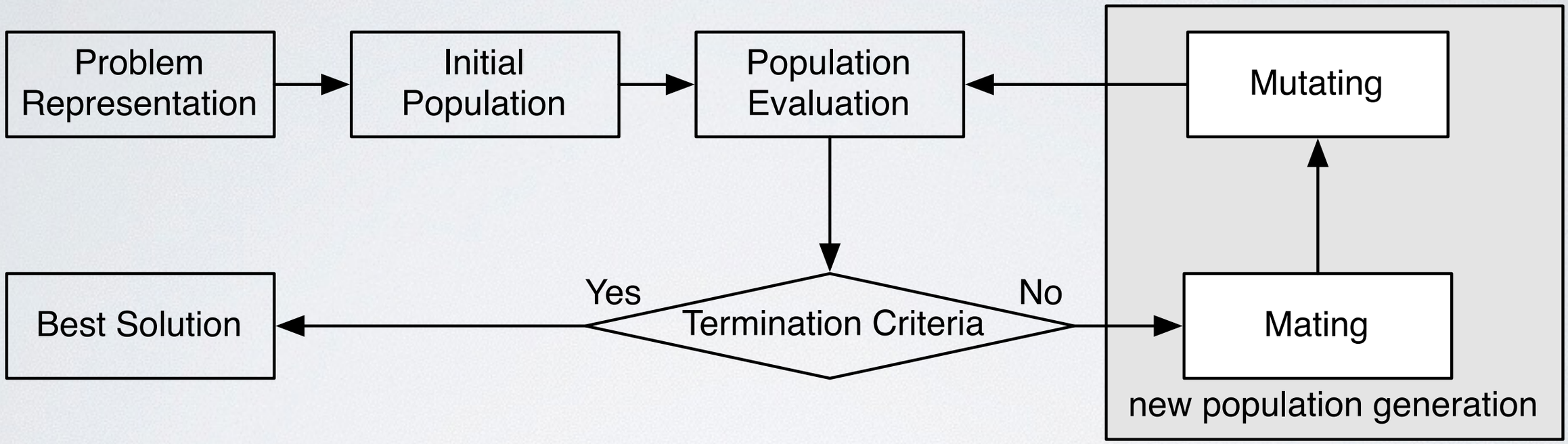
EVOLUTION ALGORITHM

- Search algorithm inspired from biological evolution

SYNTHESIS MODULE

EVOLUTION ALGORITHM

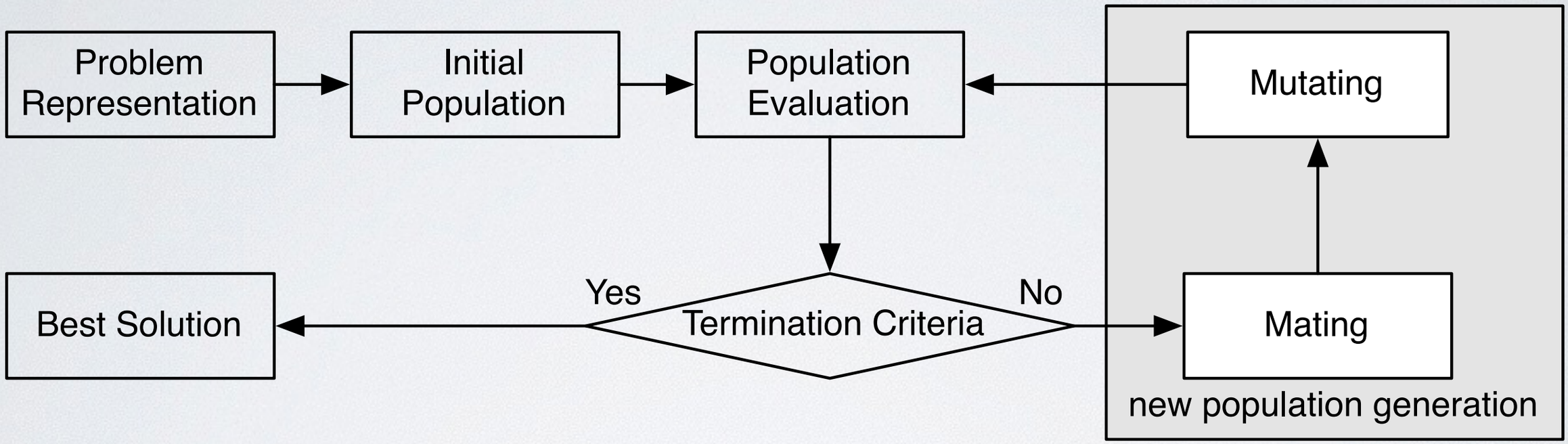
- Search algorithm inspired from biological evolution



SYNTHESIS MODULE

EVOLUTION ALGORITHM

- Search algorithm inspired from biological evolution



- Definition of mutation and mating process, based on individual representation

SYNTHESIS MODULE

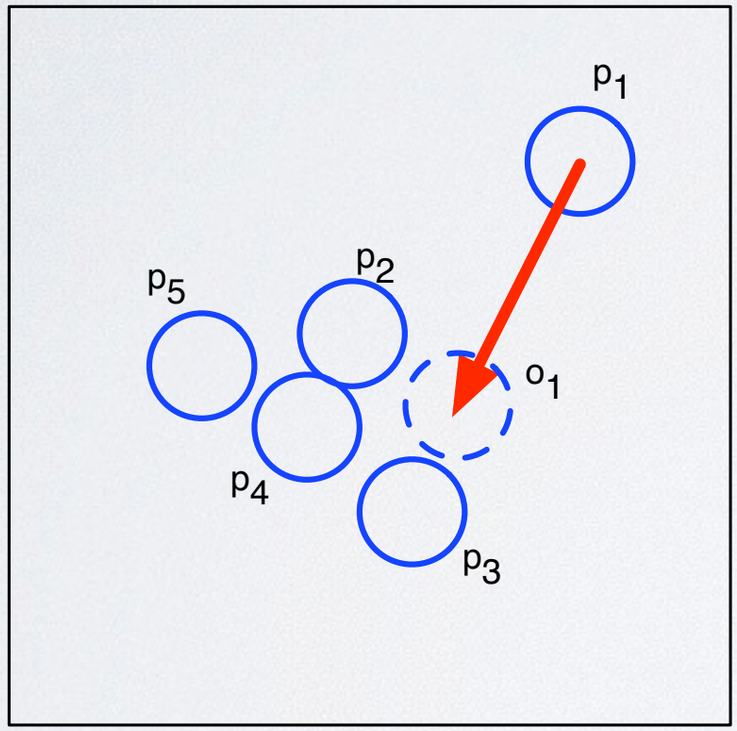
EVOLUTION ALGORITHM

SYNTHESIS MODULE

EVOLUTION ALGORITHM

Mutation : local translation

$$T_v(c_i^o) = c_i^p + v$$

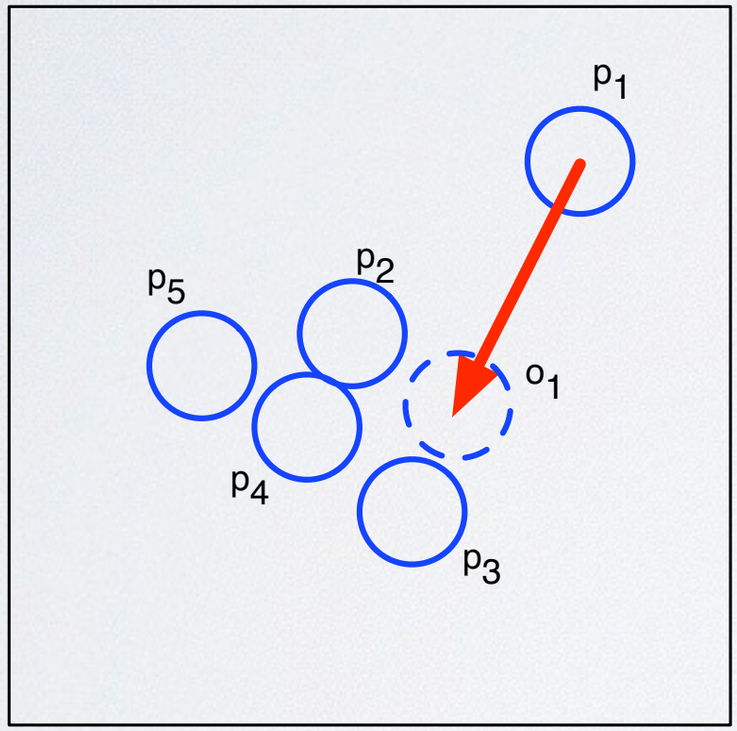


SYNTHESIS MODULE

EVOLUTION ALGORITHM

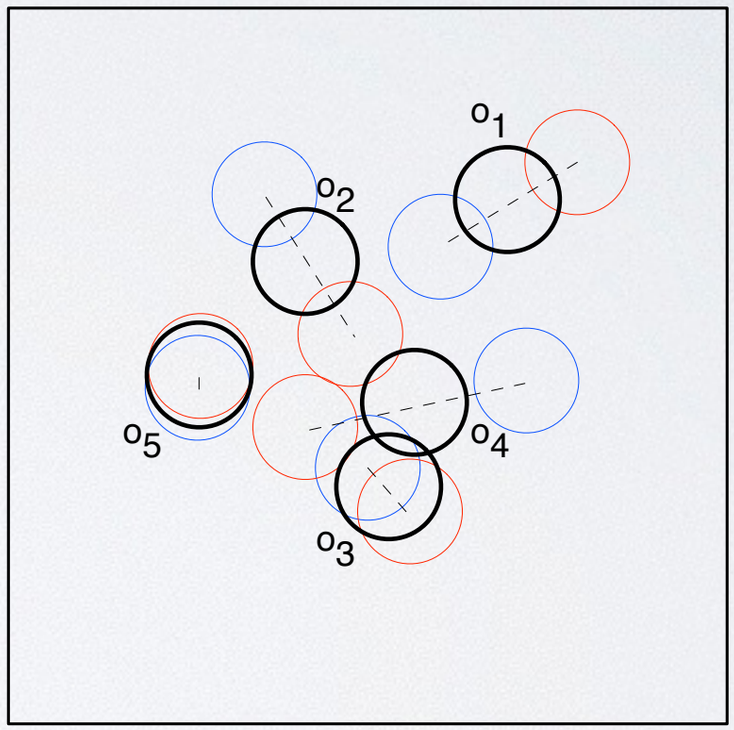
Mutation : local translation

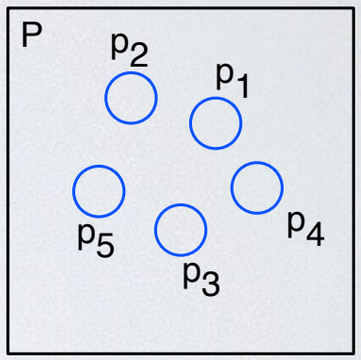
$$T_v(c_i^o) = c_i^p + v$$

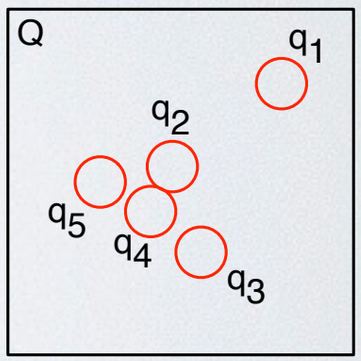


Mating : rand cross mix

$$c_i^o = \alpha c_i^p + \beta c_i^q$$

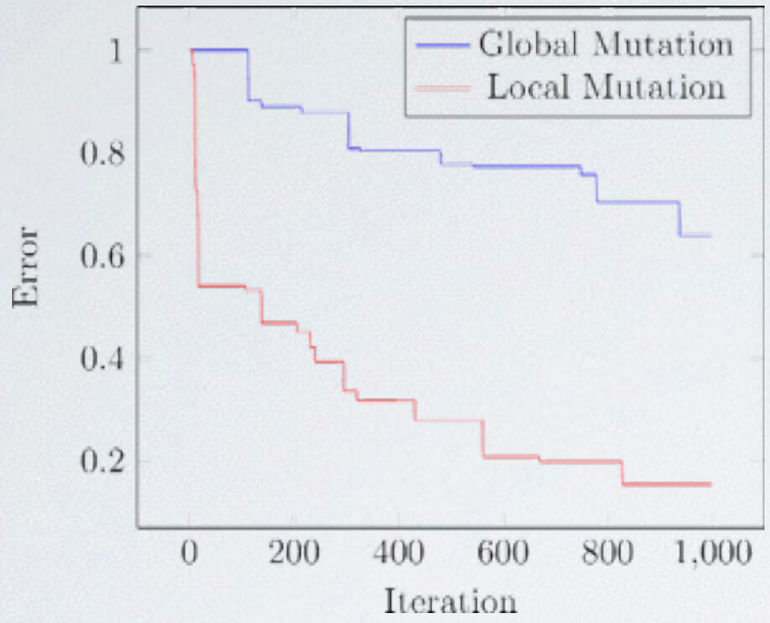


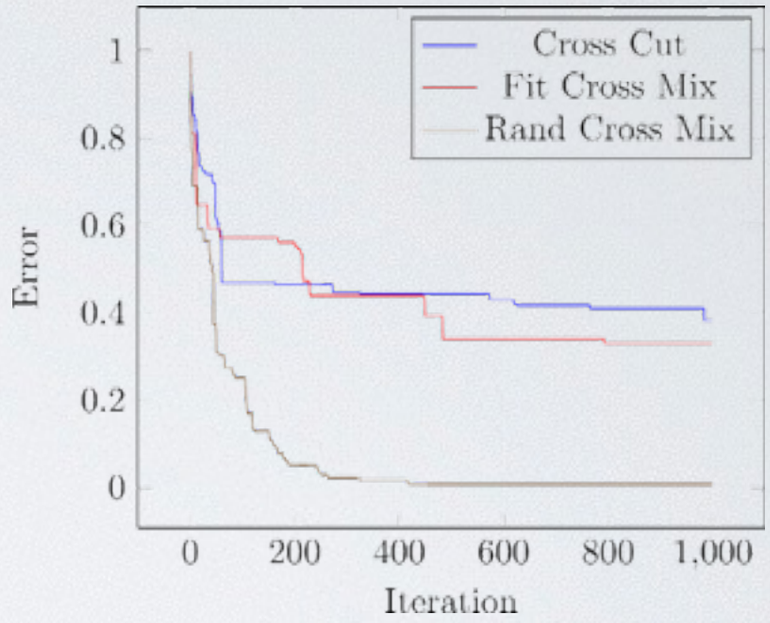


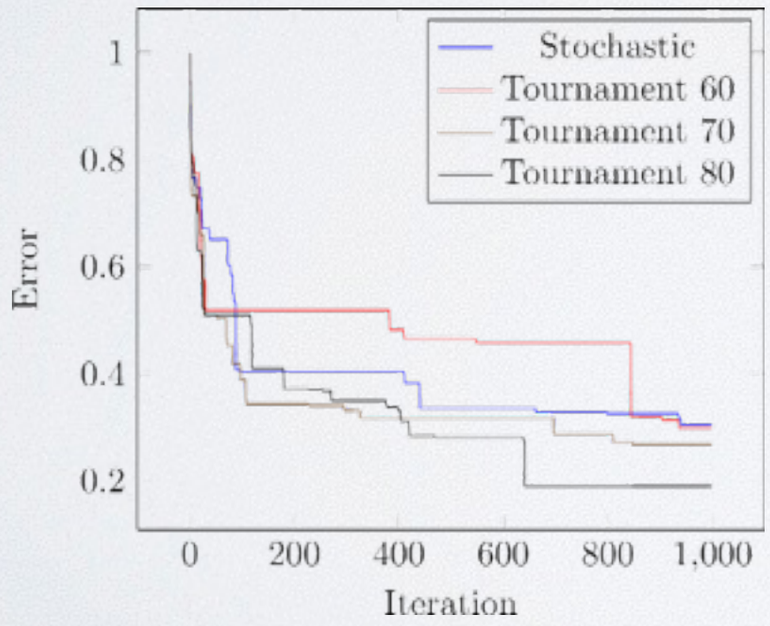


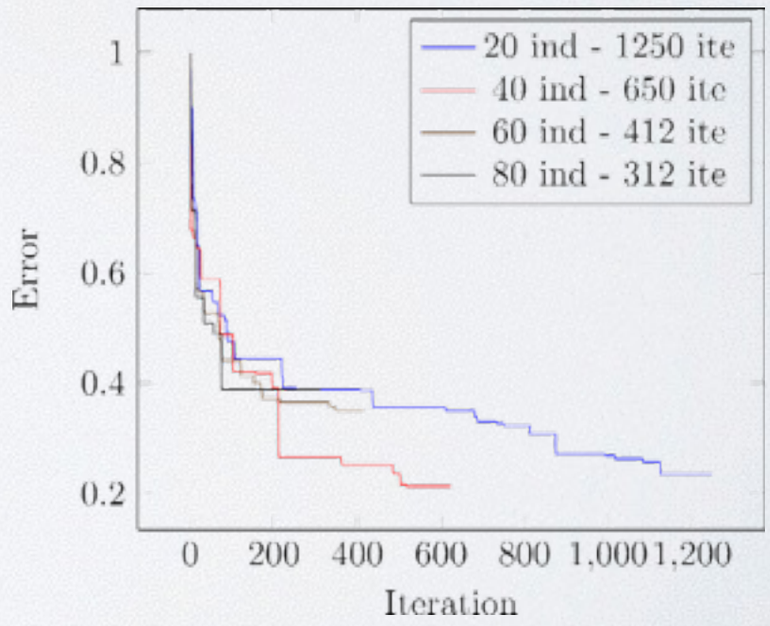
SYNTHESIS MODULE

EVOLUTION ALGORITHM









SYNTHESIS MODULE

EVOLUTION ALGORITHM

- GPU Implementation:

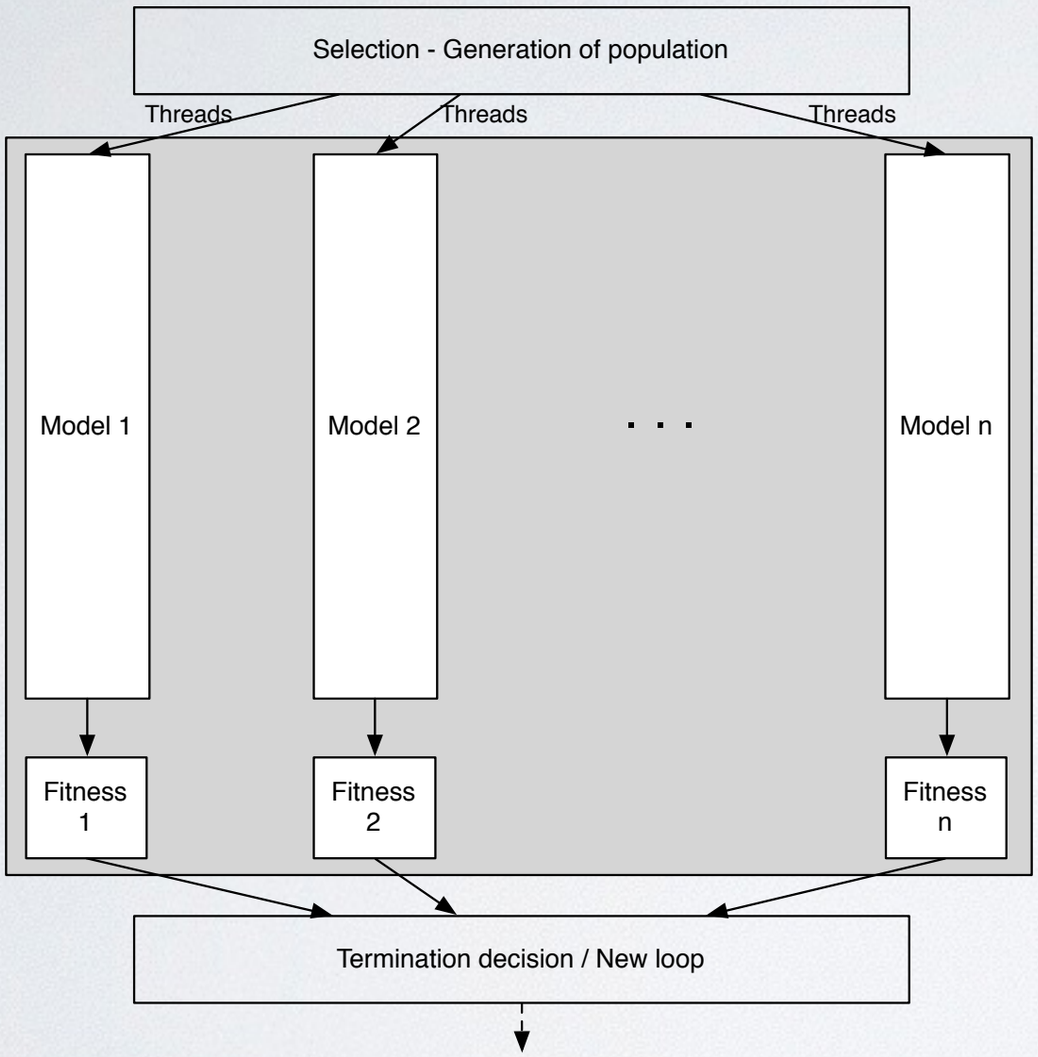
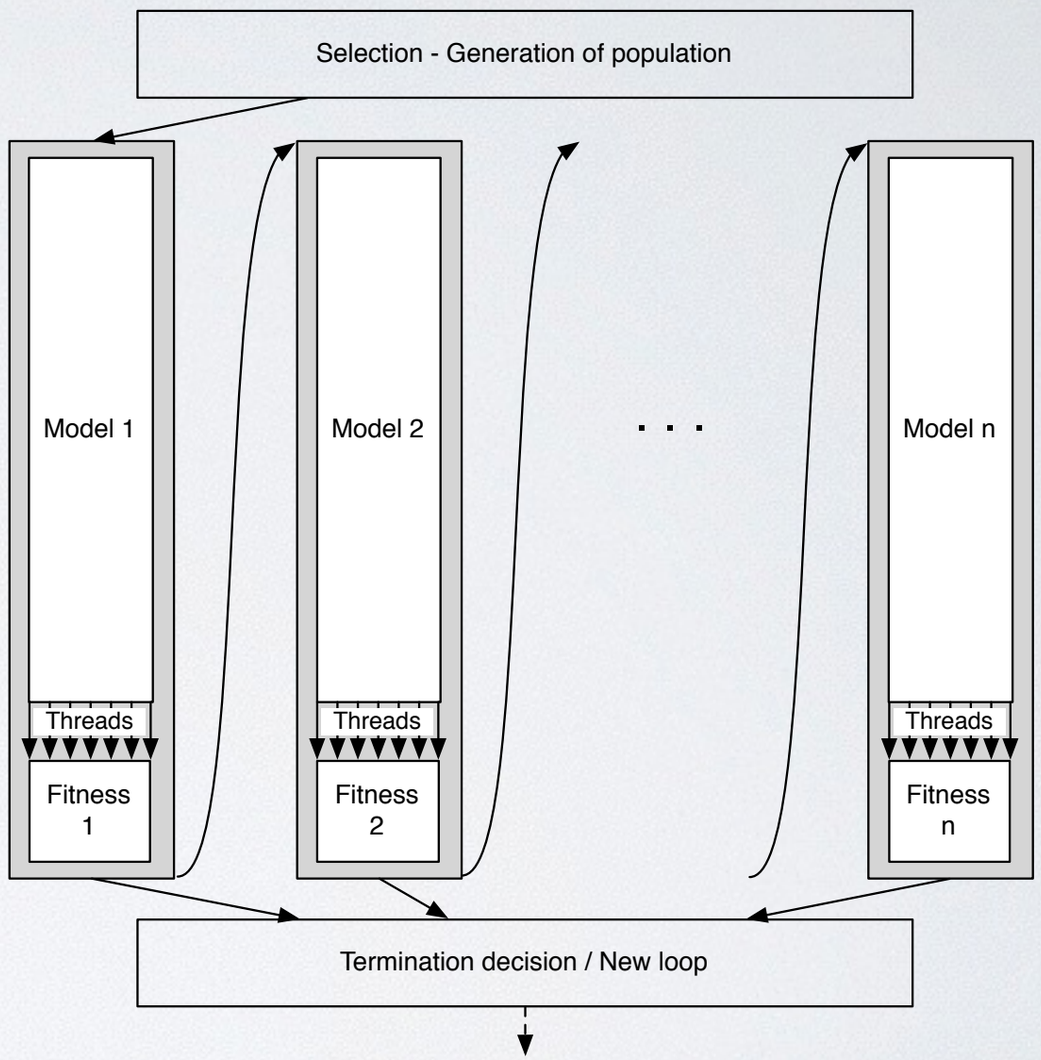


image-wise

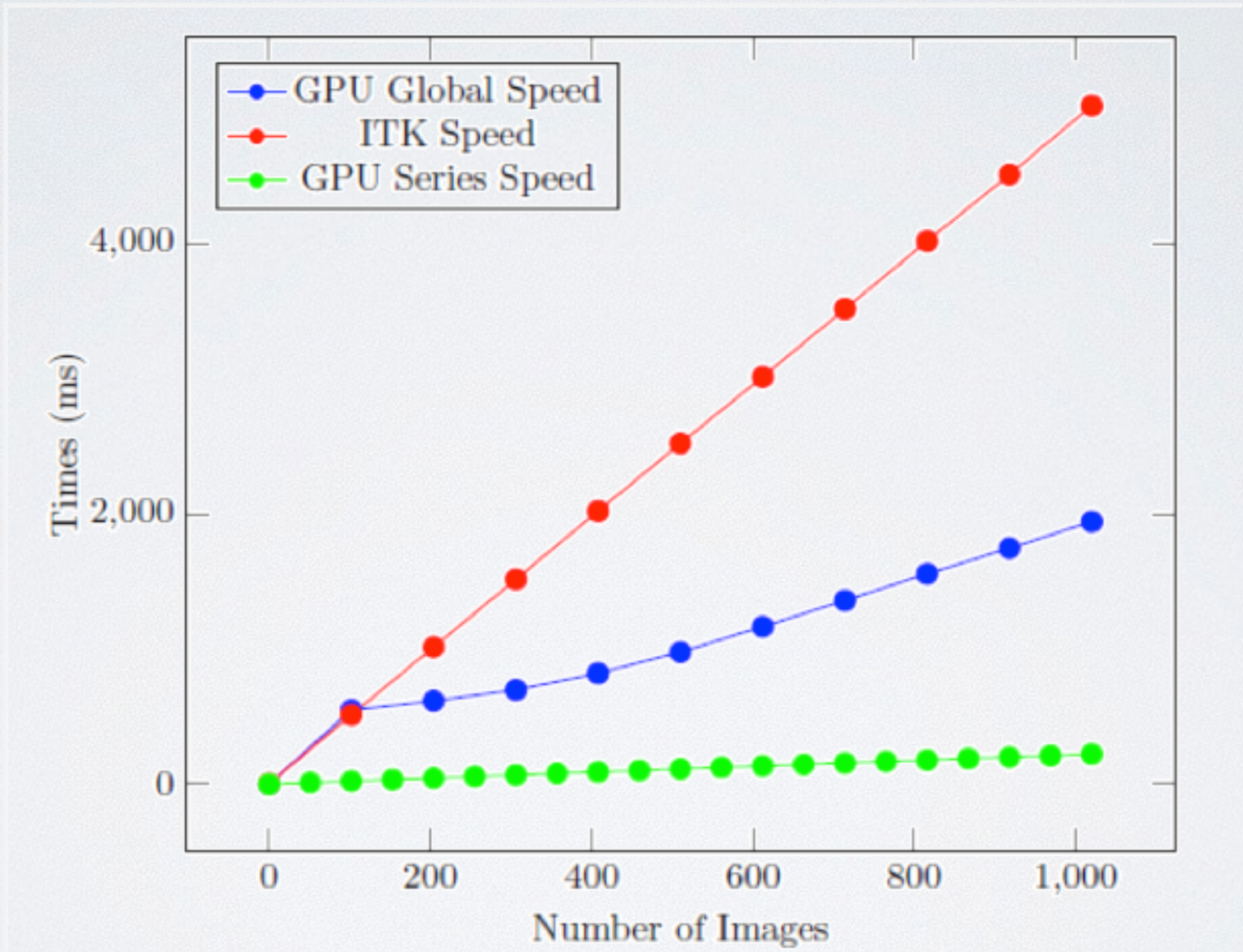


pixel-wise

SYNTHESIS MODULE

EVOLUTION ALGORITHM

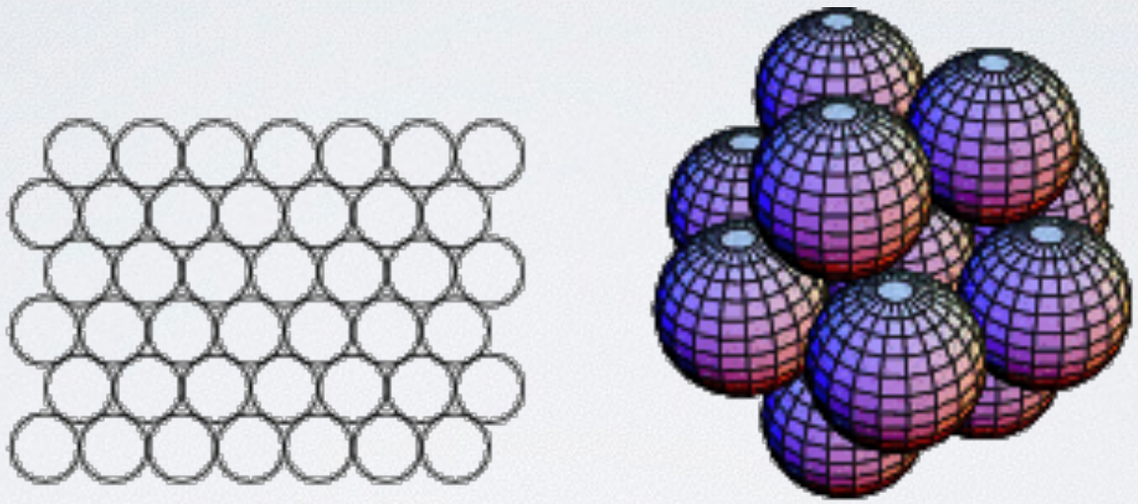
- GPU Implementation:



SYNTHESIS MODULE

DELAUNAY MESH

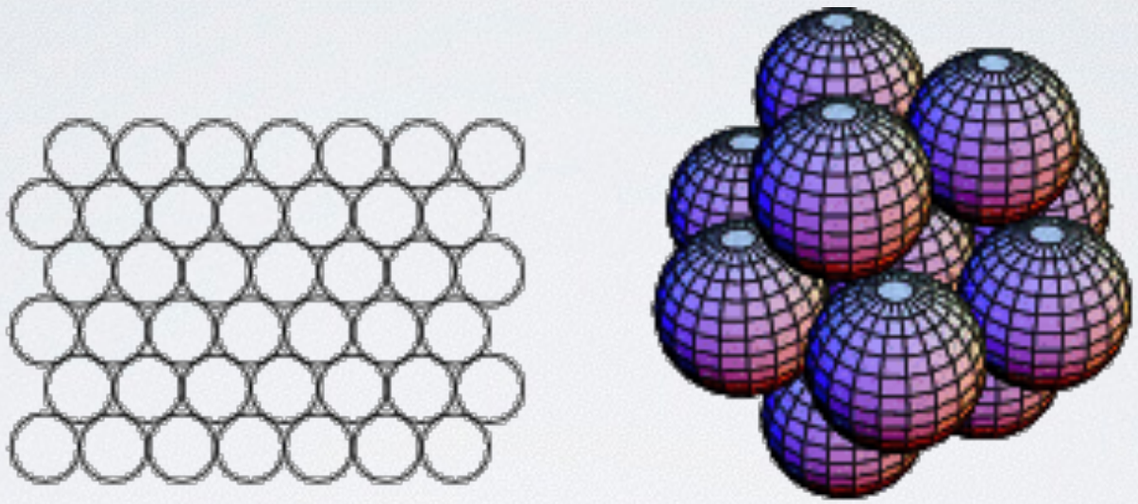
- Hypothesis of a sphere packing problem



SYNTHESIS MODULE

DELAUNAY MESH

- Hypothesis of a sphere packing problem

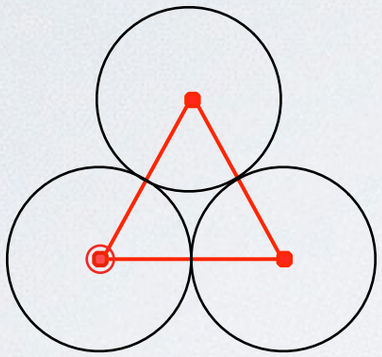


- Use of a Quad Edge Mesh structure (Guibas and Stolfi, 85)
  - constant radius
  - favor horizontal proliferation before vertical

SYNTHESIS MODULE

DELAUNAY MESH

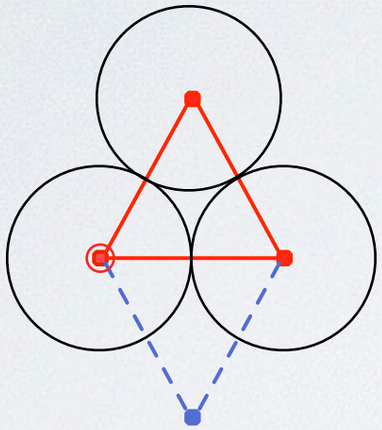
- Horizontal layer proliferation



SYNTHESIS MODULE

DELAUNAY MESH

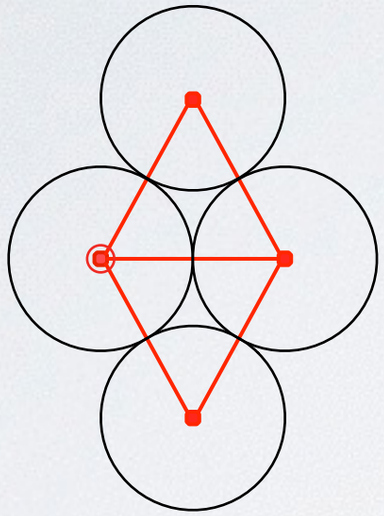
- Horizontal layer proliferation



SYNTHESIS MODULE

DELAUNAY MESH

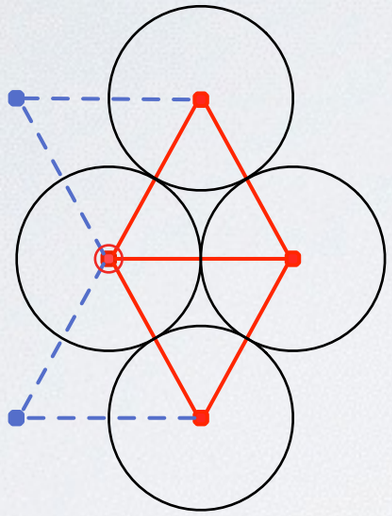
- Horizontal layer proliferation



SYNTHESIS MODULE

DELAUNAY MESH

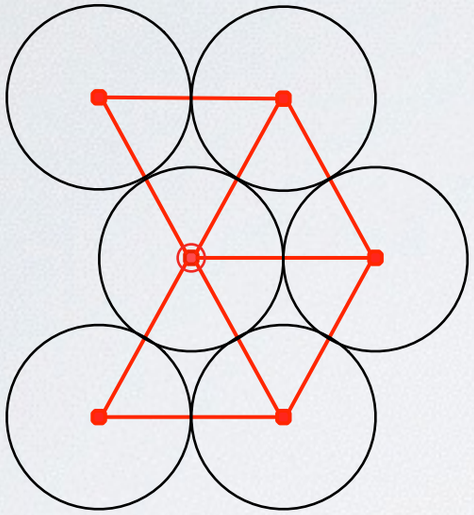
- Horizontal layer proliferation



SYNTHESIS MODULE

DELAUNAY MESH

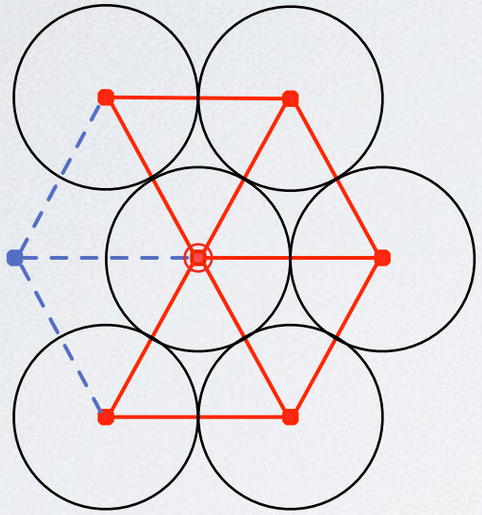
- Horizontal layer proliferation



SYNTHESIS MODULE

DELAUNAY MESH

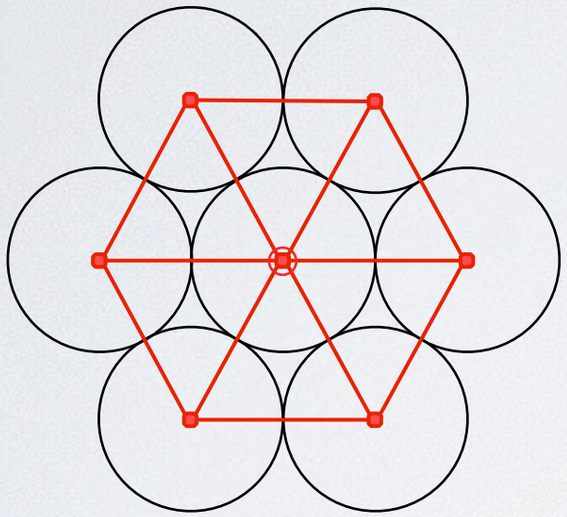
- Horizontal layer proliferation



SYNTHESIS MODULE

DELAUNAY MESH

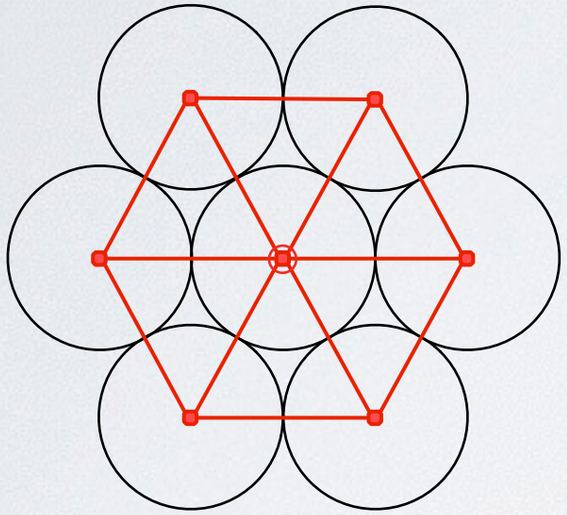
- Horizontal layer proliferation

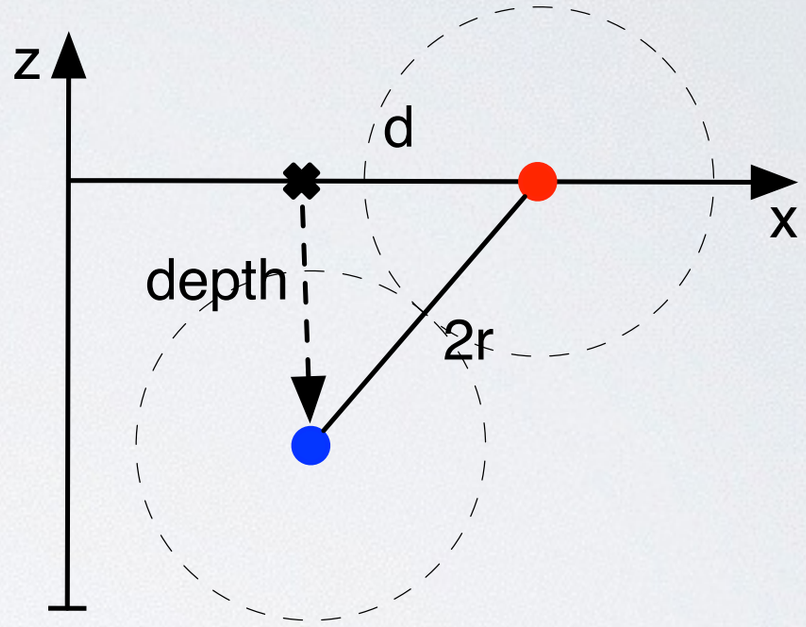


SYNTHESIS MODULE

DELAUNAY MESH

- Horizontal layer proliferation



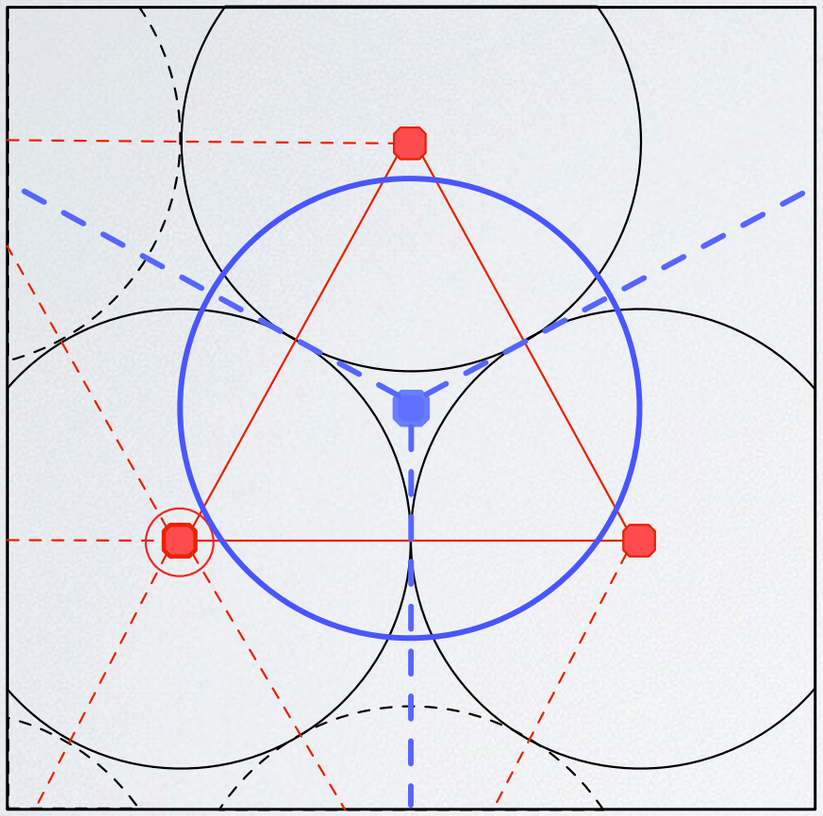


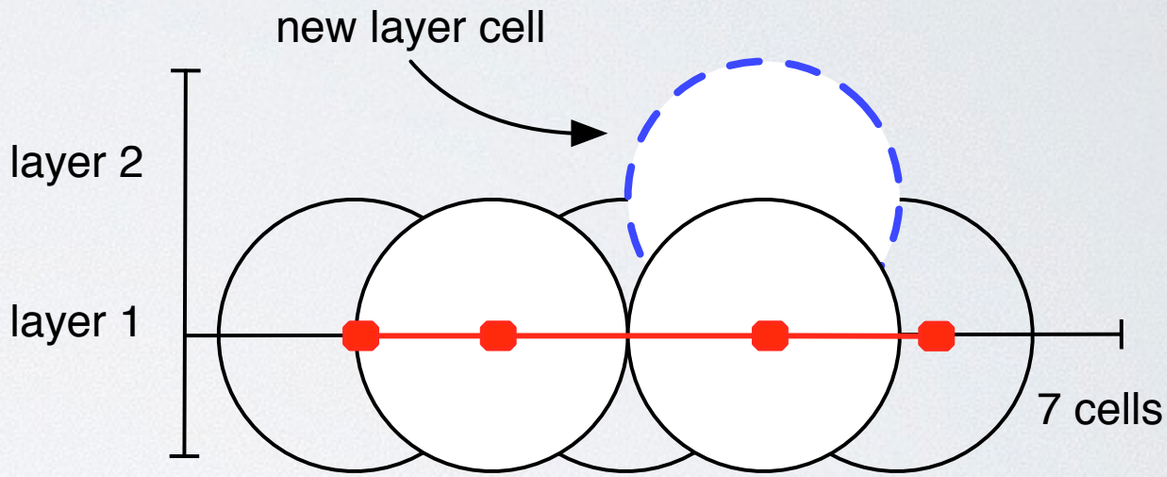
Depth calculation

SYNTHESIS MODULE

DELAUNAY MESH

- New layer proliferation





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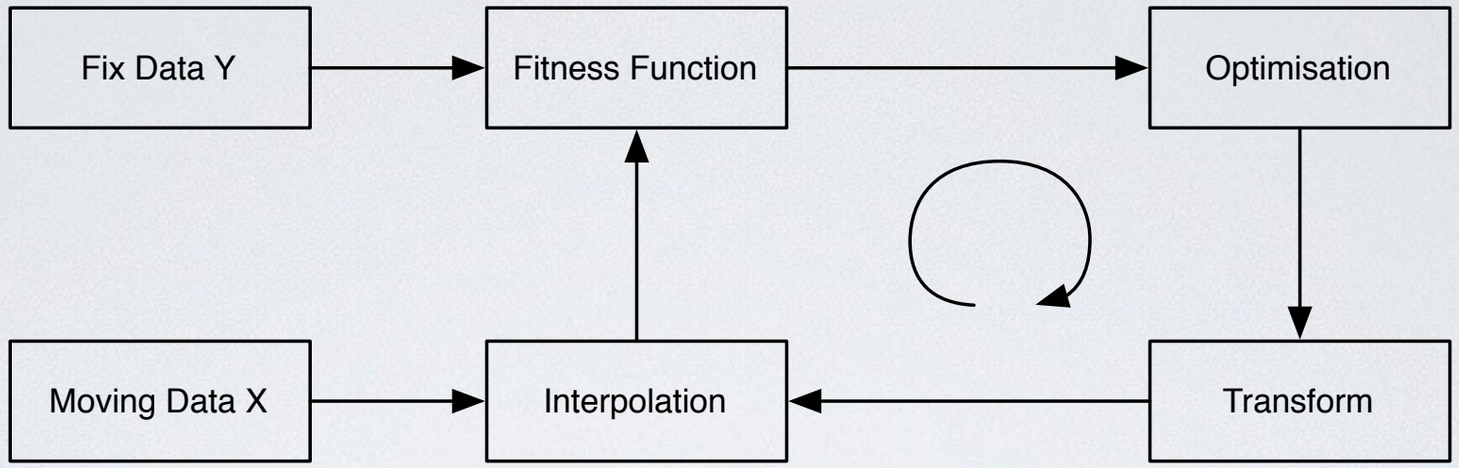
SELECTION MODULE

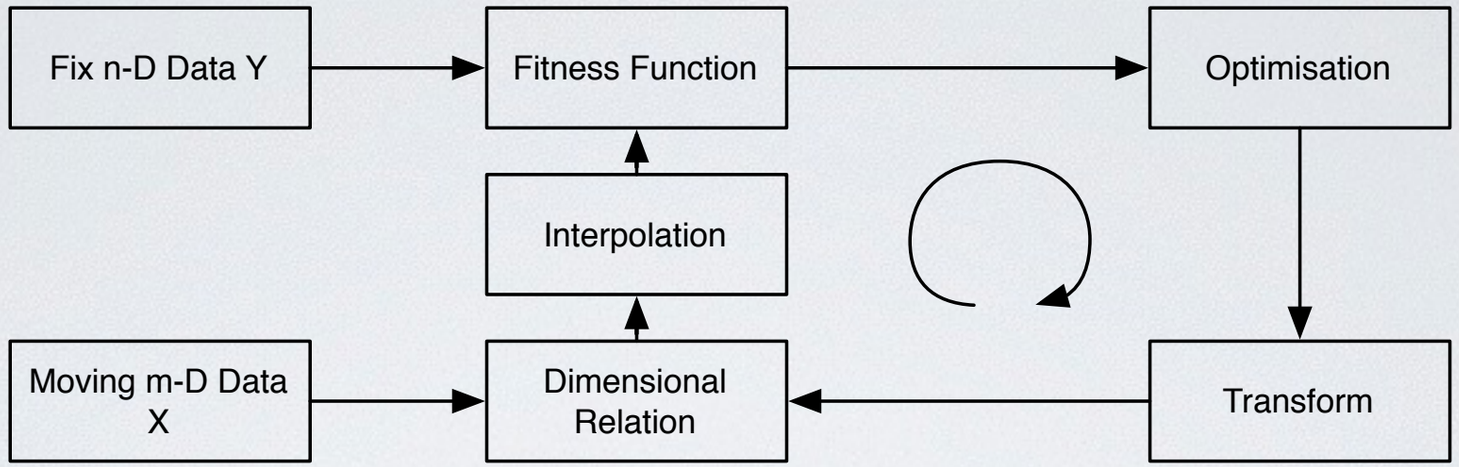
- Evaluate each generated model based on similarity with the current microscope observation

- 3-D to 2-D registration problematic

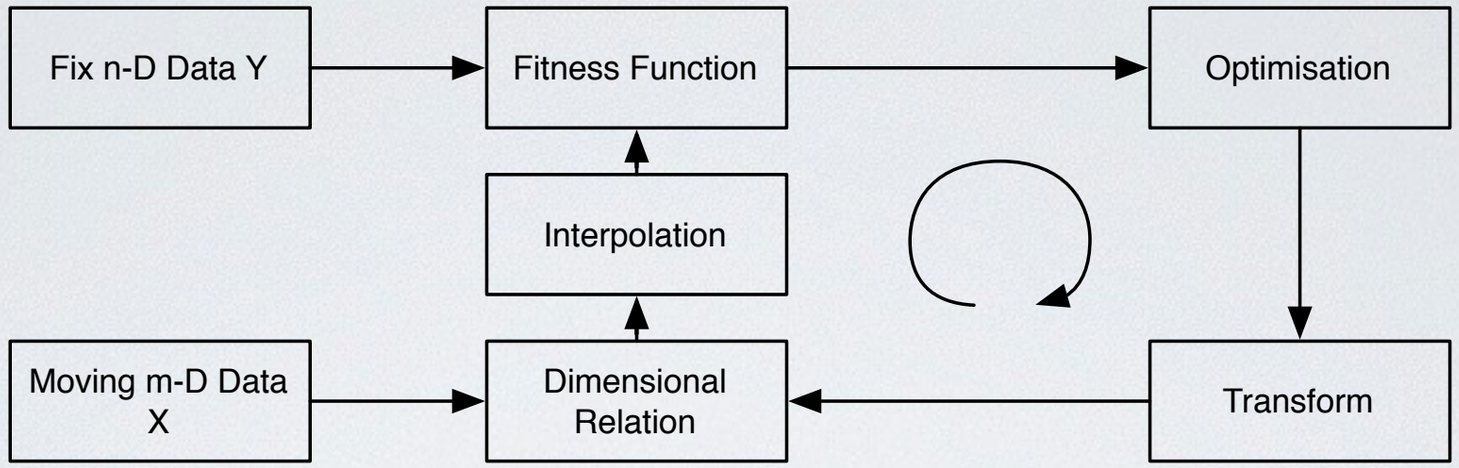
SELECTION MODULE



SELECTION MODULE

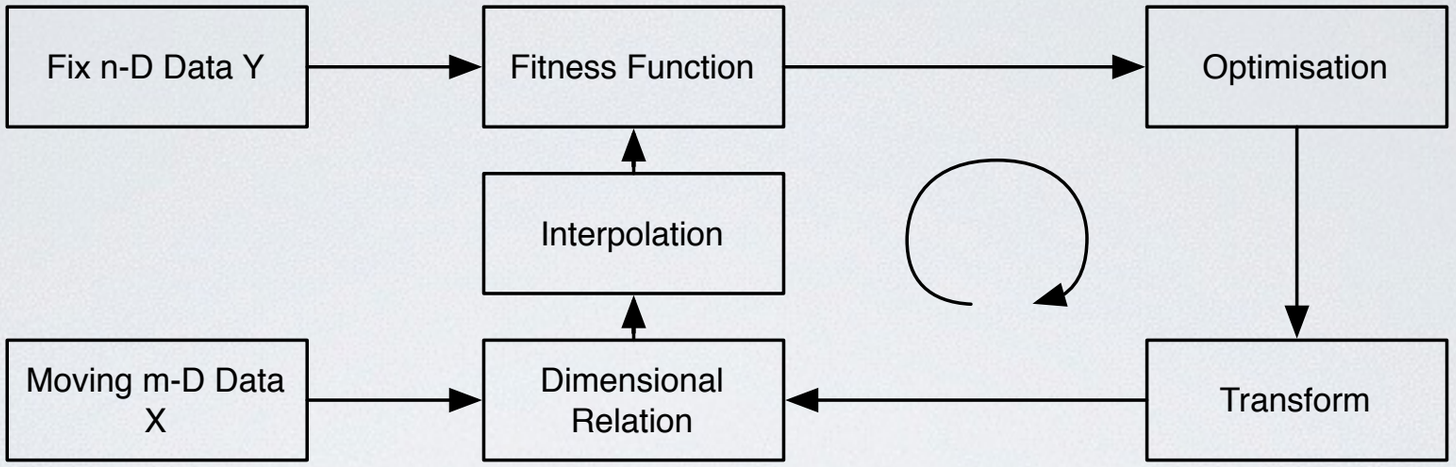


SELECTION MODULE



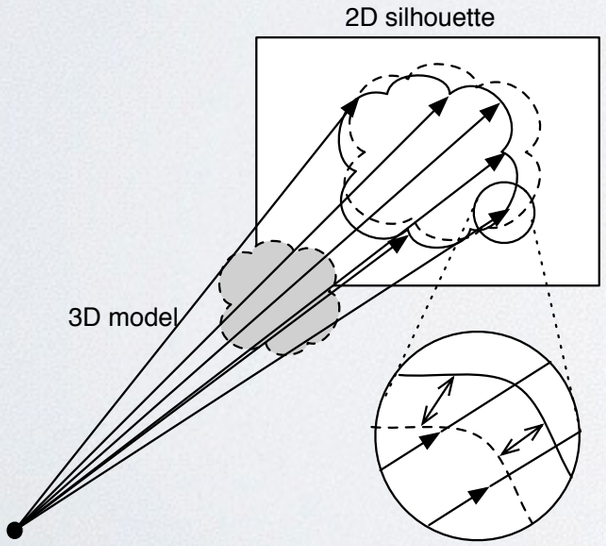
- Dimensional relation in registration (Markelj et. al., 12)

SELECTION MODULE

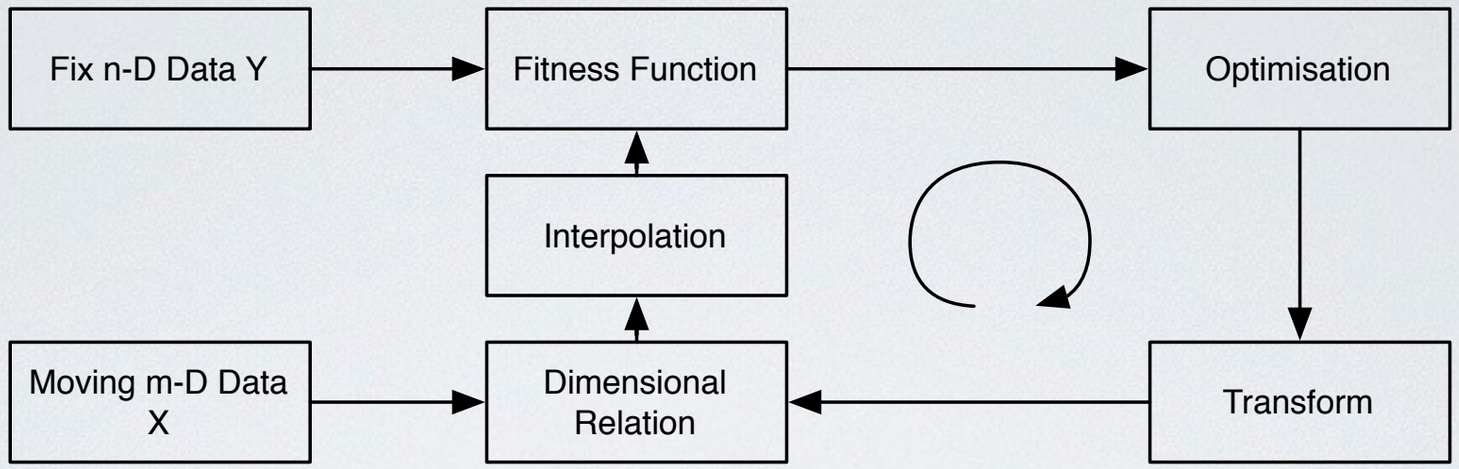


- Dimensional relation in registration (Markelj et. al., 12)

$$Proj(T(X^{3d}_{mov})) = T(X^{2d}_{mov}) = Y^{2d}_{fix}$$



SELECTION MODULE



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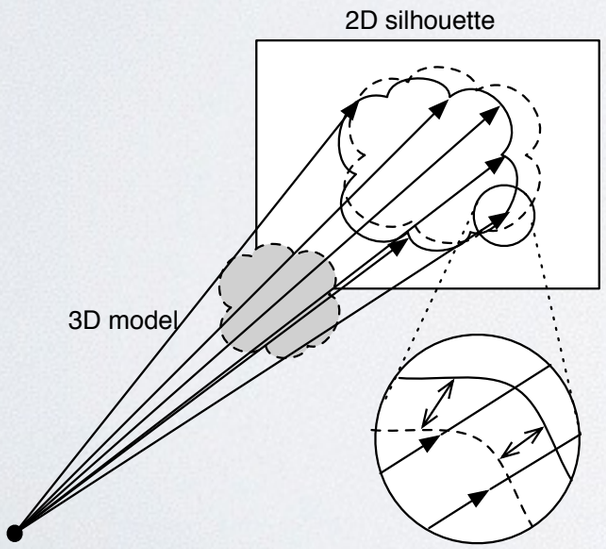
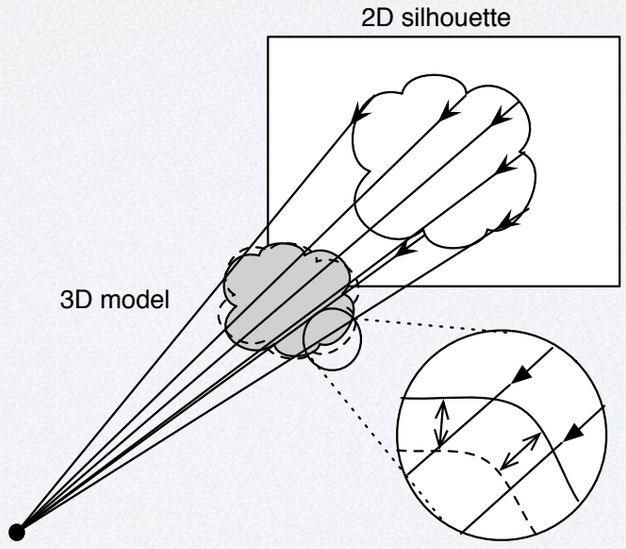
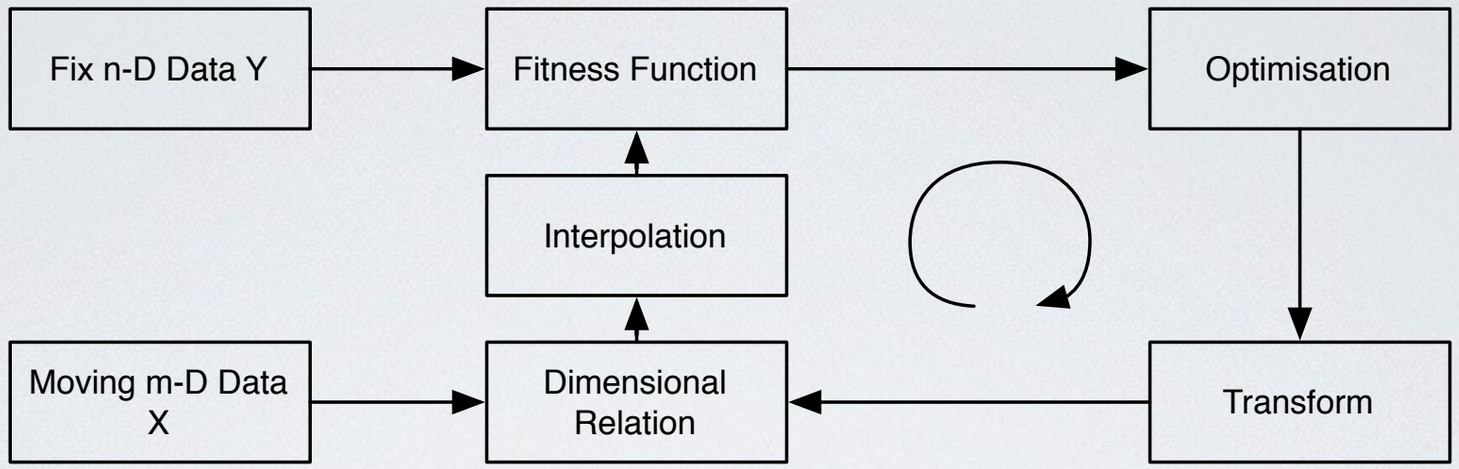
$$Proj(T(X^{3d}_{mov})) = T(X^{2d}_{mov}) = Y^{2d}_{fix}$$



$$Y^{3d}_{fix} = T(X^{3d}_{mov}) = Bproj(T(X^{2d}_{mov}))$$



SELECTION MODULE



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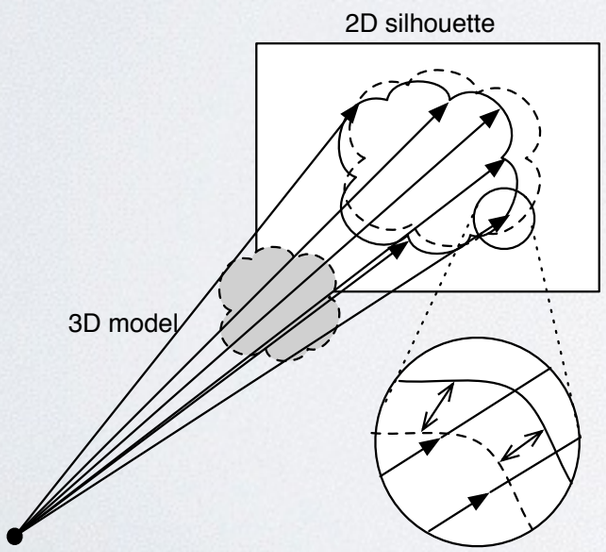
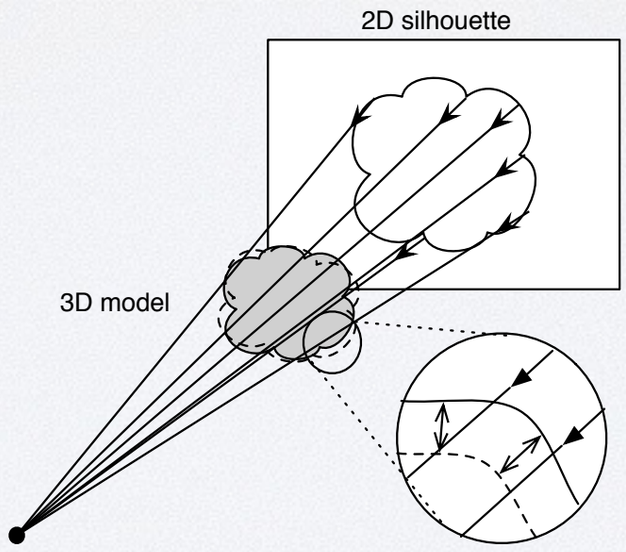
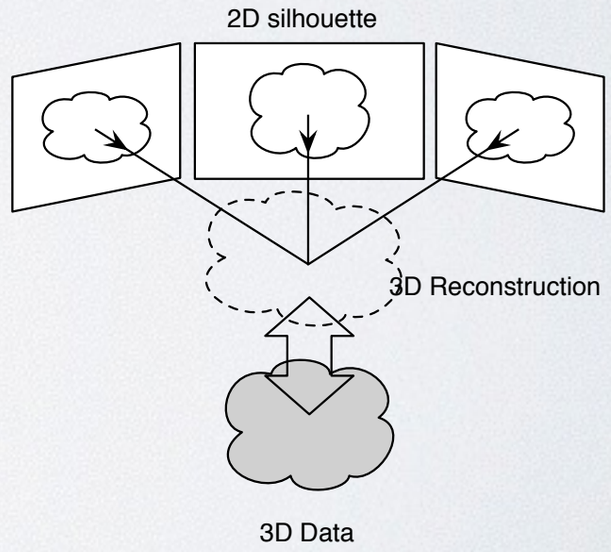
$$Proj(T(X^{3d}_{mov})) = T(X^{2d}_{mov}) = Y^{2d}_{fix}$$



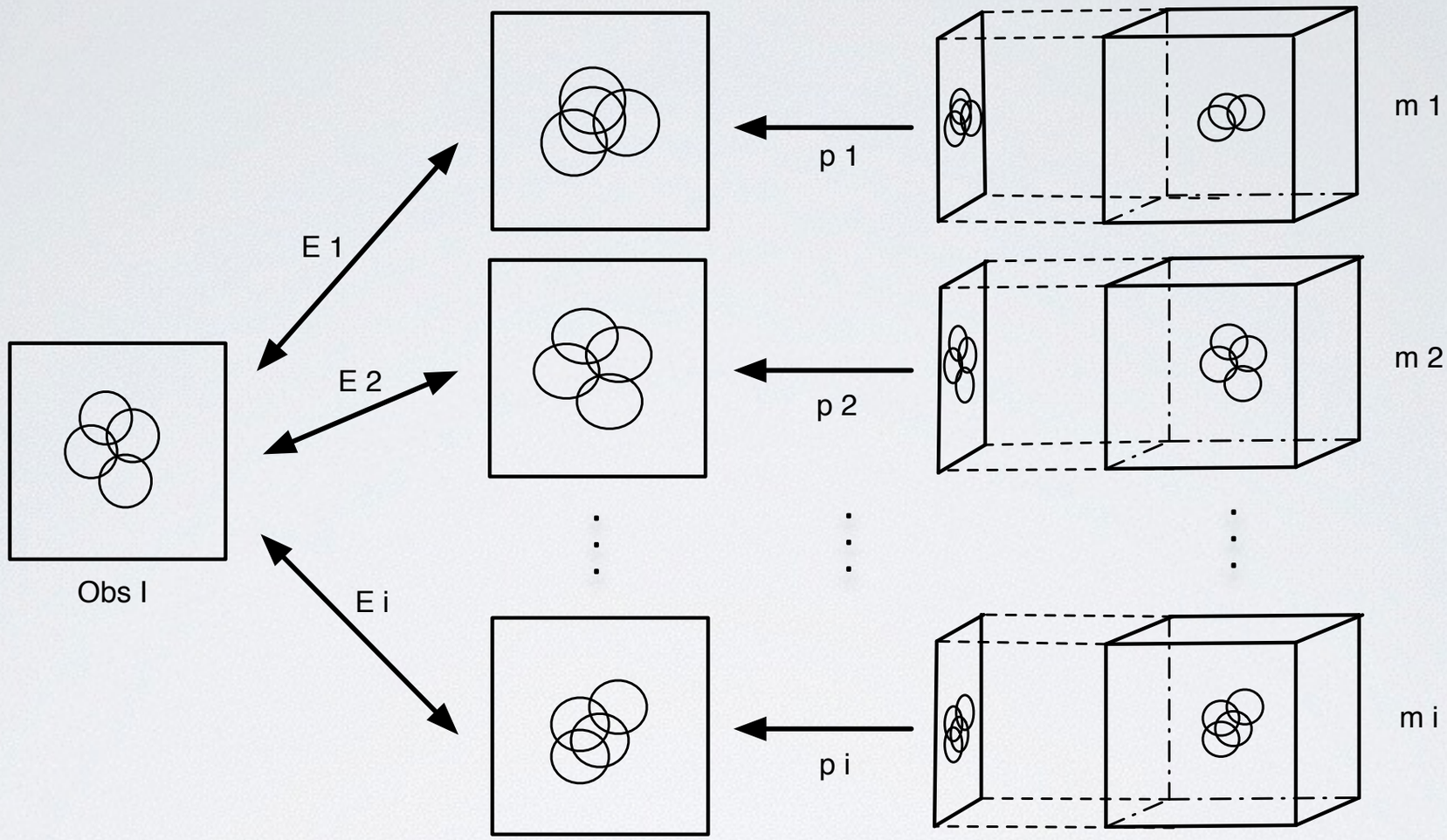
$$Y^{3d}_{fix} = T(X^{3d}_{mov}) = Bproj(T(X^{2d}_{mov}))$$



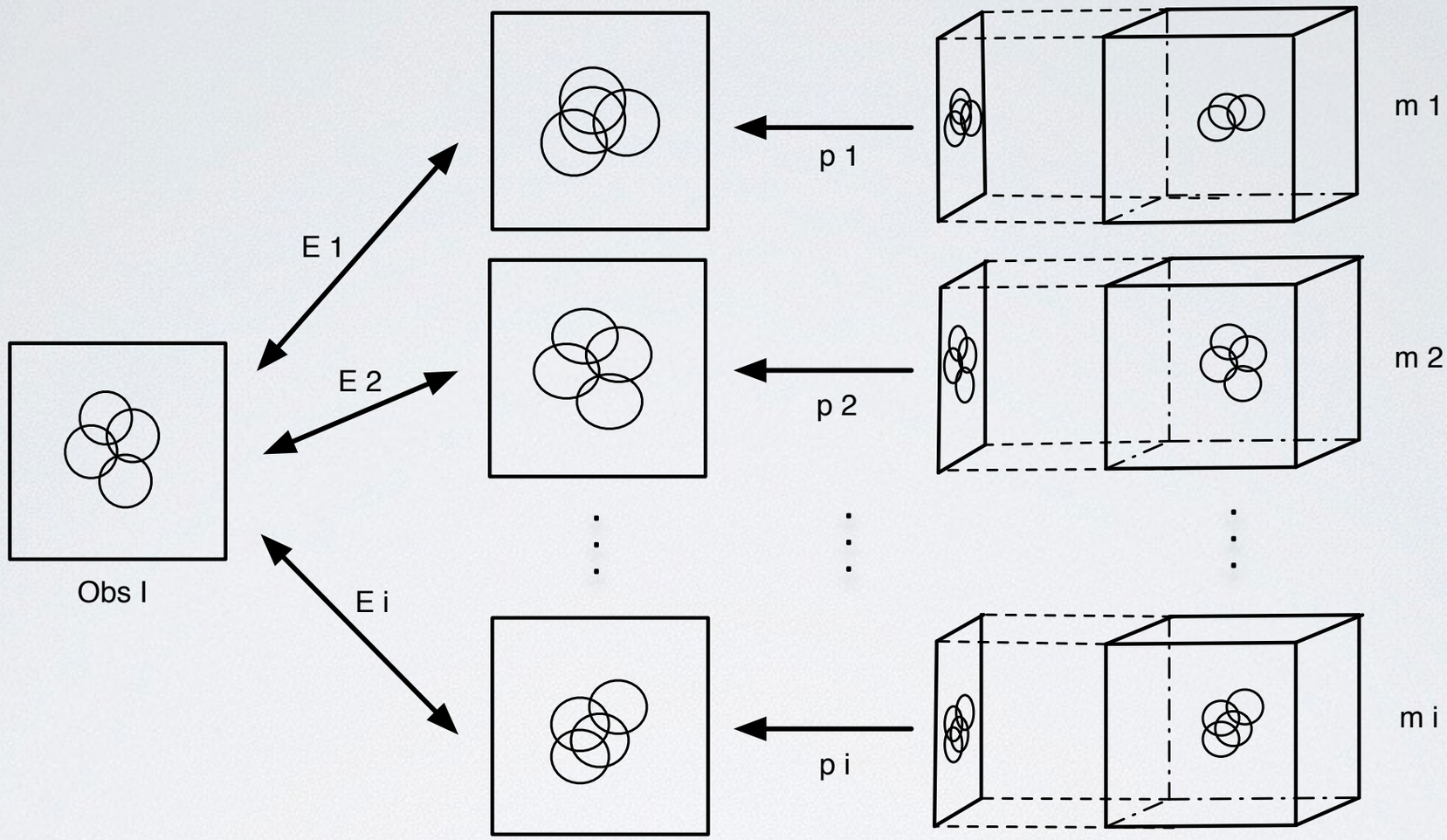
$$Y^{3d}_{fix} = T(X^{3d}_{mov}) = Rec(T(X^{2d}_{mov_i}))$$



SELECTION MODULE



SELECTION MODULE



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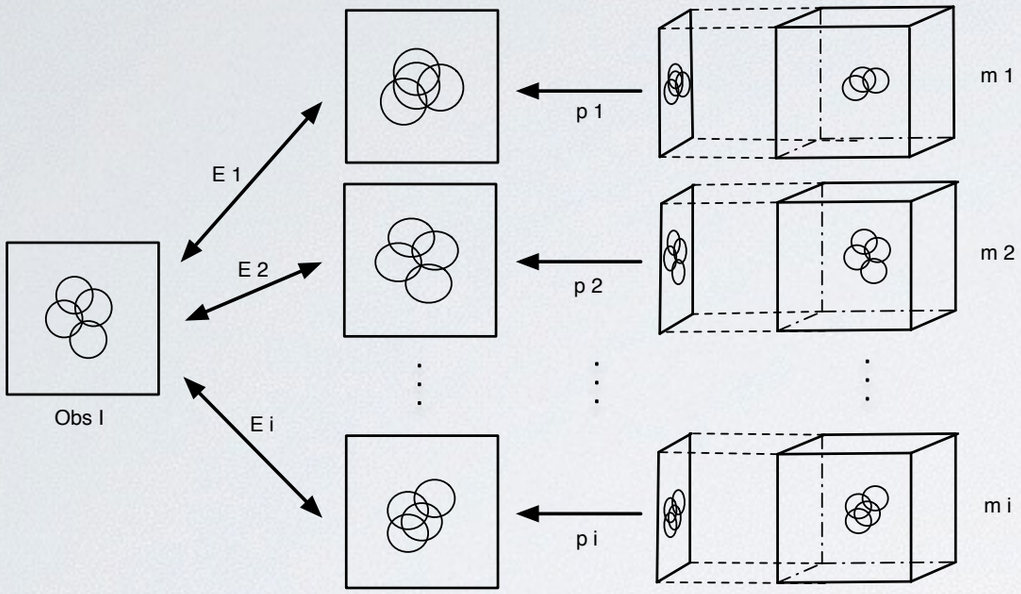

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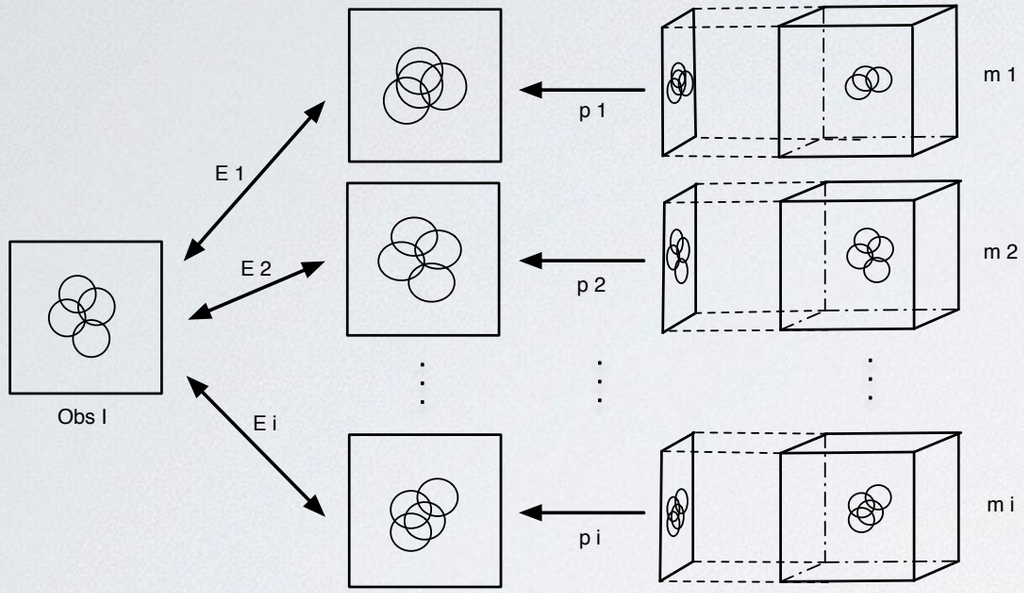
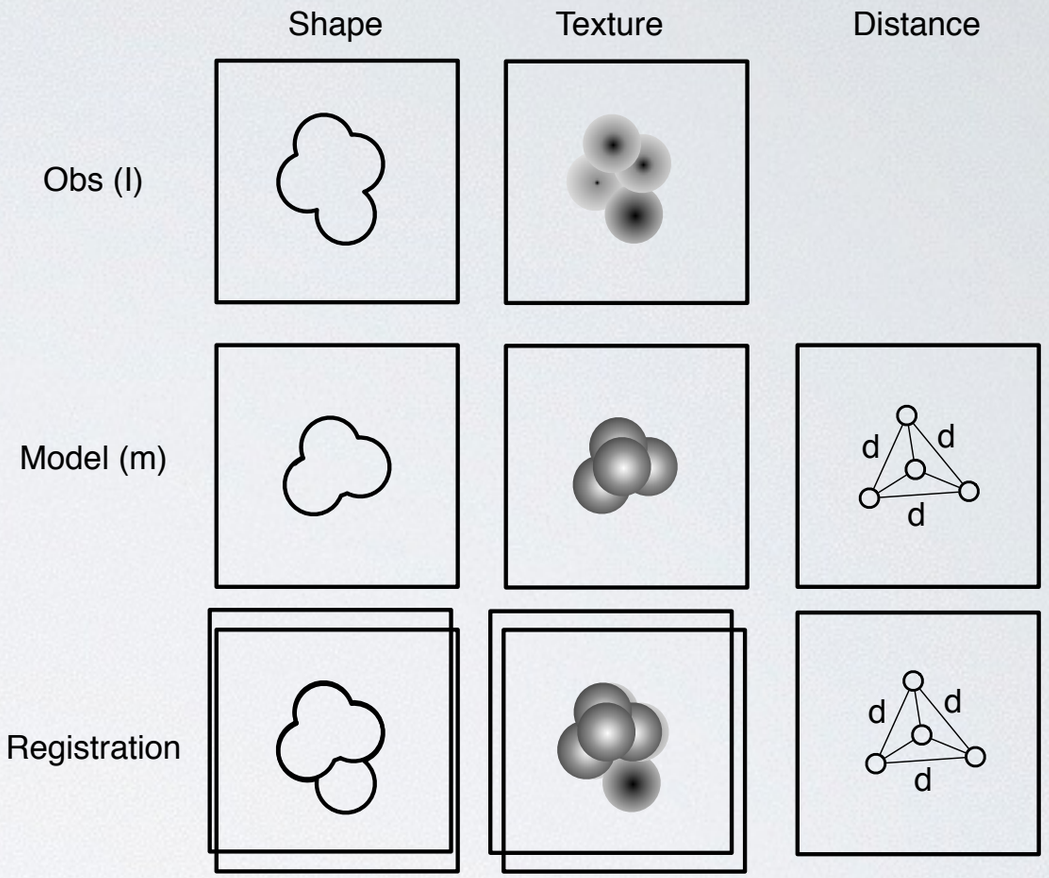
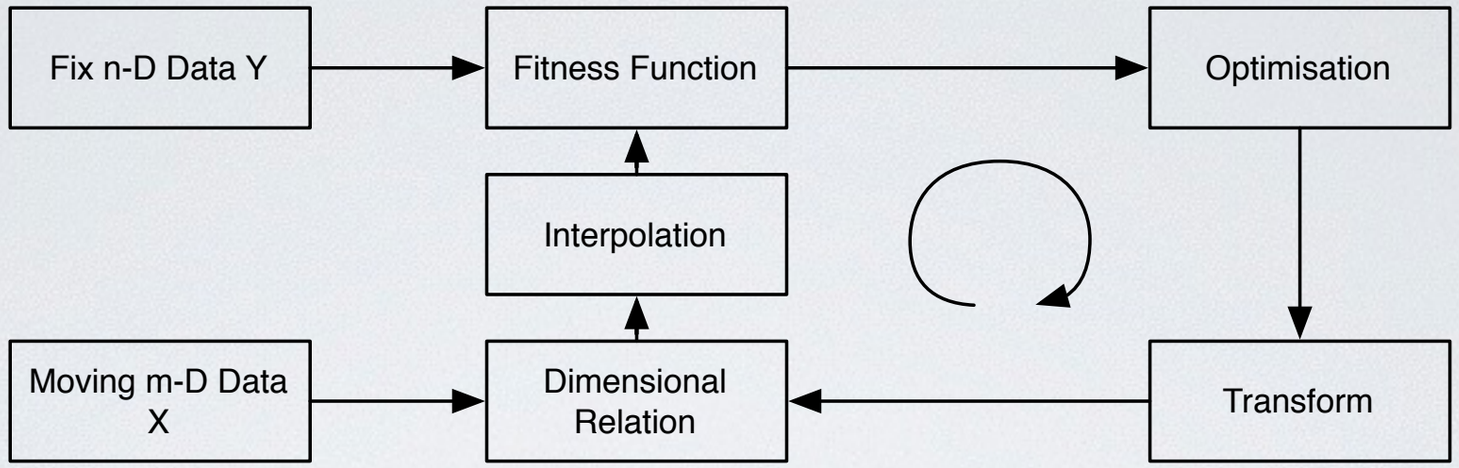




$$E(m) = \underbrace{E_{shape}(p(m),I) + E_{texture}(p(m),I)}_{external} + \underbrace{E_{violation}(m)}_{internal}$$

SELECTION MODULE



- Gradient descent optimisation process
- Rigid geometrical transform
- Linear interpolation

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- Introduction
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RESULTS AND VISUALISATION

- Application of the framework on different datasets

RESULTS AND VISUALISATION

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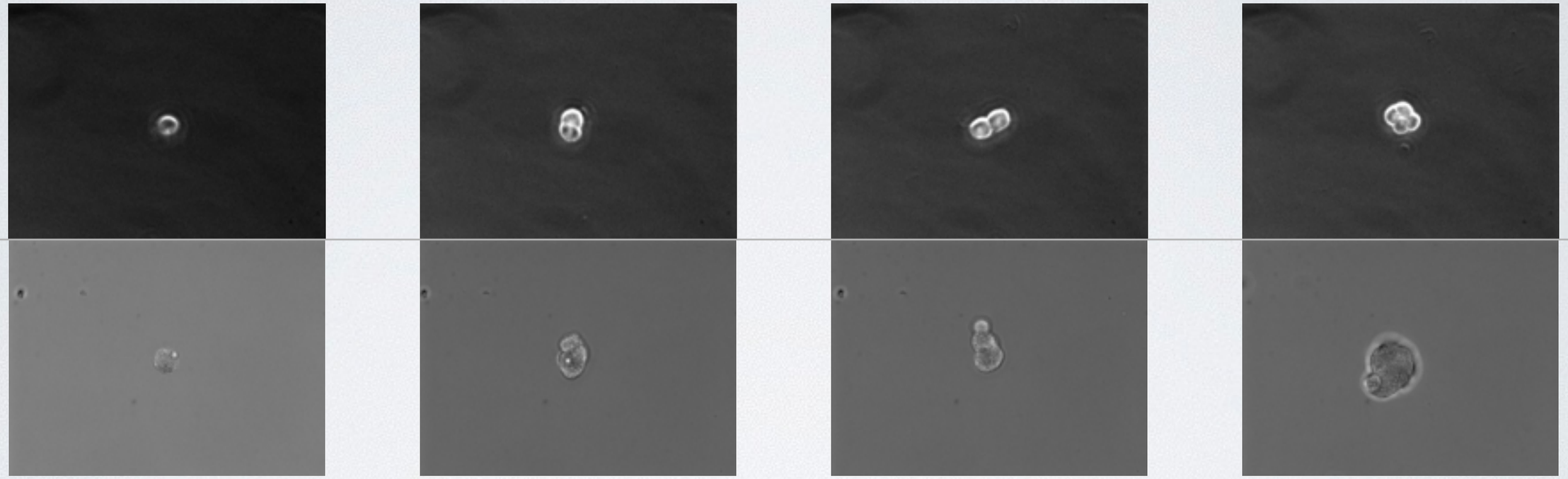
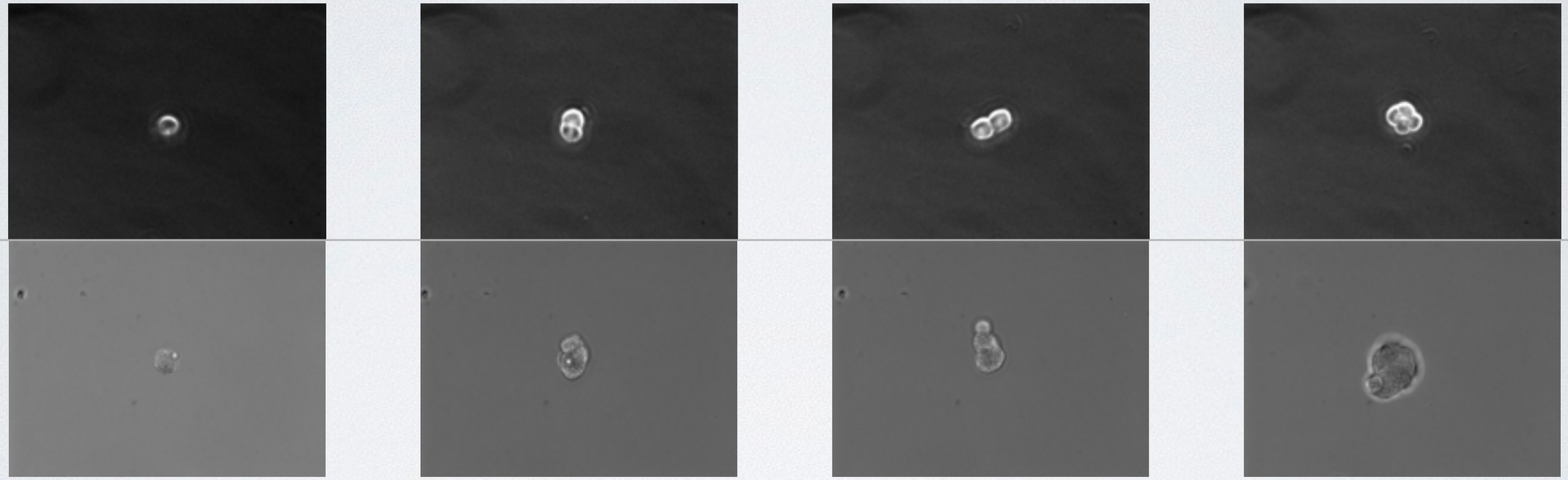


RESULTS AND VISUALISATION

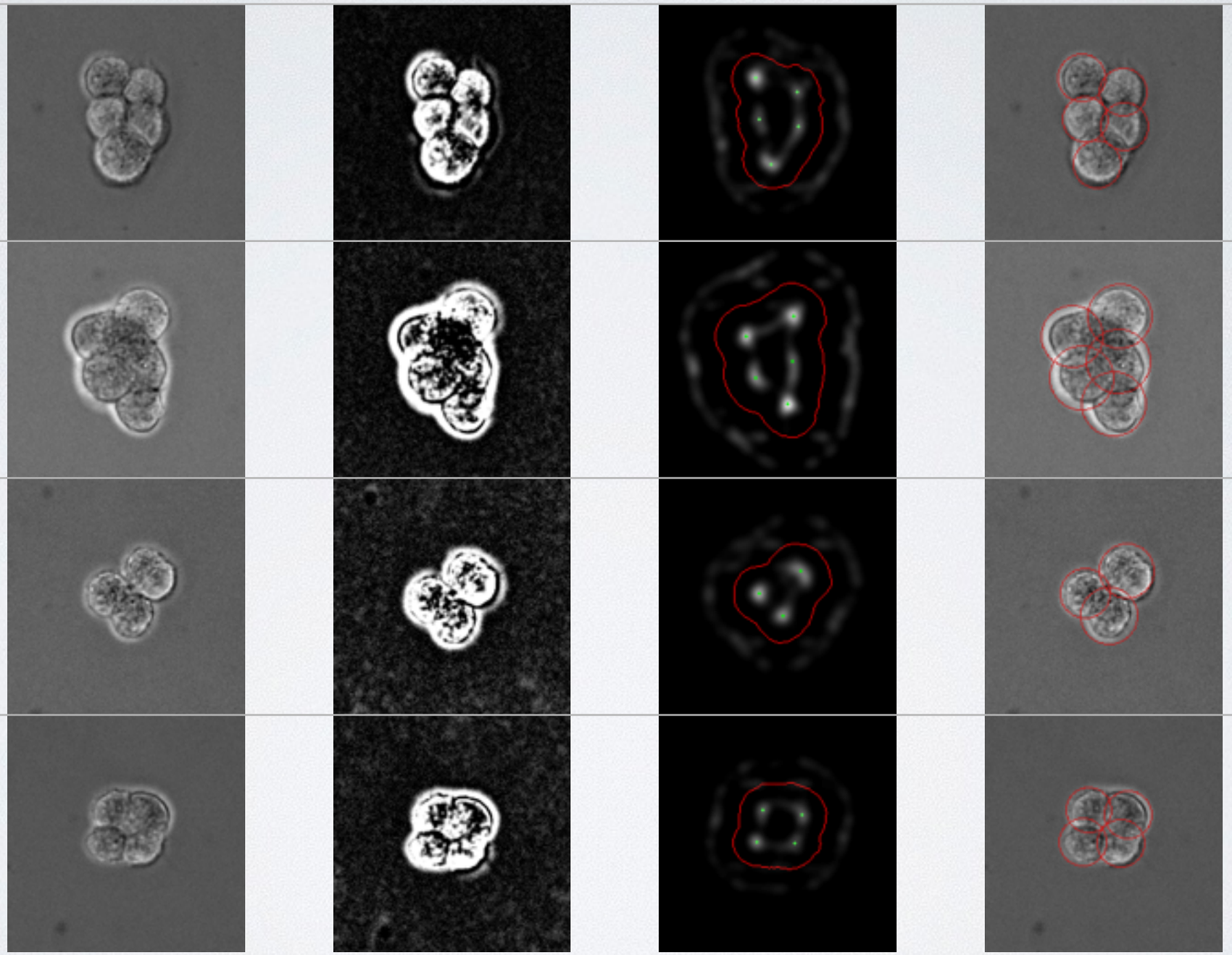
- Application of the framework on different datasets



- Observation of the results
  - over an entier sequence
  - at different time of the proliferation

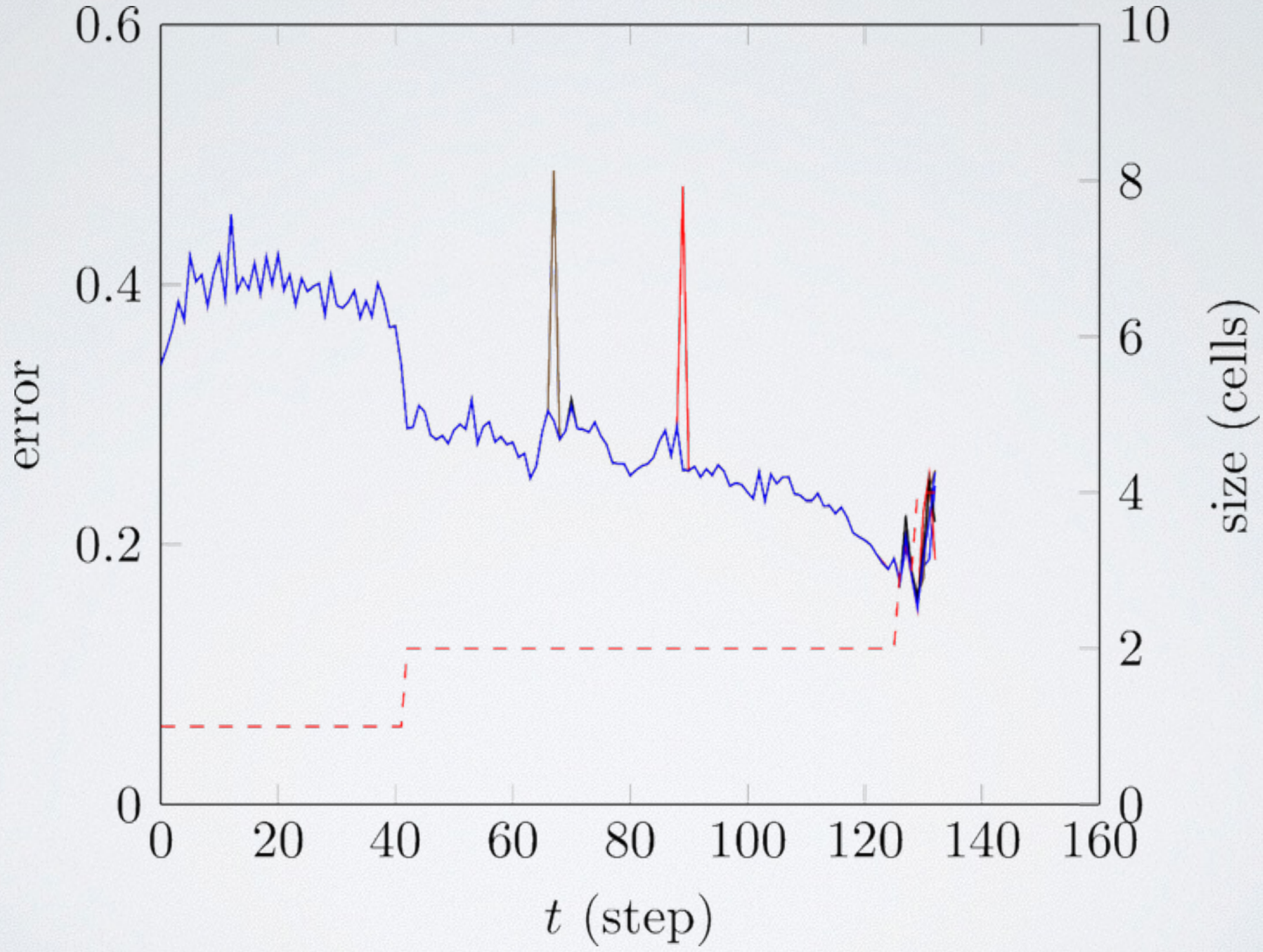
RESULTS AND VISUALISATION

raw restored process results



RESULTS AND VISUALISATION

EVOLUTION ALGORITHM METHOD



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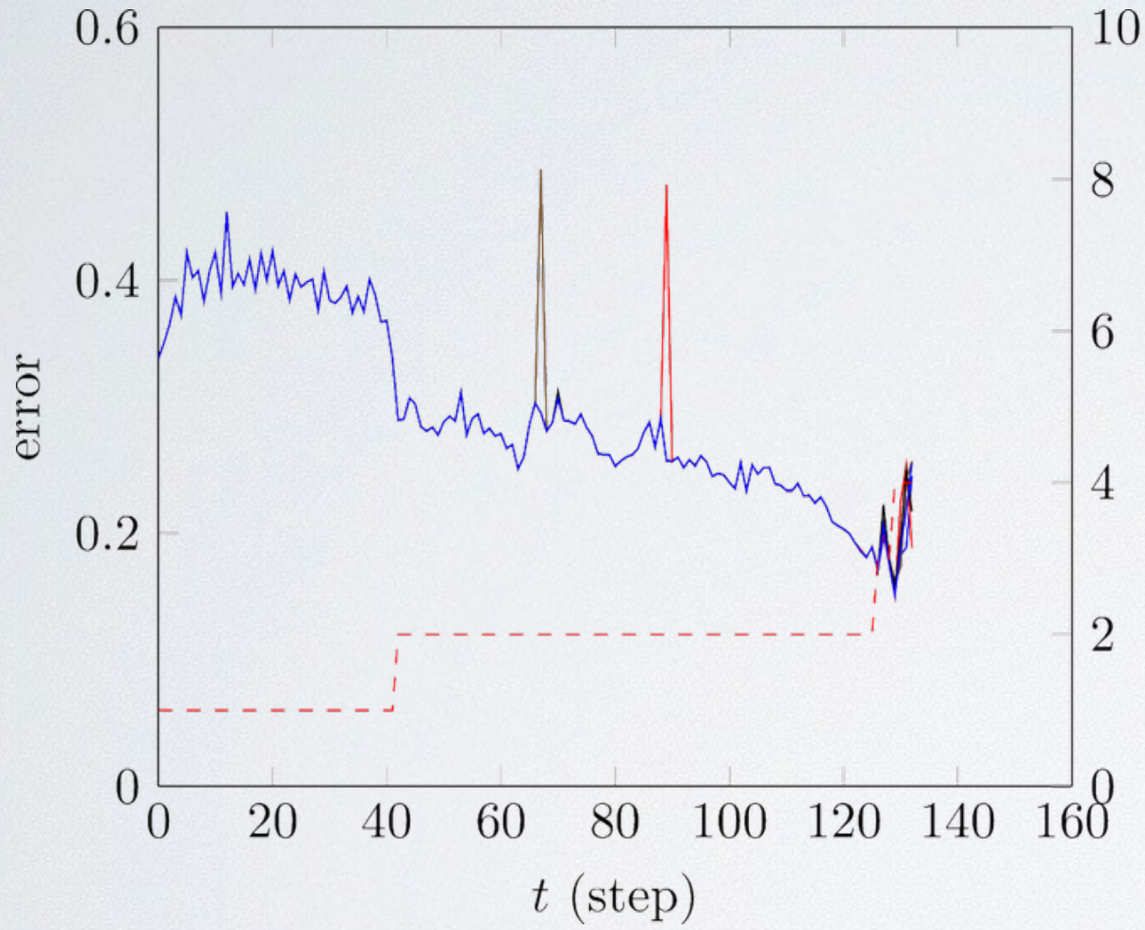

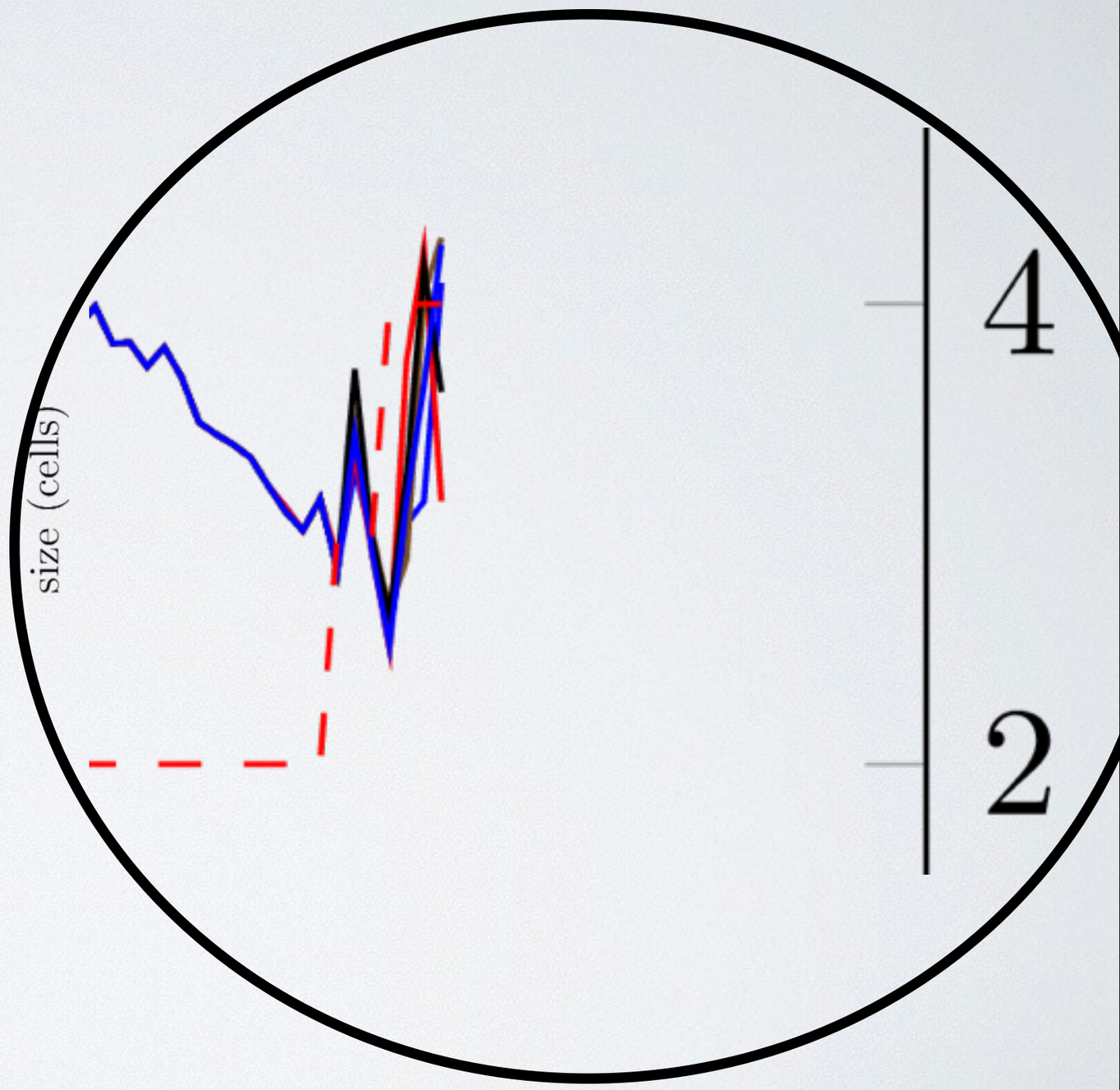

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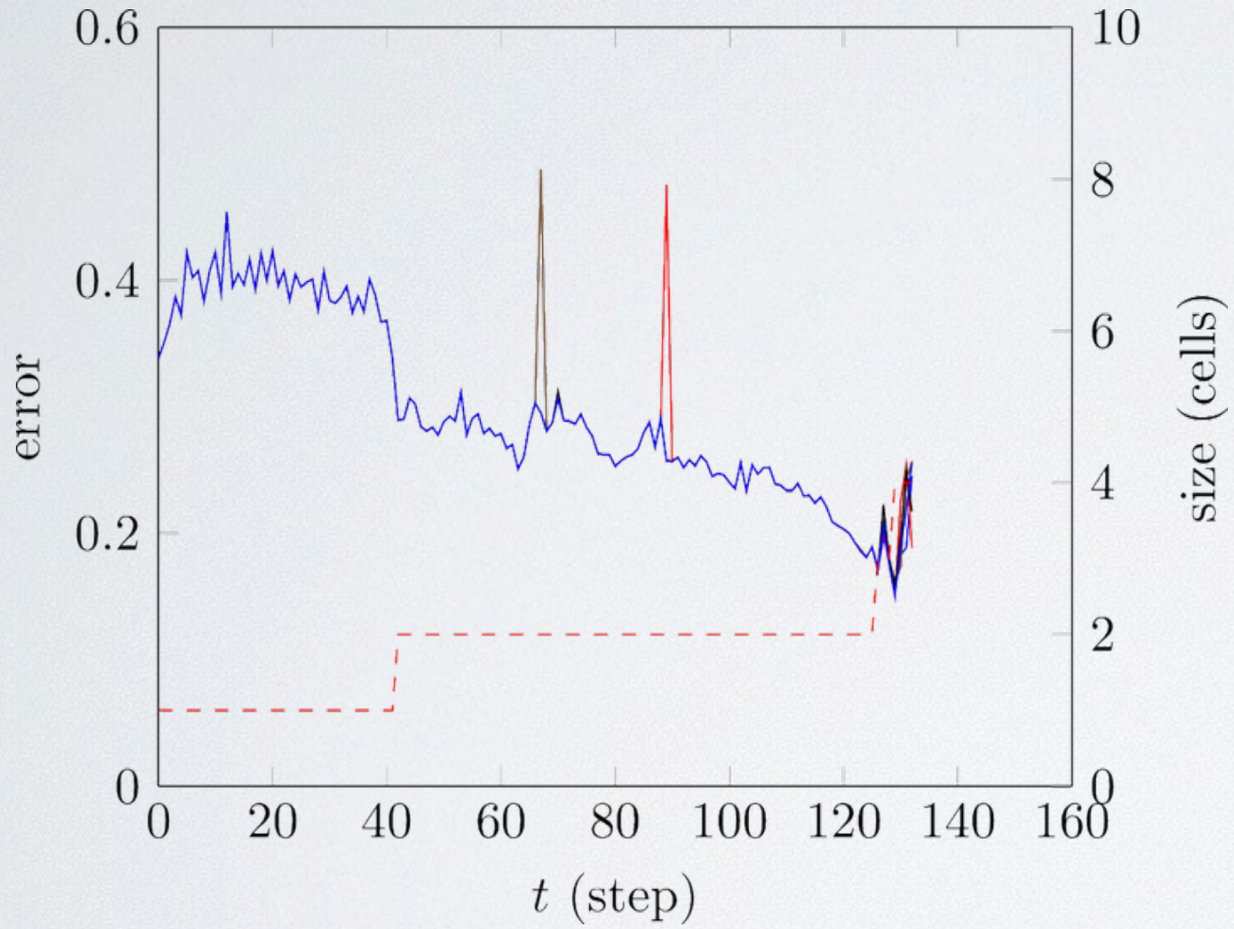
EVOLUTION ALGORITHM METHOD



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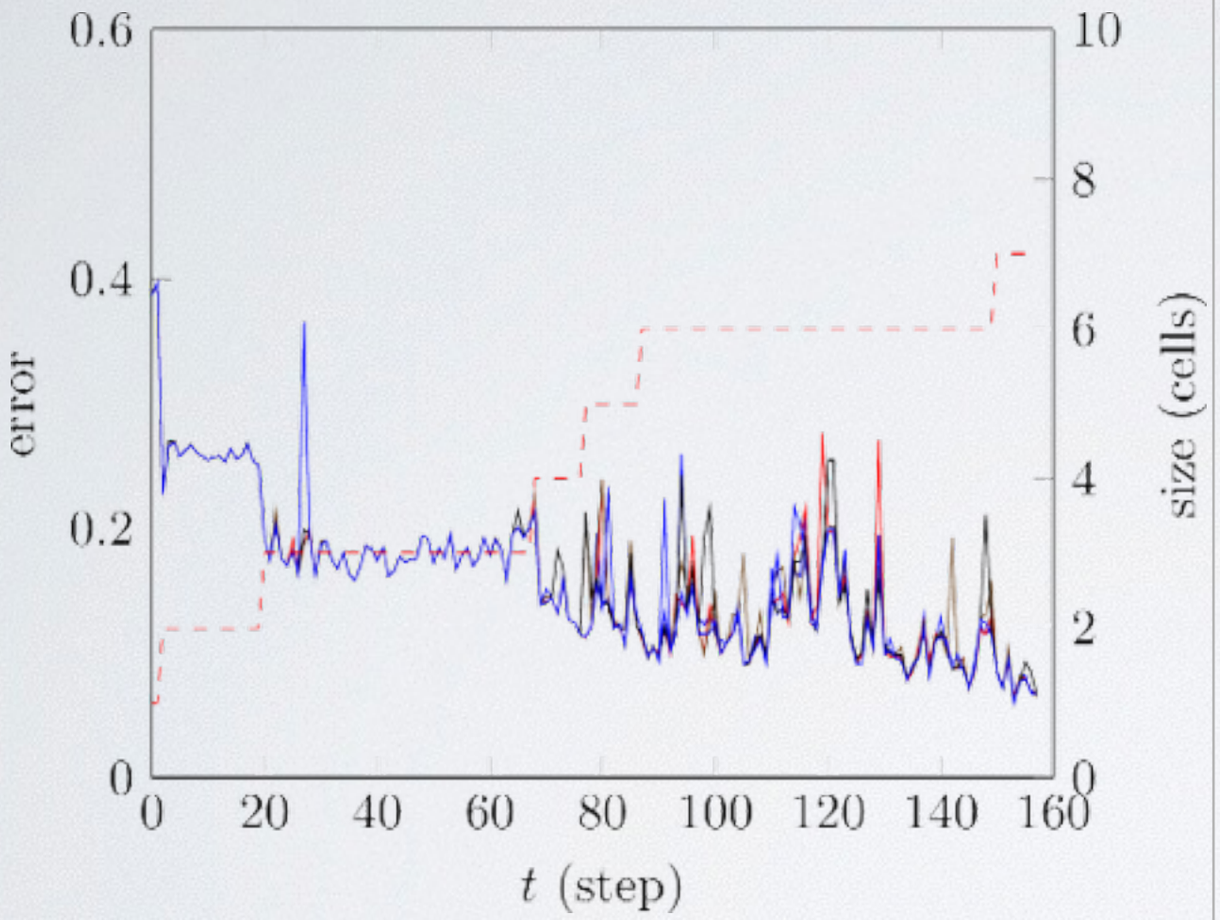
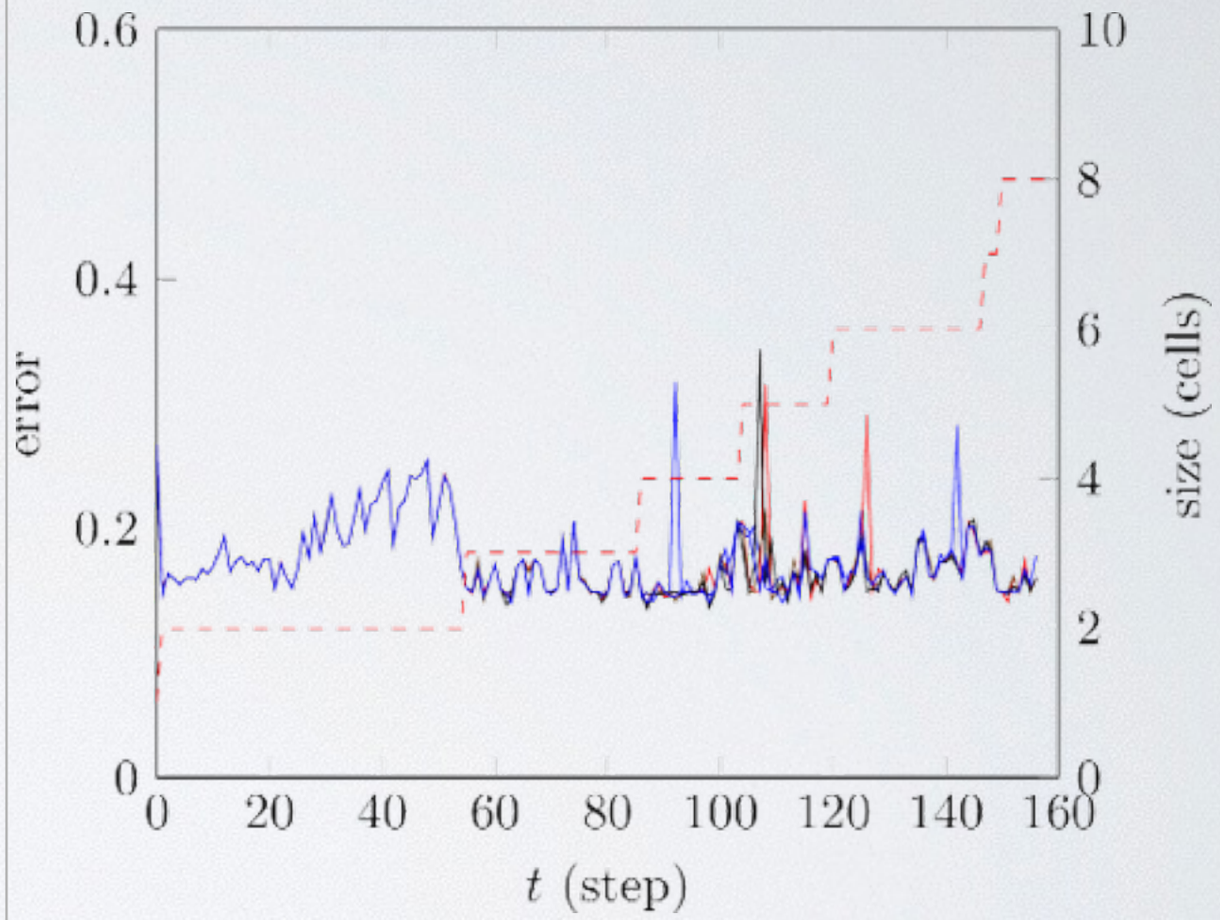
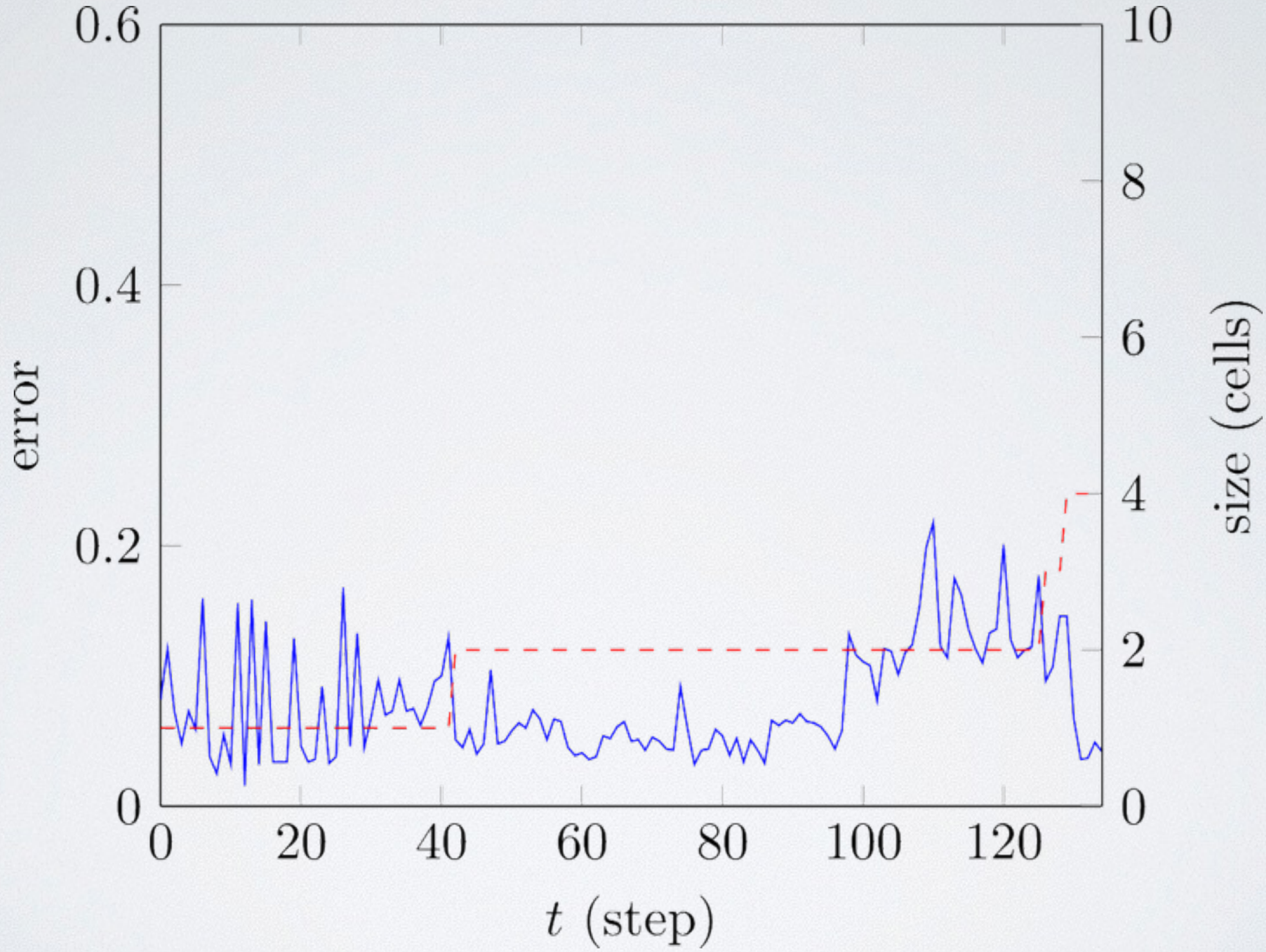




RESULTS AND VISUALISATION

PRIMAL DUAL DELAUNAY



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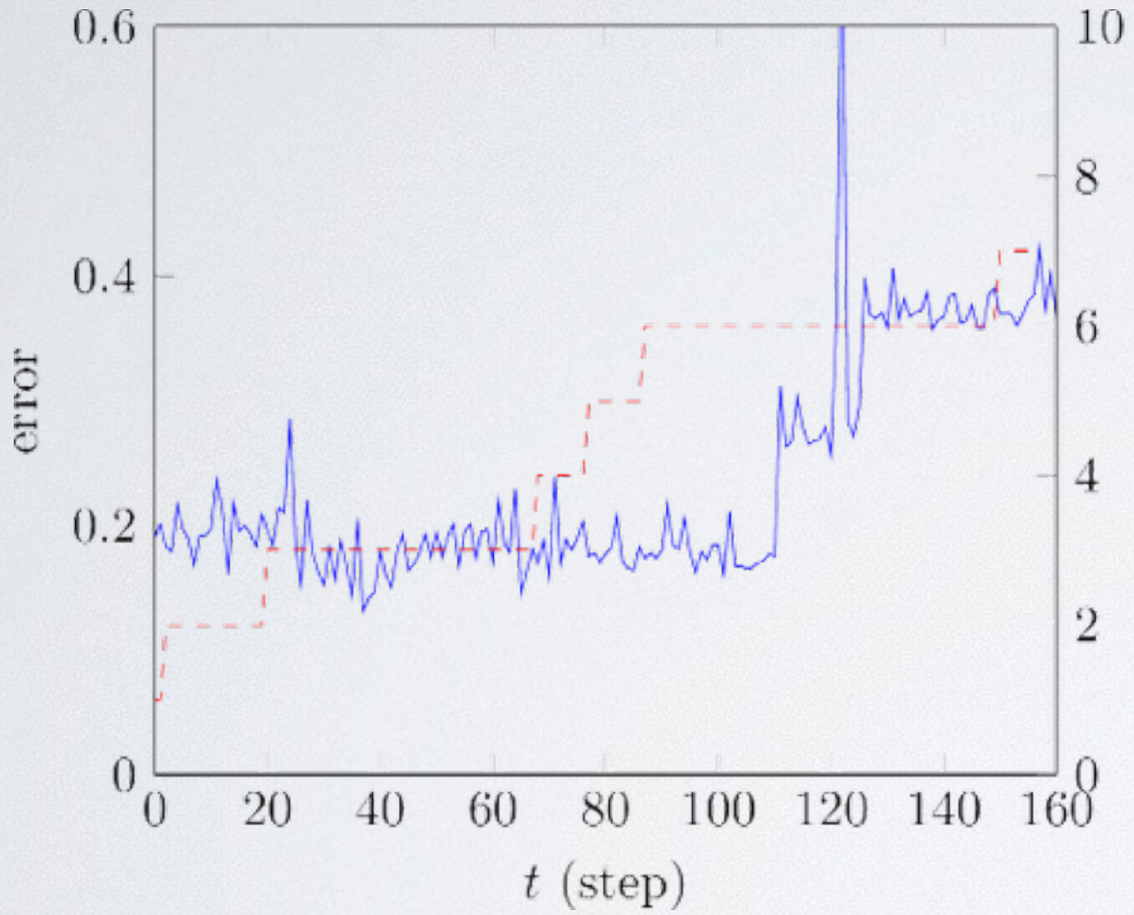

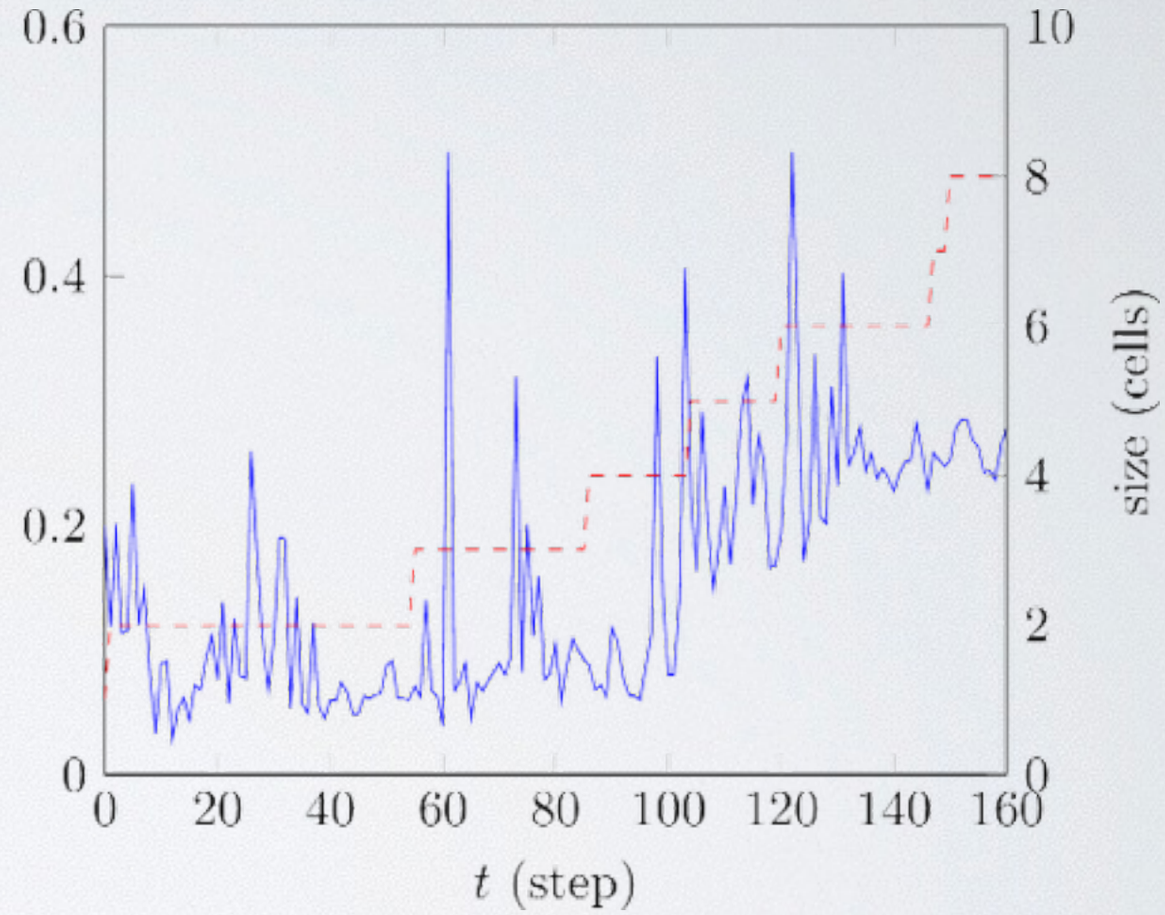

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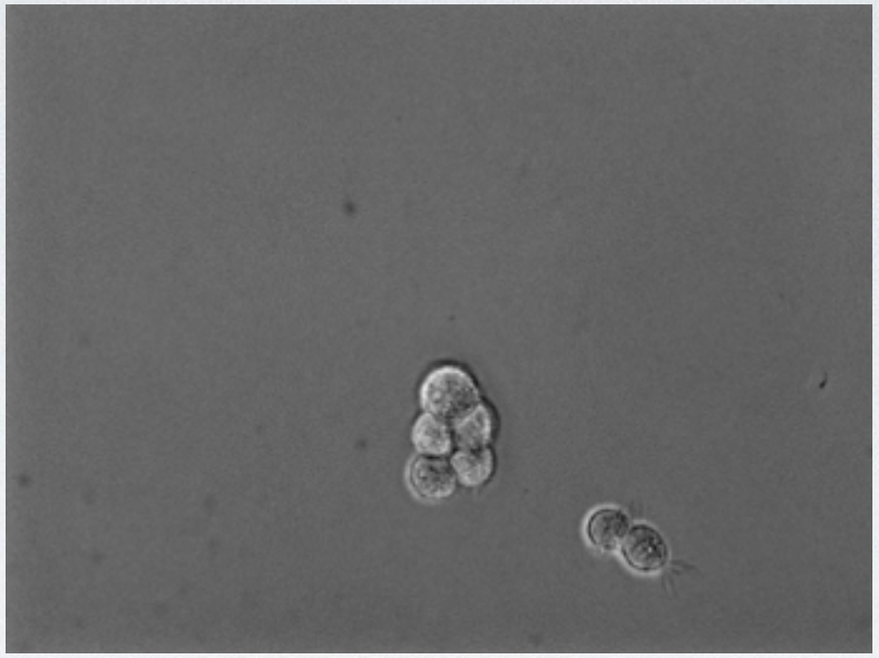

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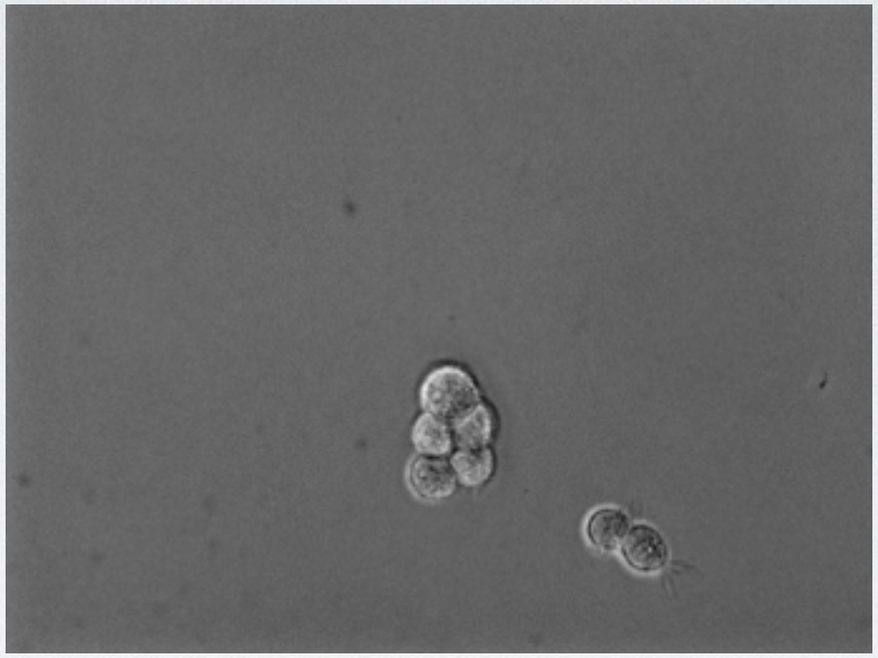

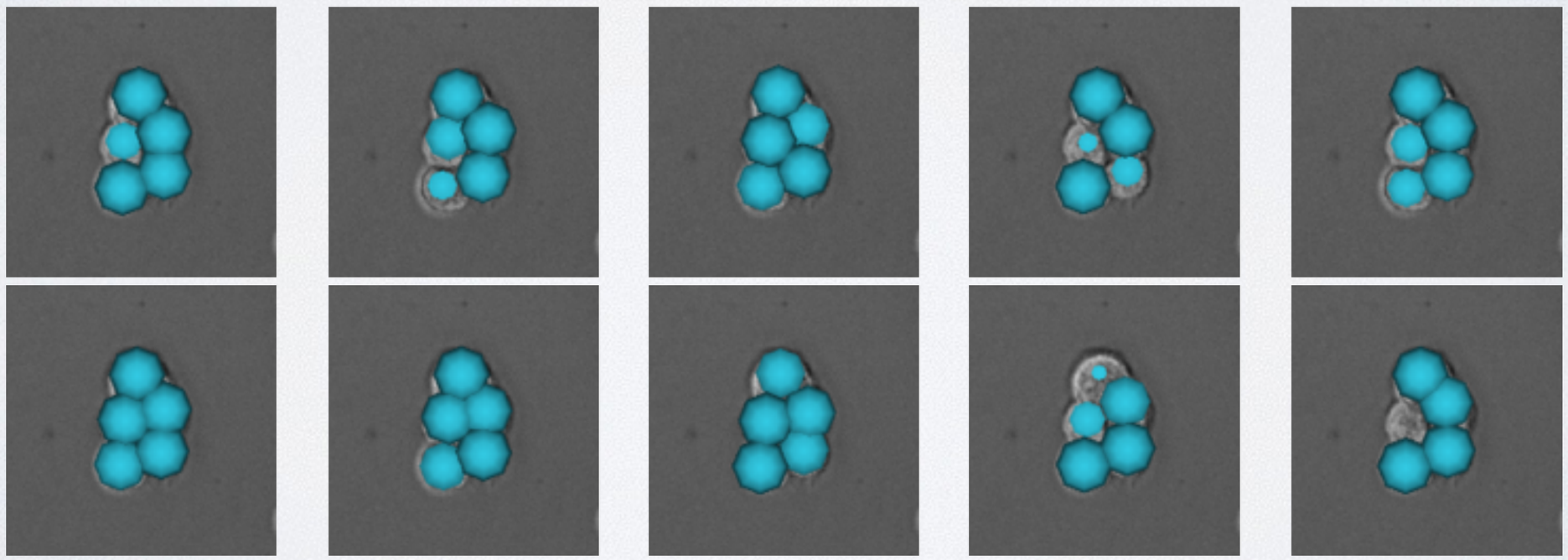

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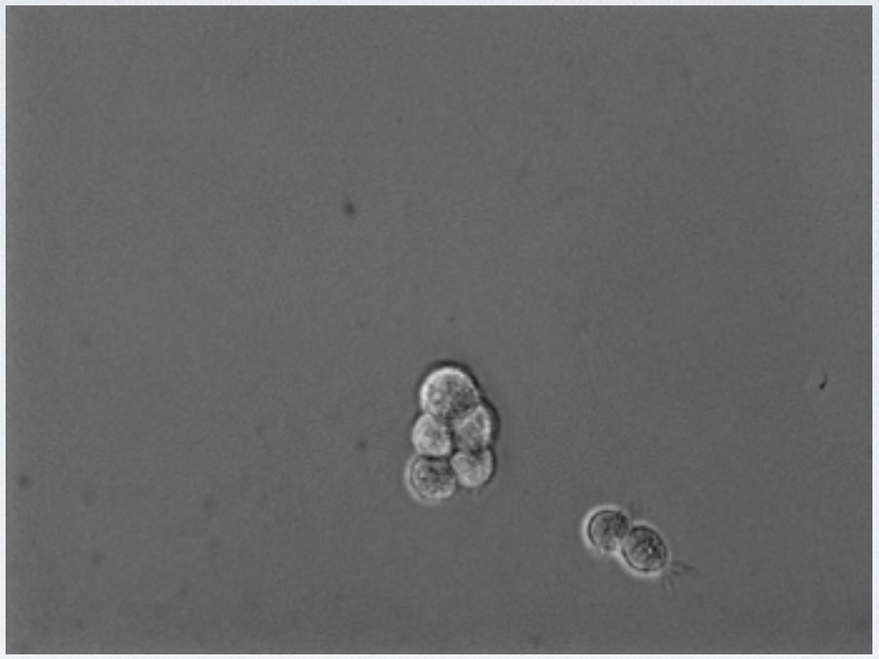

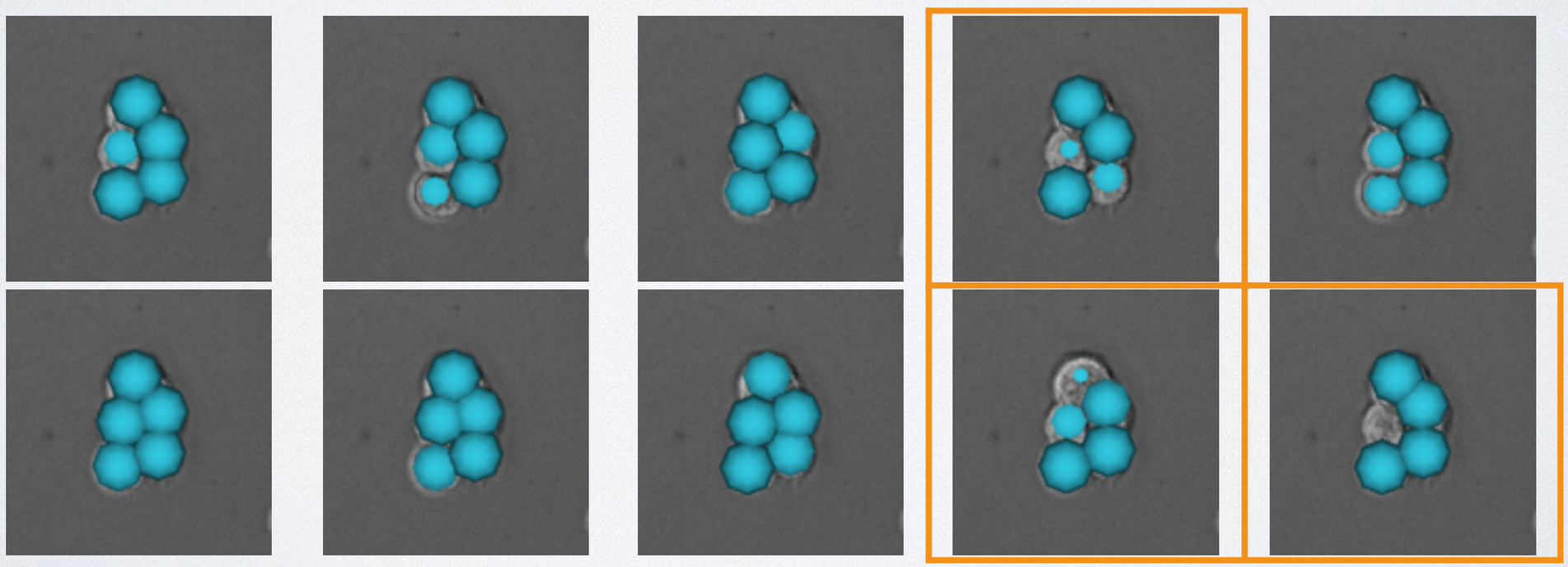

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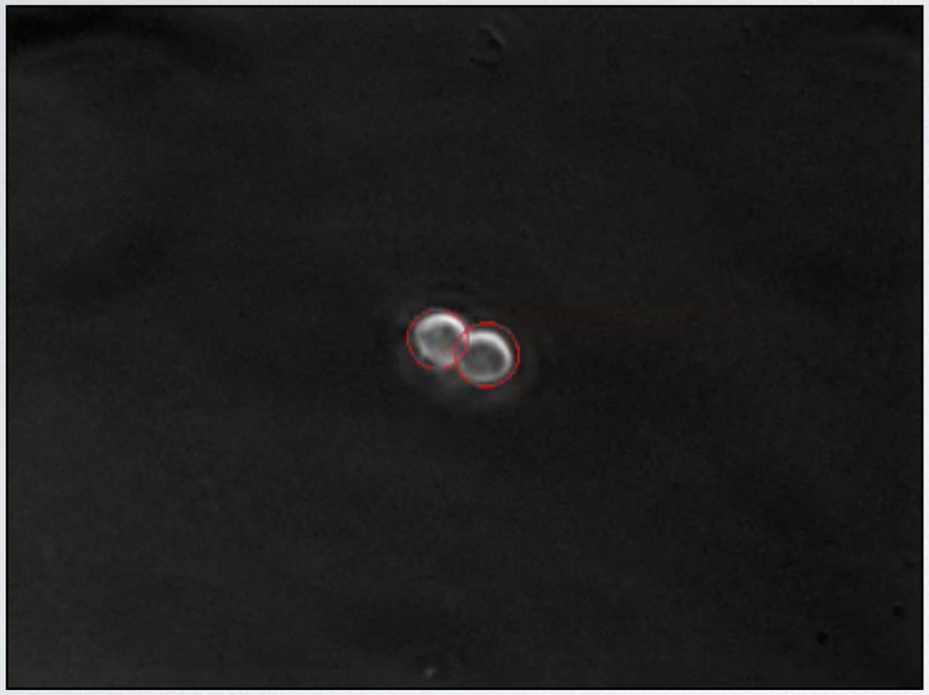

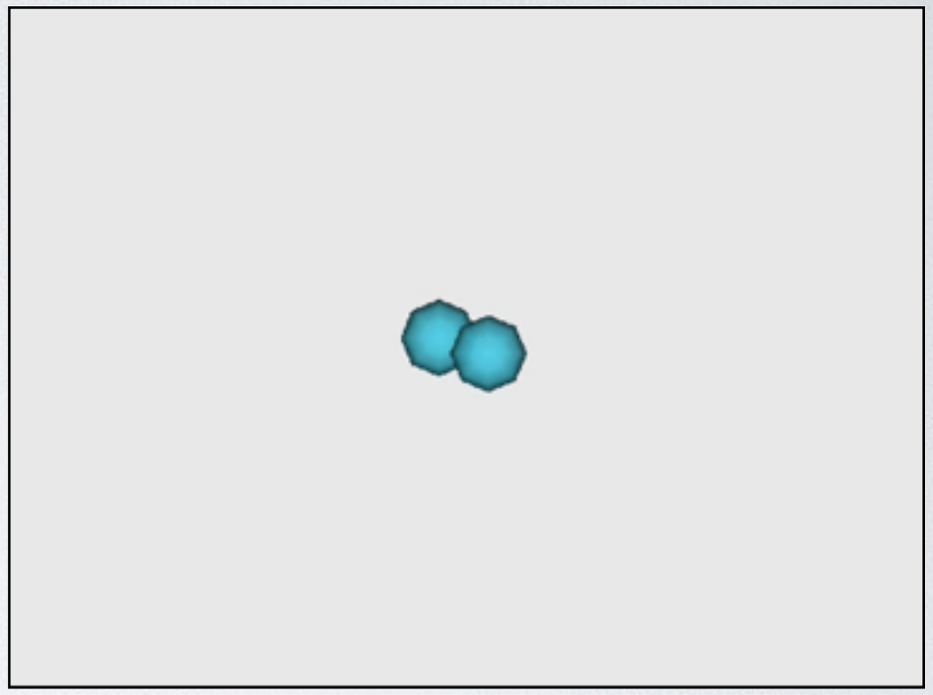

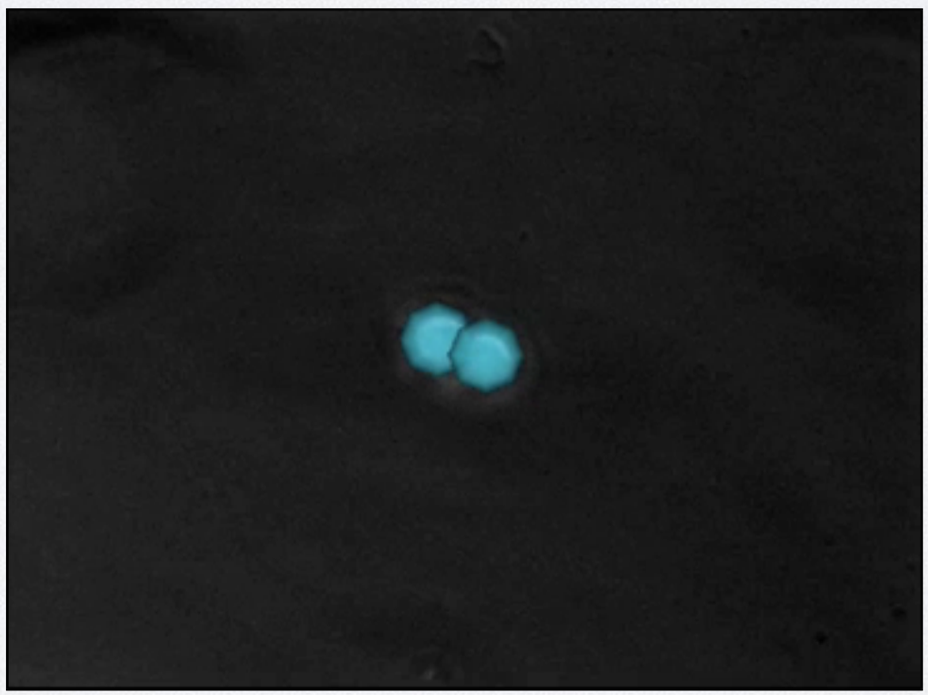

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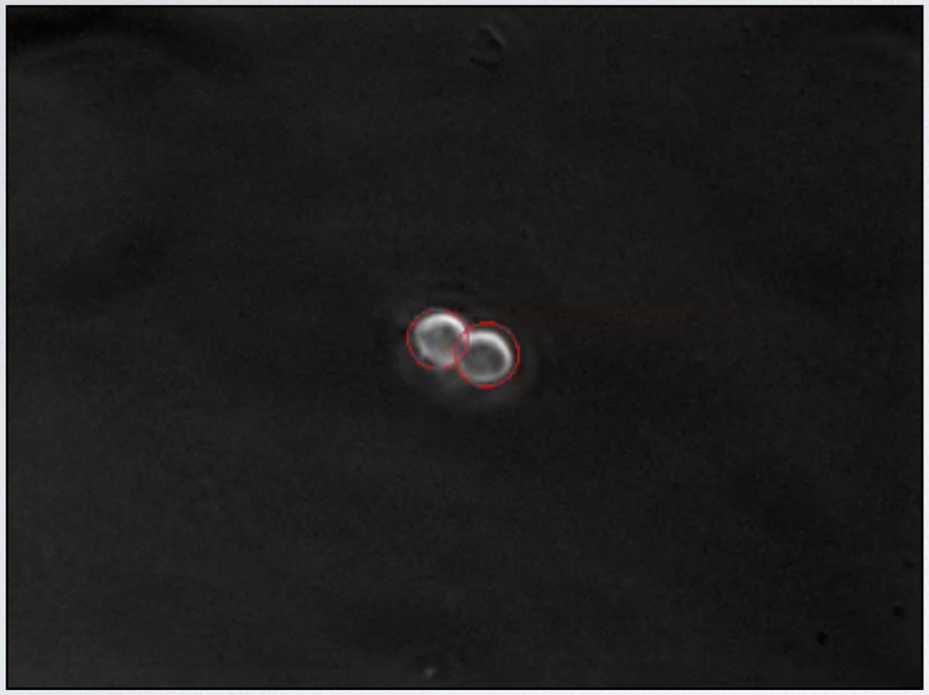

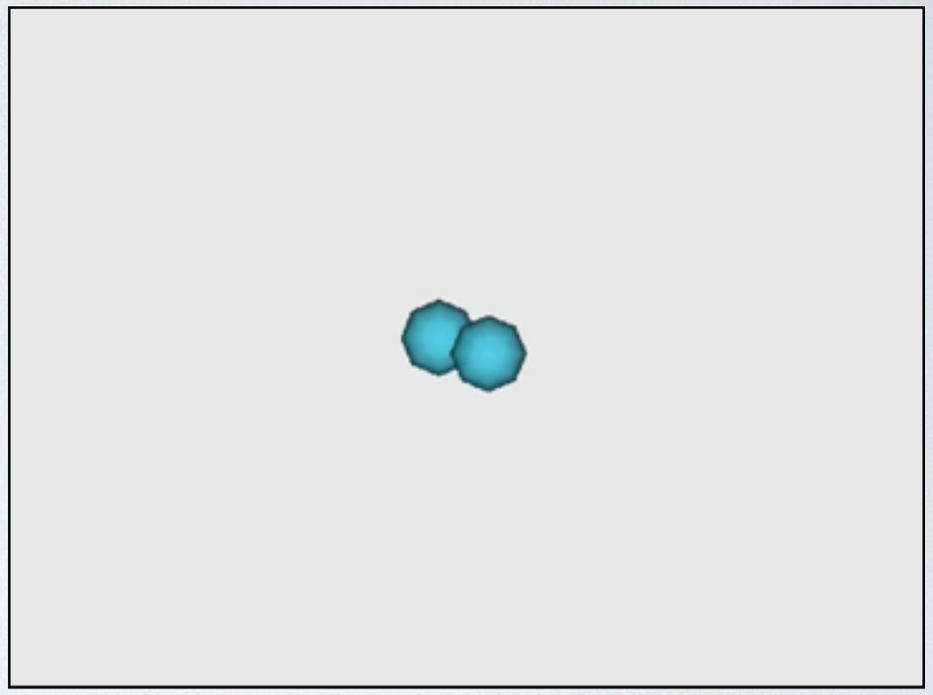

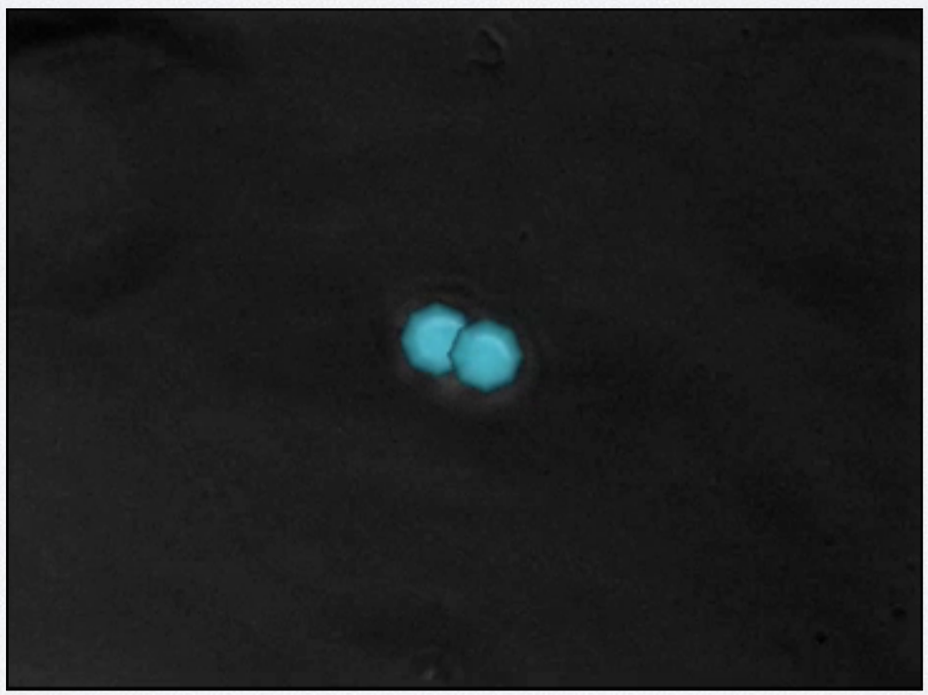

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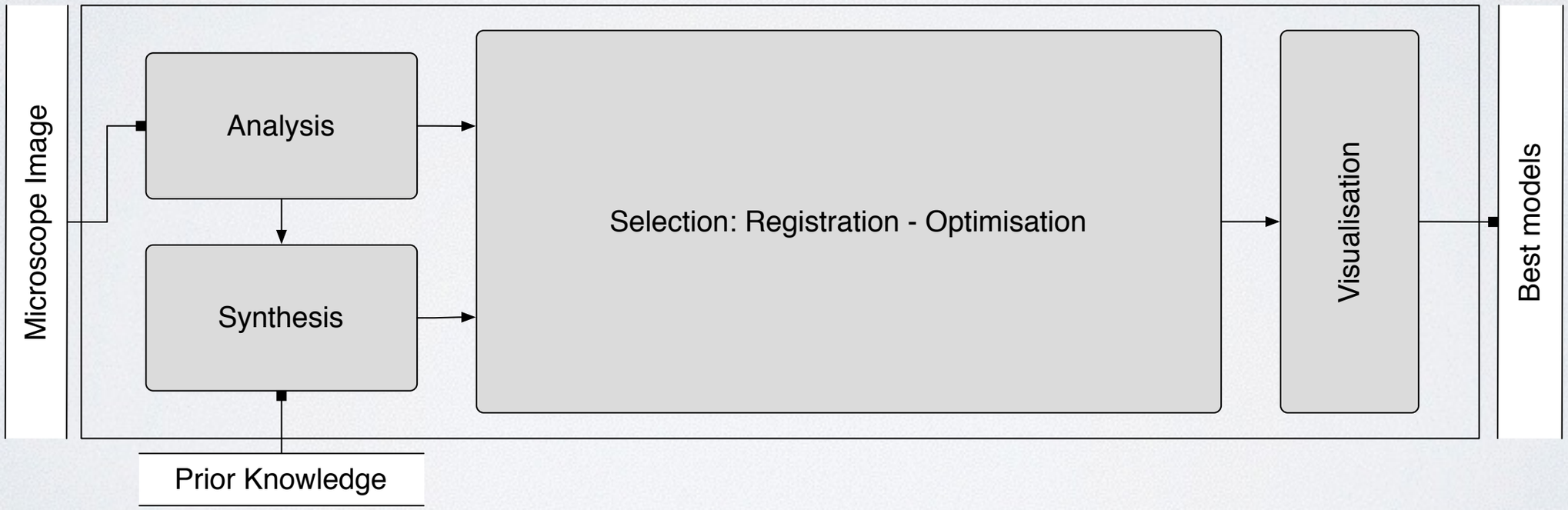
CONCLUSION

- Modelling framework for the observation of neural stem cell proliferation *in vitro* culture

- Three modules based framework



CONCLUSION

- Methodology for neurosphere observation
  - visualisation modality
  - structure monitoring

- A push toward the promotion of 3-dimensional culture

CONCLUSION

- Two modelling methods

CONCLUSION

- Two modelling methods

  - evolution algorithm

High flexibility

Low control
Low dynamical information

CONCLUSION

- Two modelling methods
  - evolution algorithm
  - primal dual mesh structure

High flexibility	High control High dynamical information
Low control Low dynamical information	Low flexibility

CONCLUSION

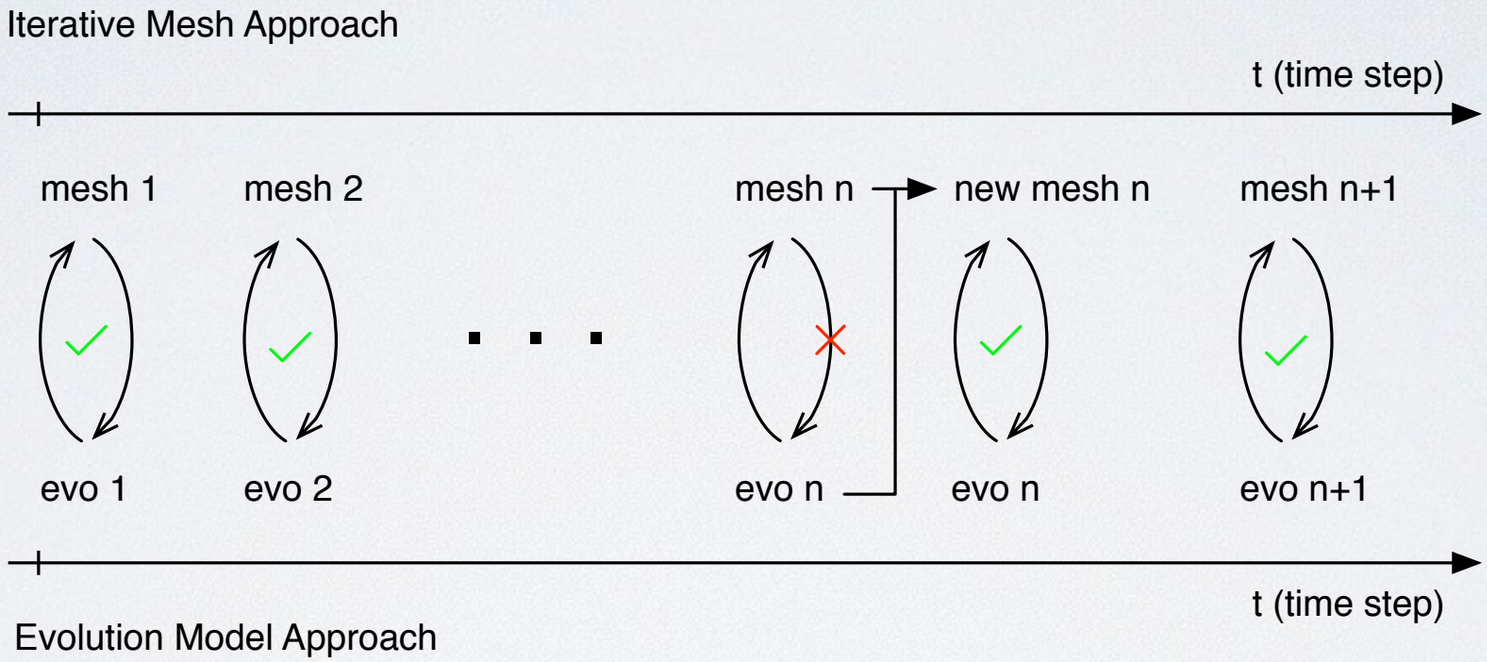
PERSPECTIVES

- Middle ground between EA and Delaunay generation process

CONCLUSION

PERSPECTIVES

- Middle ground between EA and Delaunay generation process
- Cross validation of both models



CONCLUSION

PERSPECTIVES

- Middle ground between EA and Delaunay generation process
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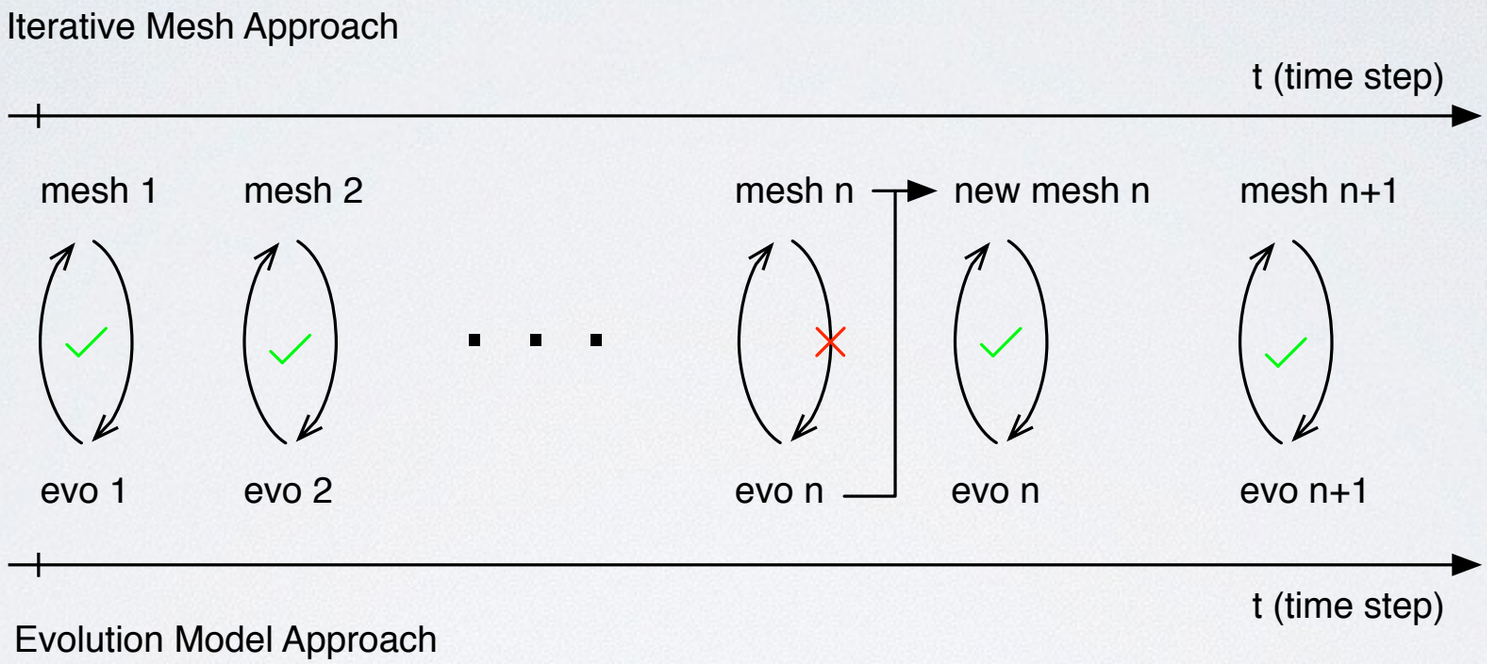


- Merge both processes toward a mesh structure generated using evolution algorithm

CONCLUSION

PERSPECTIVES

- Build a model database

- Analysis on

  - possible **patterns** of configuration

  - drug effects on **proliferation** and **configuration**

CONCLUSION

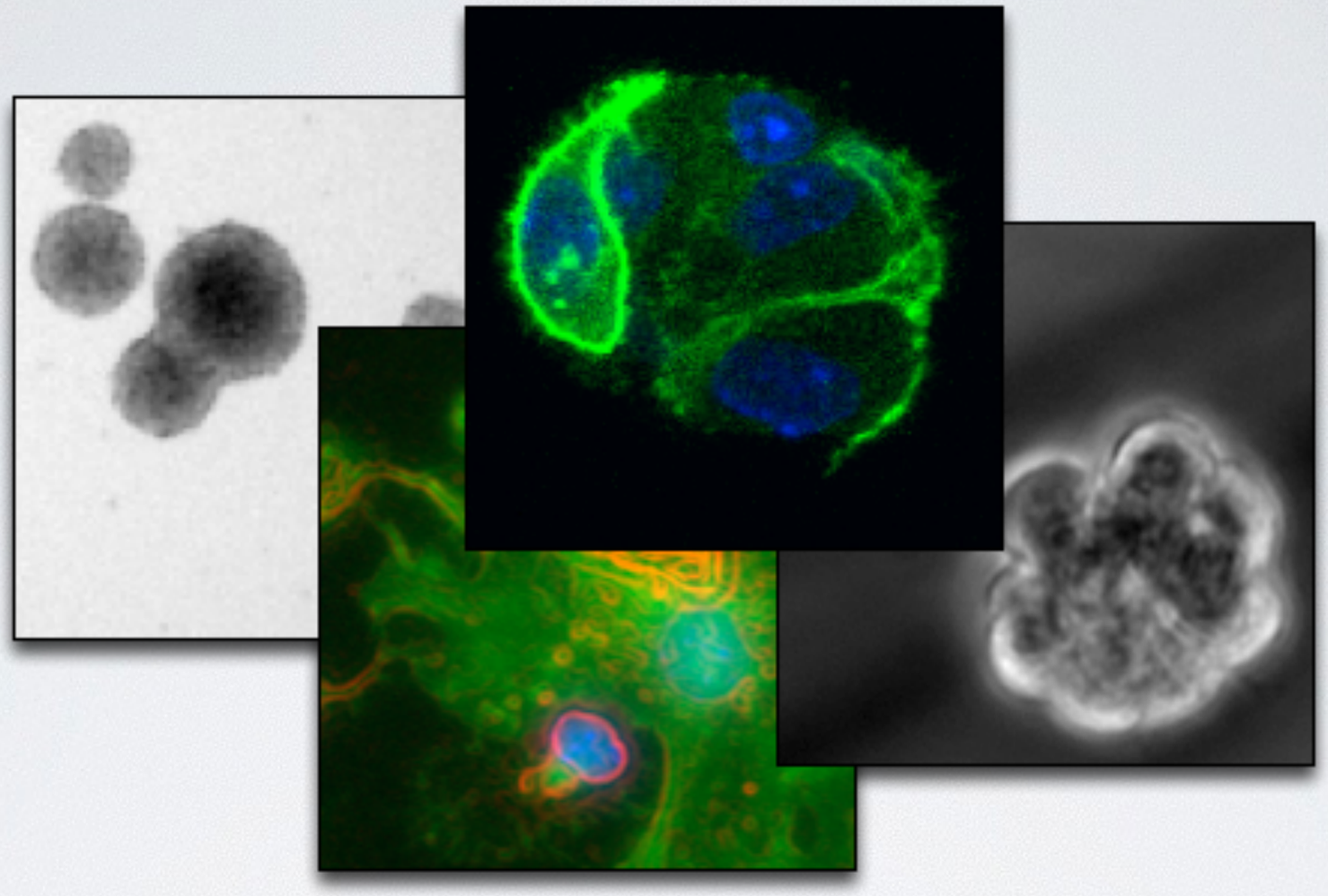
PERSPECTIVES

- Apply on new microscopy modalities
  - light sheet microscopy
  - Integrated Autonomous Microscope System project (A*STAR JCO grant)

- International Conferences
  - S. U. Rigaud, C.-H. Huang, S. Ahmed, Joo-Hwee Lim, and D. Racoceanu. "An analysis- synthesis approach for neurosphere modeling." *EMBC*, pp 1–6, 2013.
  - S. U. Rigaud, N. Loménie, S. Sankaran, S. Ahmed, Joo-Hwee Lim, and D. Racoceanu. "Neurosphere fate prediction: An analysis-synthesis approach for feature extraction". *IJCNN*, pp 1–7, 2012.
  - S. U. Rigaud and Nicolas Loménie. "Neural stem cell tracking with phase contrast video microscopy". *SPIE Medical Imaging*, pp 796230–796236, 2011.

- White Journals
  - H. Irshad, S. U. Rigaud, and A. Gouaillard. "Primal/dual mesh with application to triangular/simplex mesh and Delaunay/Voronoi". *Insight Journal*, pp 1–14, 2012.
  - S. U. Rigaud and A. Gouaillard. "Incremental Delaunay triangulation". *Insight Journal,* pp 1–5, 2012.
  - S. U. Rigaud and A. Gouaillard. "Walk in a triangulation : Straight walk". *Insight Journal*, pp 1–3, 2012.

- Peer-reviewed Journals
  - In preparation



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