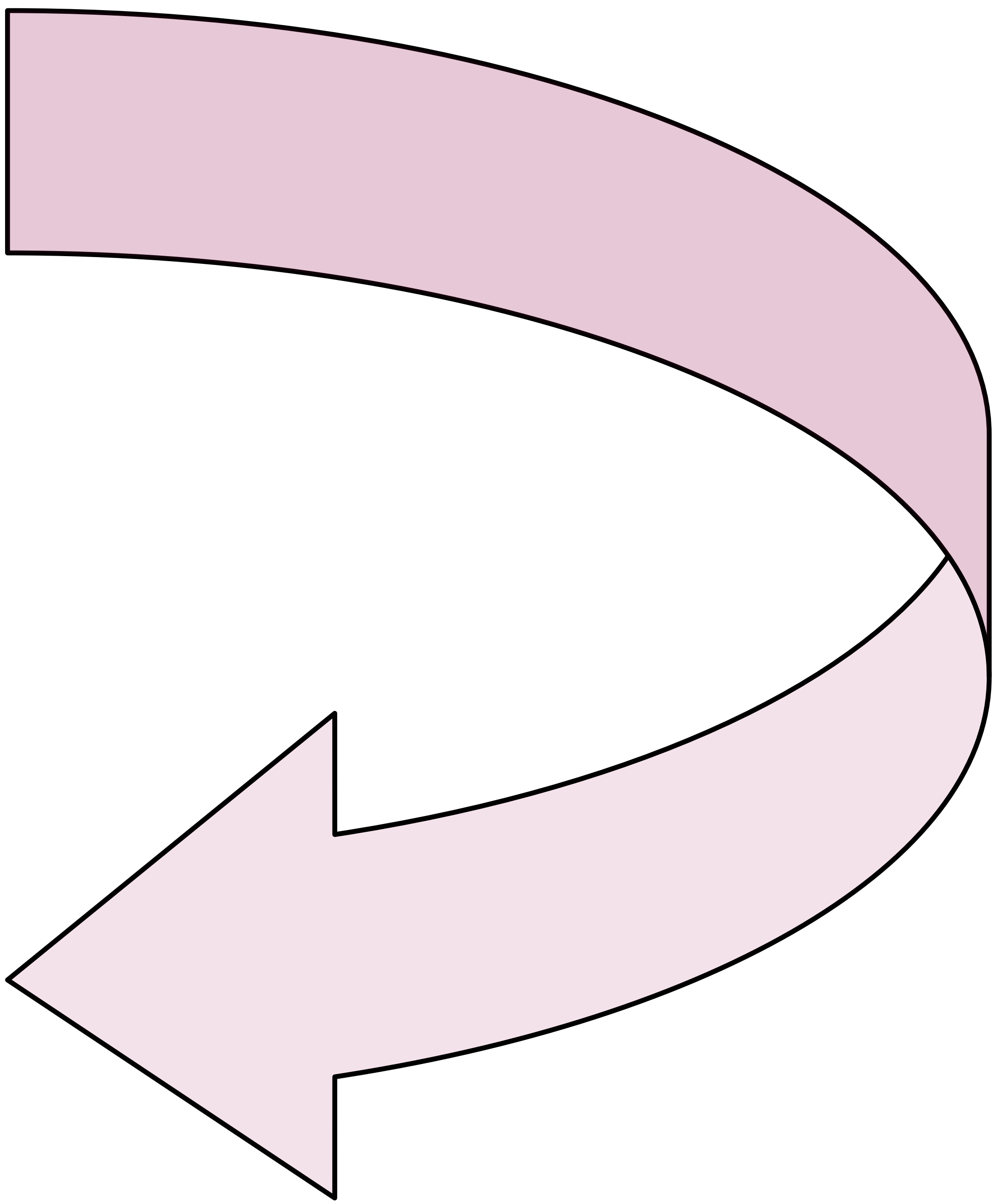
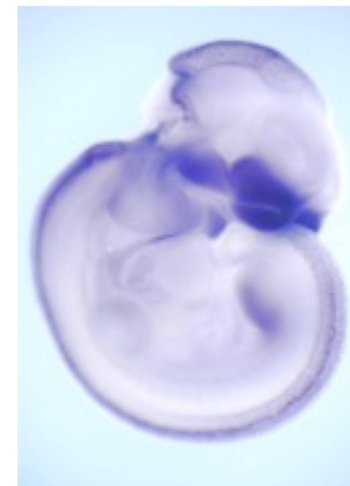
Atlas-Based Bioinformatics

Richard Baldock
MRC Human Genetics Unit
Institute of Genetics and Molecular Medicine
Edinburgh, UK

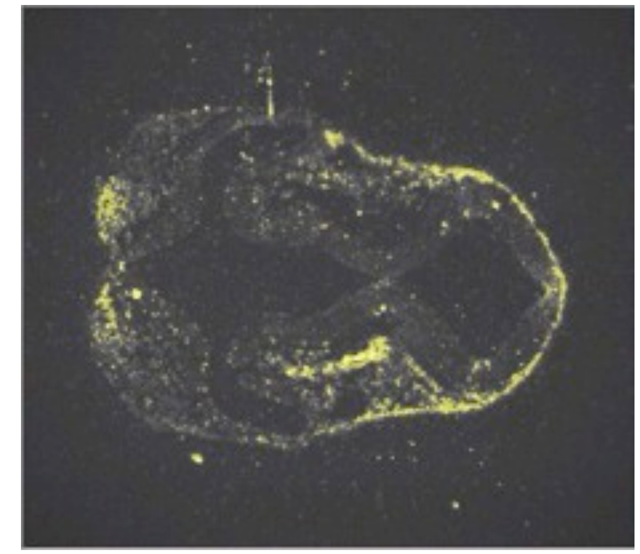
eMouseAtlas - Development and Gene-Expression

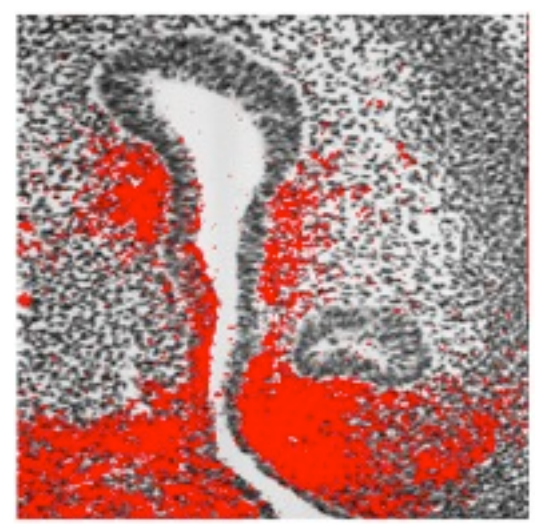


GENE EXPRESSION



Carol Wicking, University of Queensland





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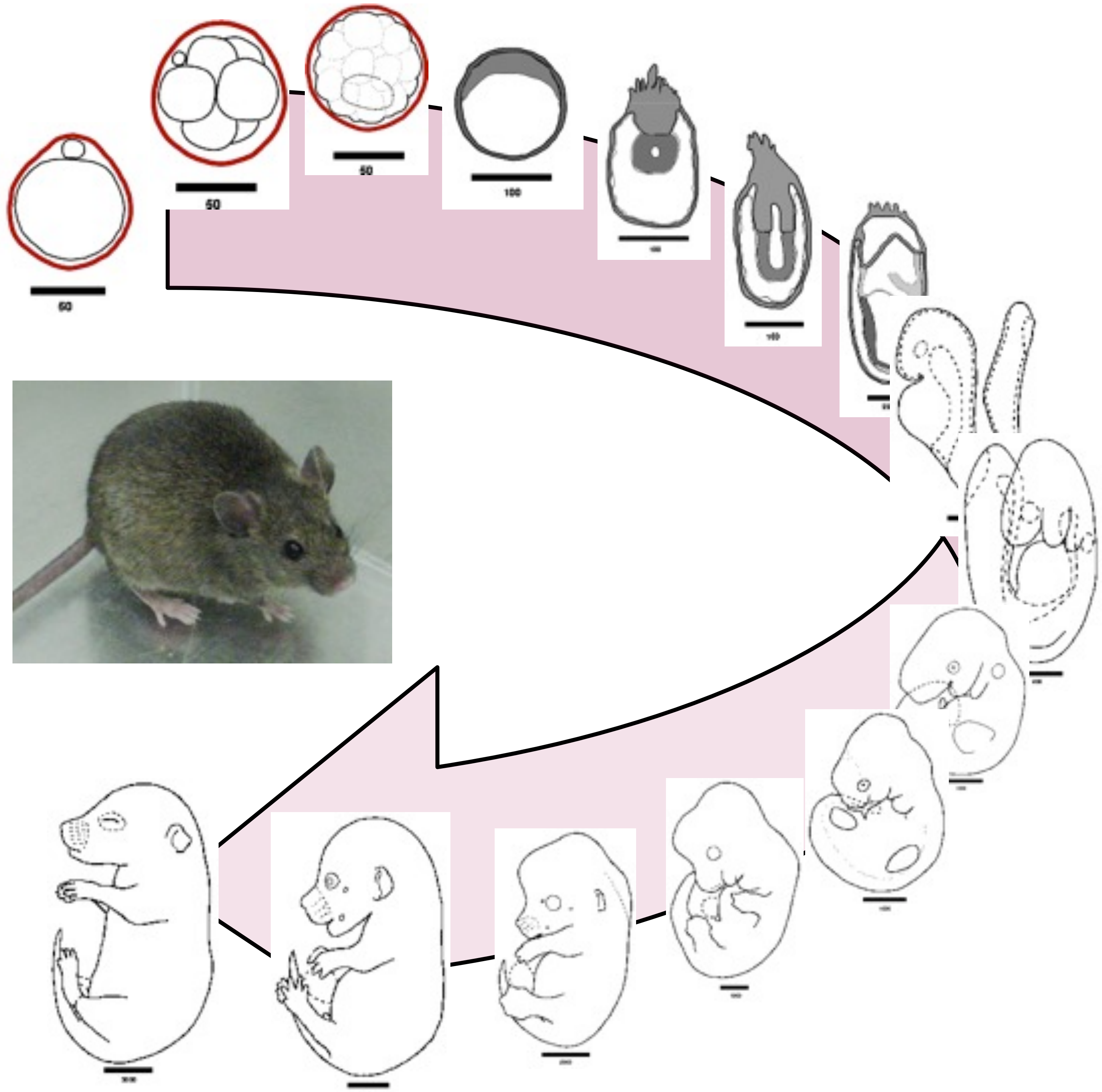
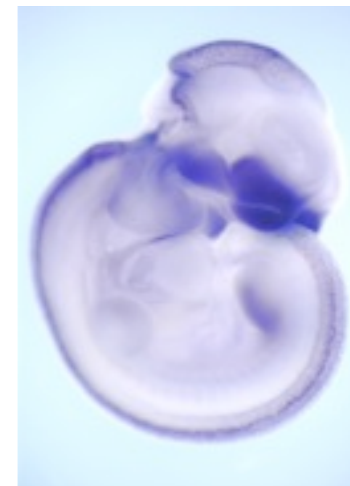


GENE EXPRESSION



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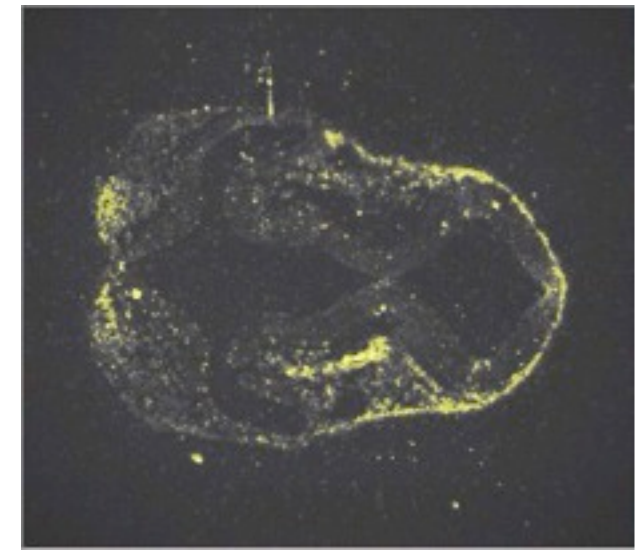
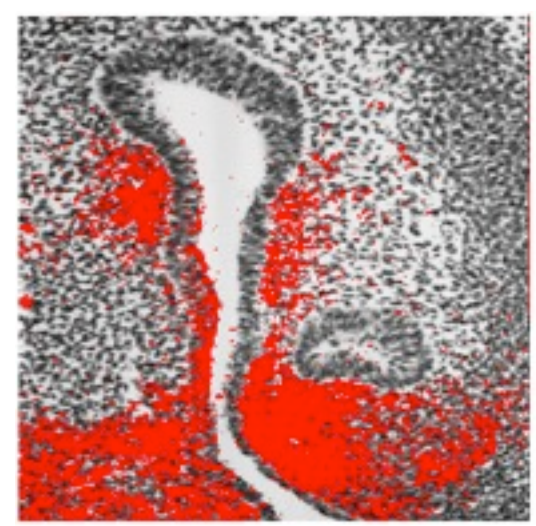
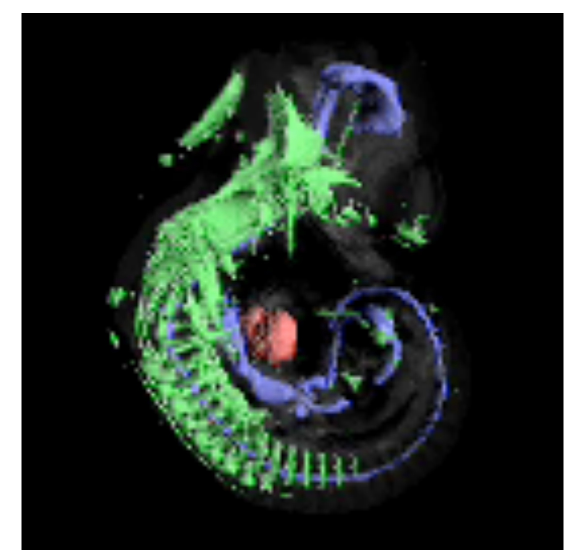
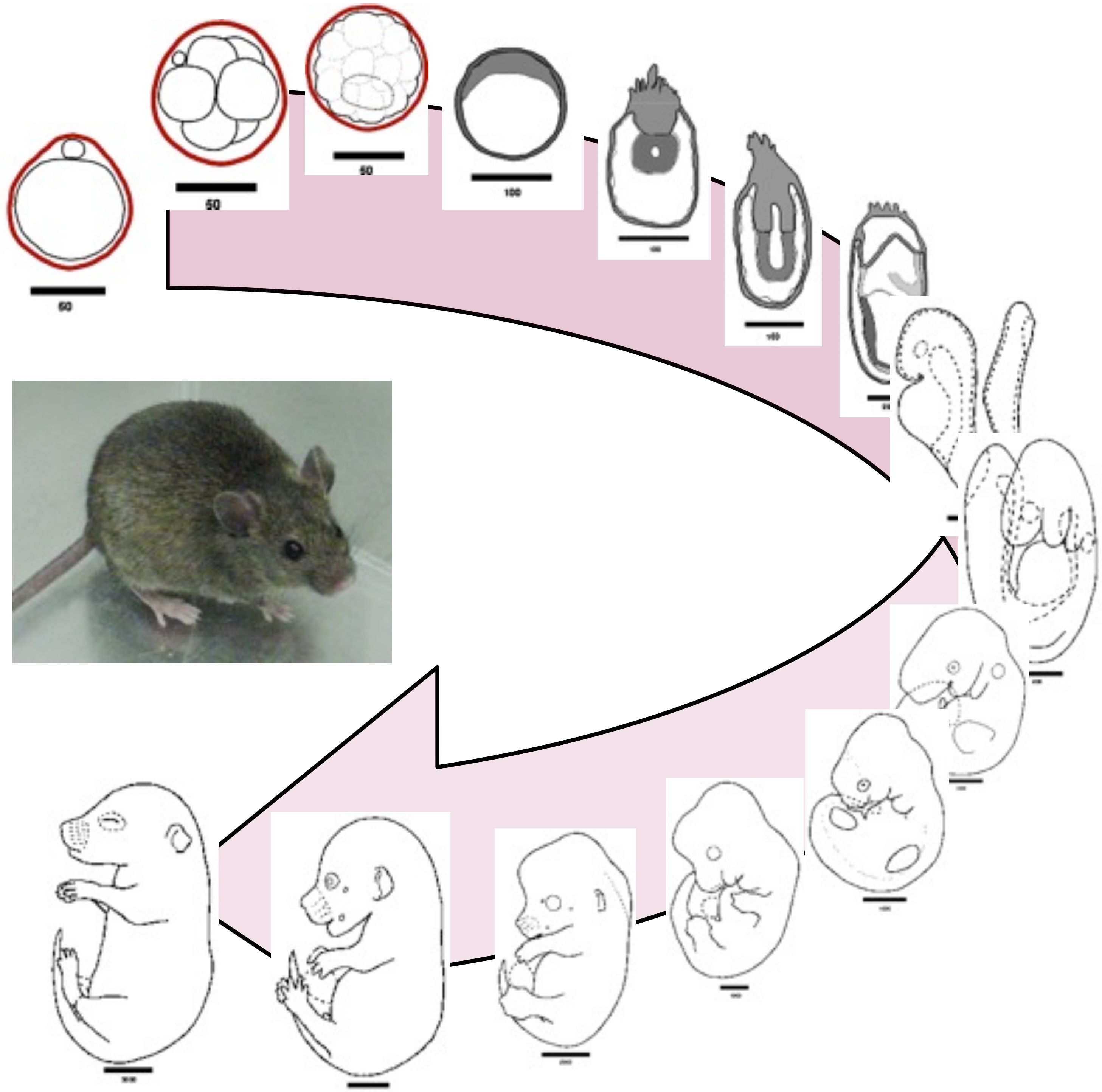


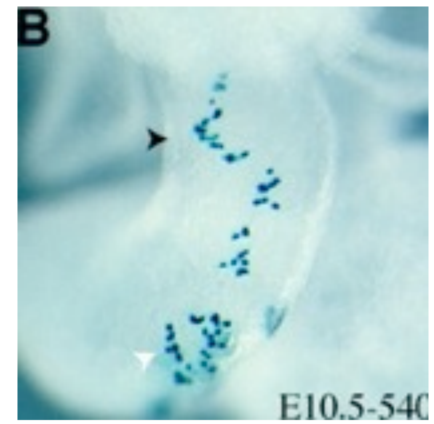




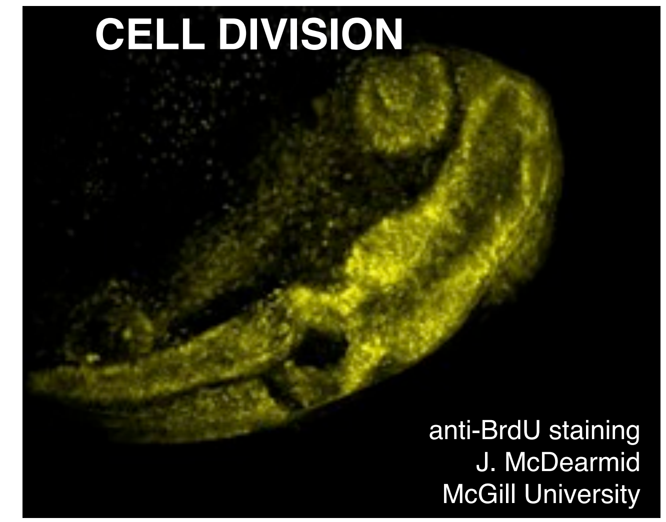
eMouseAtlas - Development and Gene-Expression



CELL LINEAGE



Sigolène Meilhac
Institut Pasteur

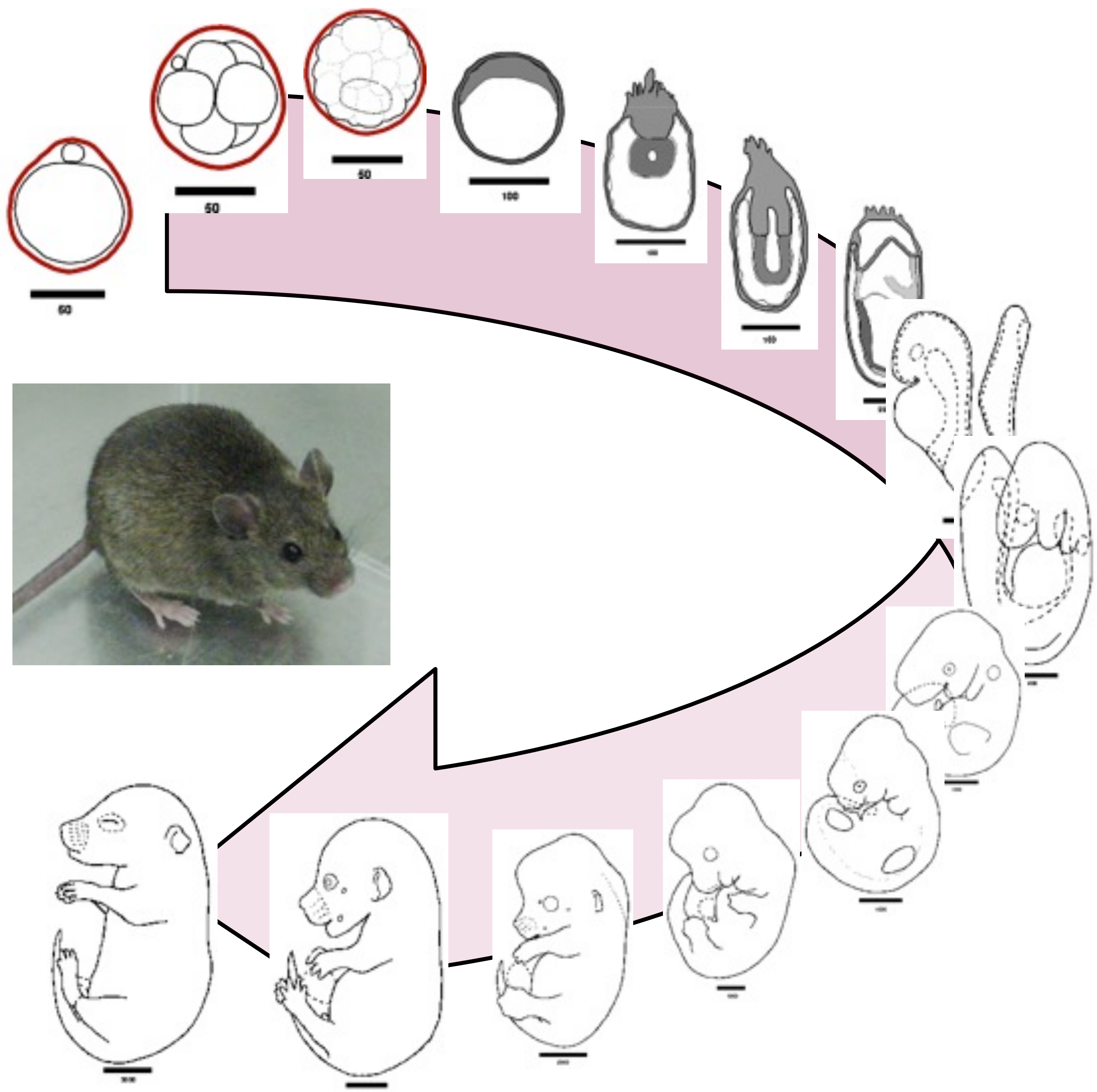


APOPTOSIS

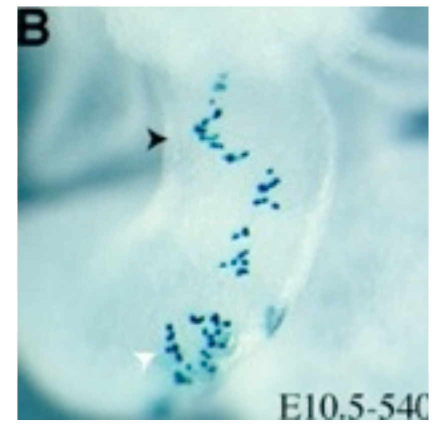
Acridine Orange
J. Burns
University of Bristol

TRANSGENICS

eMouseAtlas - Development and Gene-Expression



CELL LINEAGE



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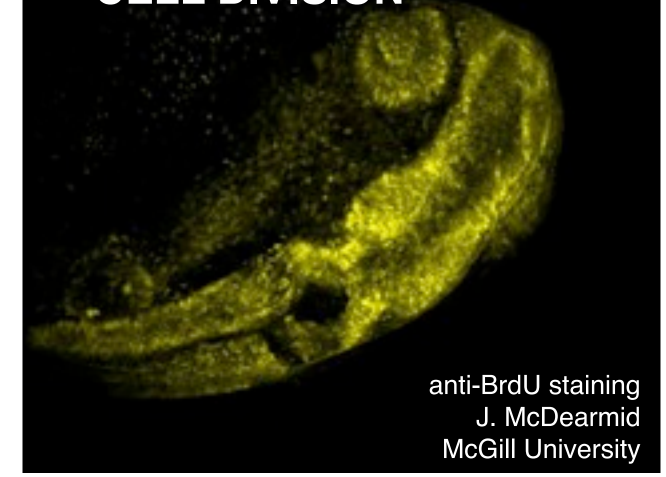
Institut Pasteur

CELL DIVISION



anti-BrdU staining
J. McDearmid
McGill University

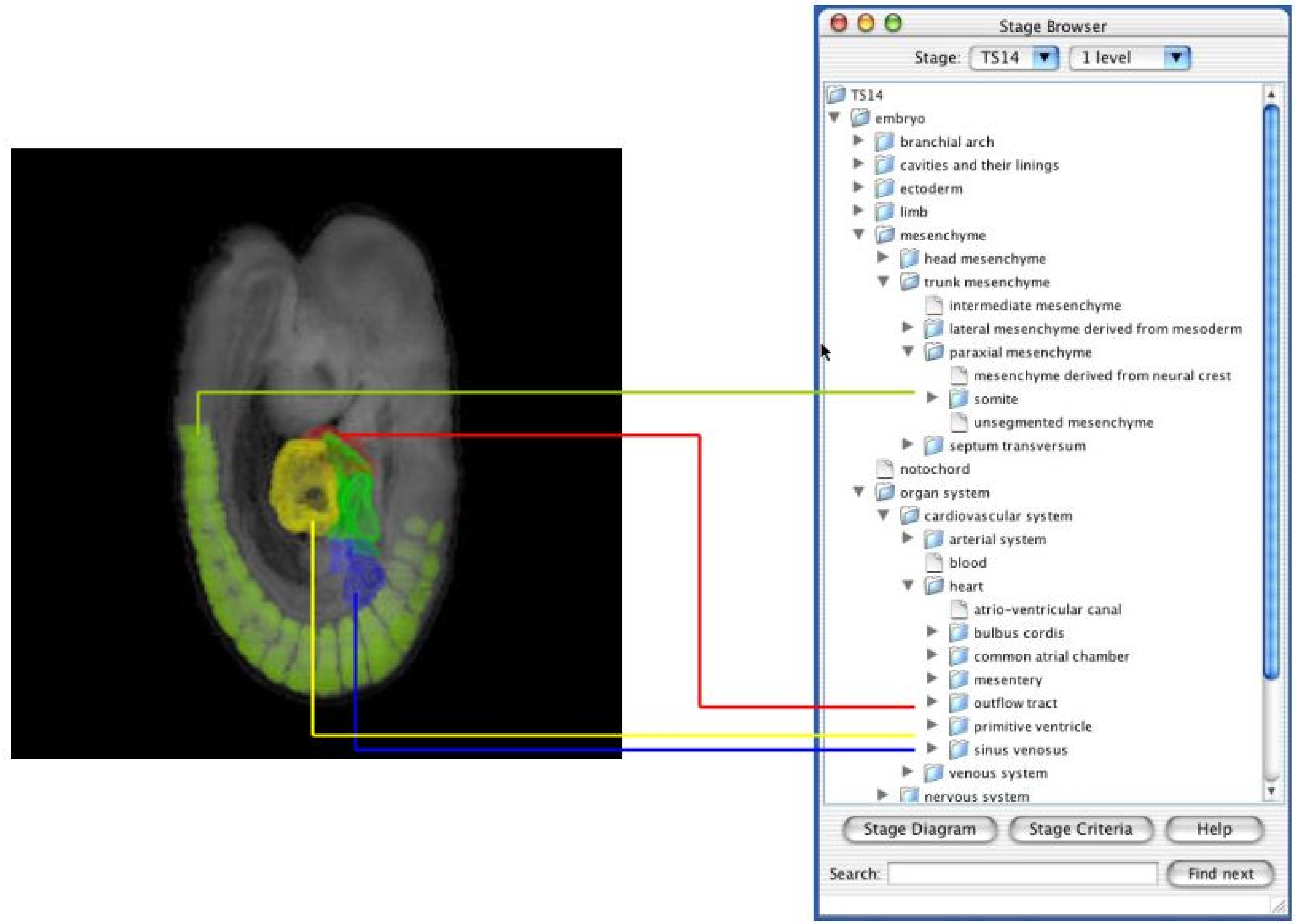
APOPTOSIS

Acridine Orange
J. Burns
University of Bristol

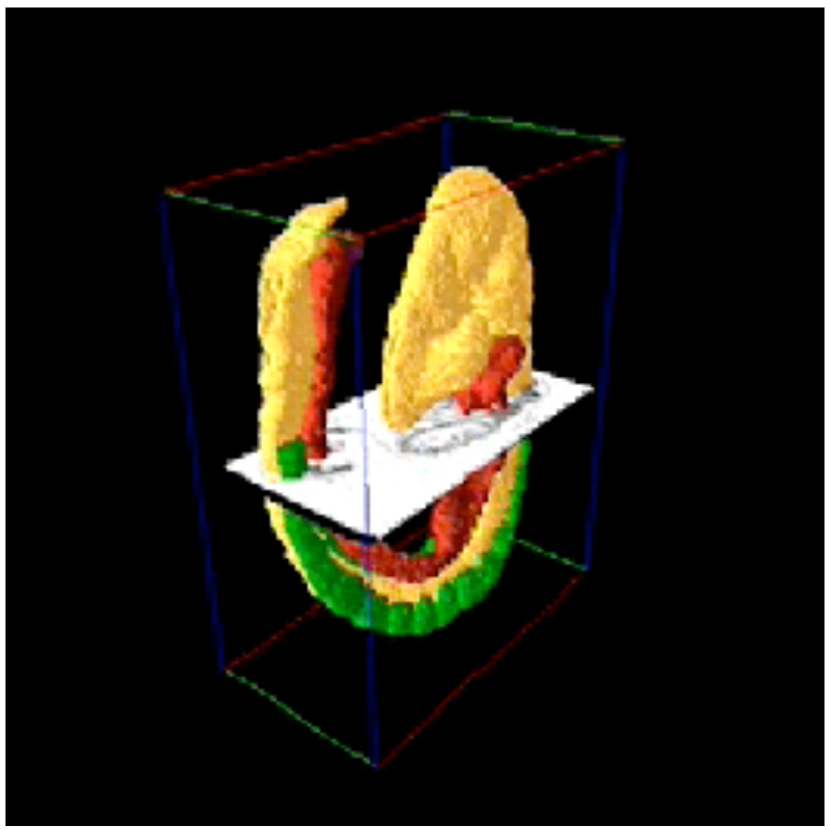
TRANSGENICS

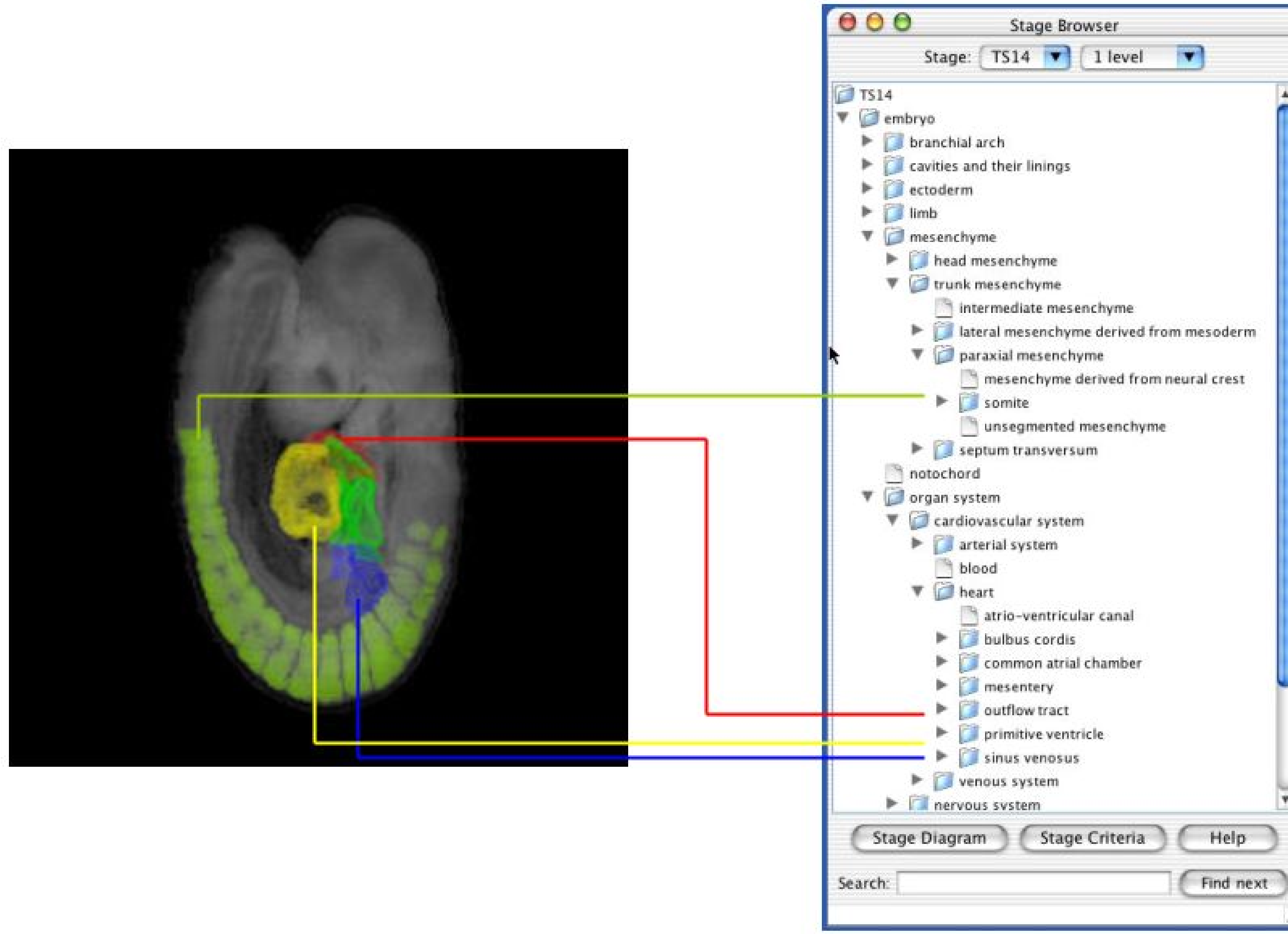
cre induced-
LacZ expression
W. Hsu, University of Rochester

eMouseAtlas Framework

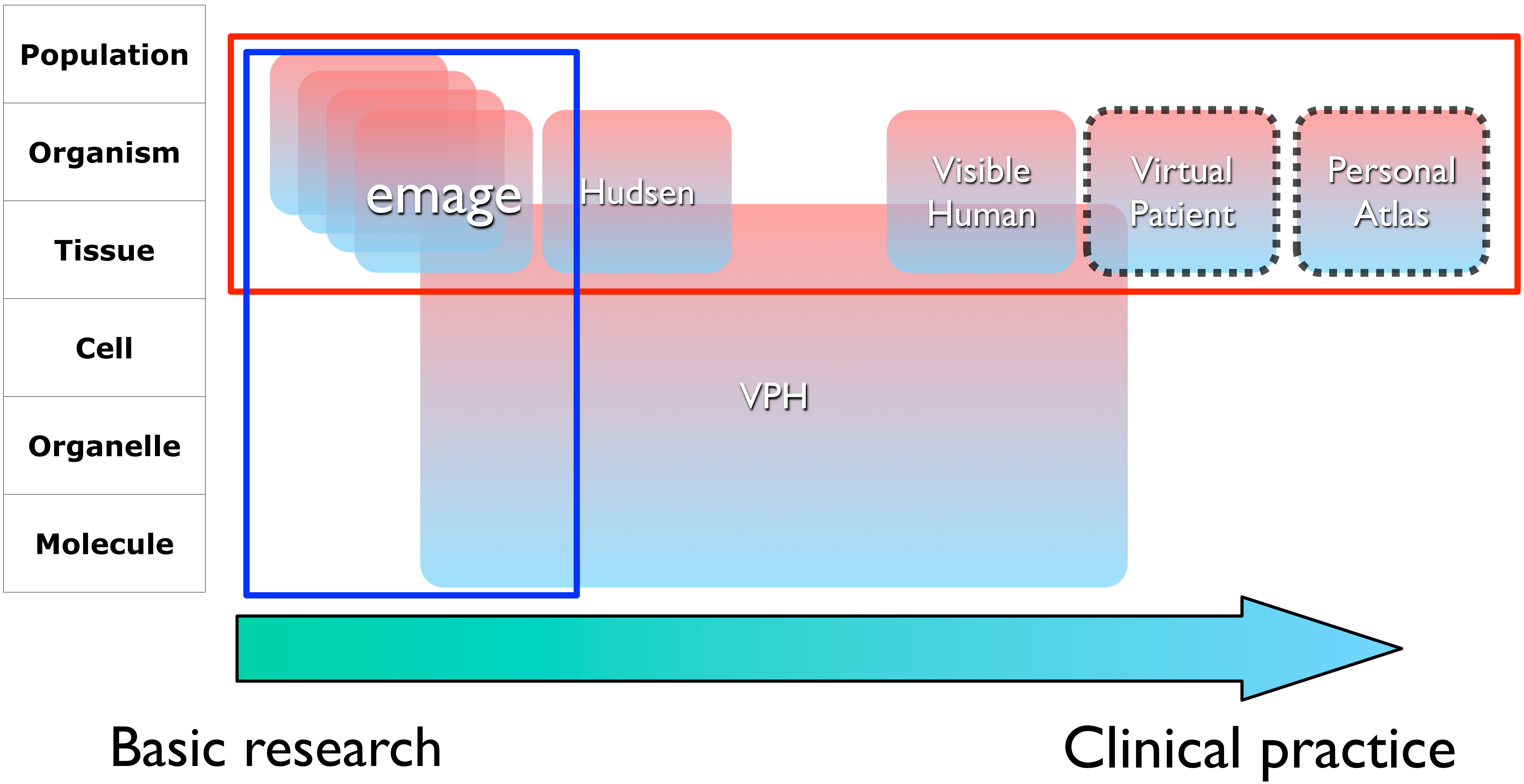


eMouseAtlas Framework



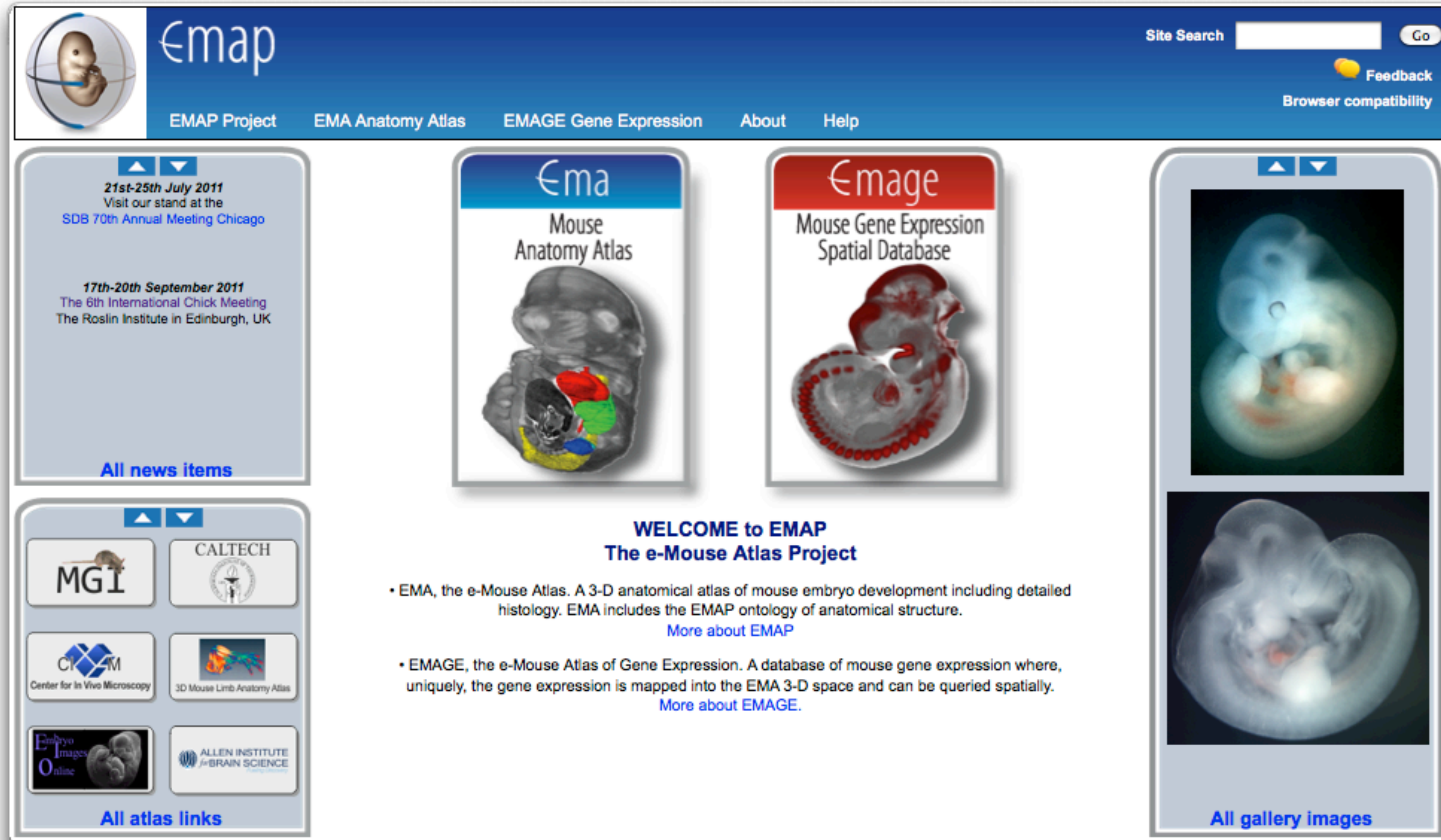


Atlas-Based Infrastructures

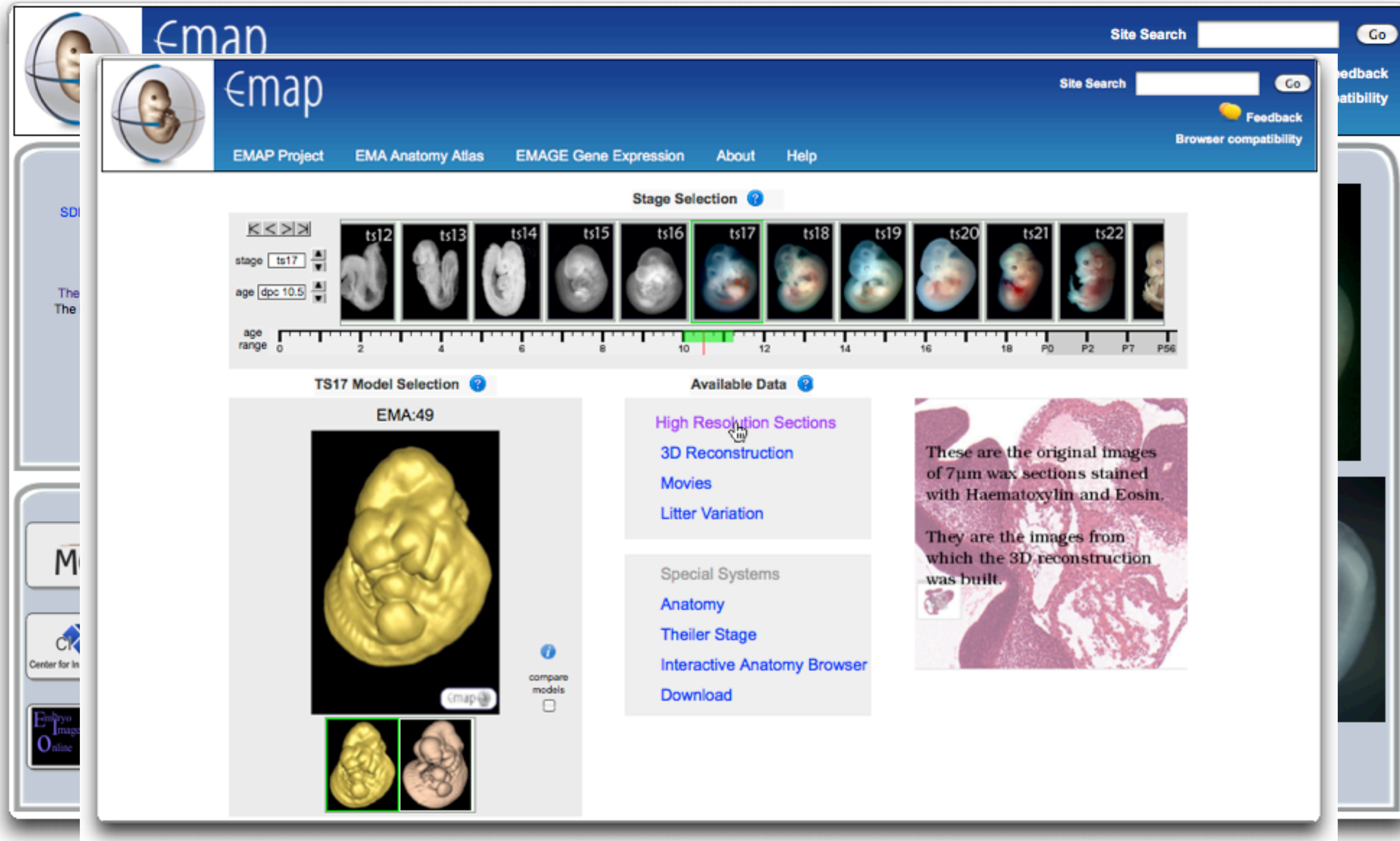


MRC Human Genetics Unit

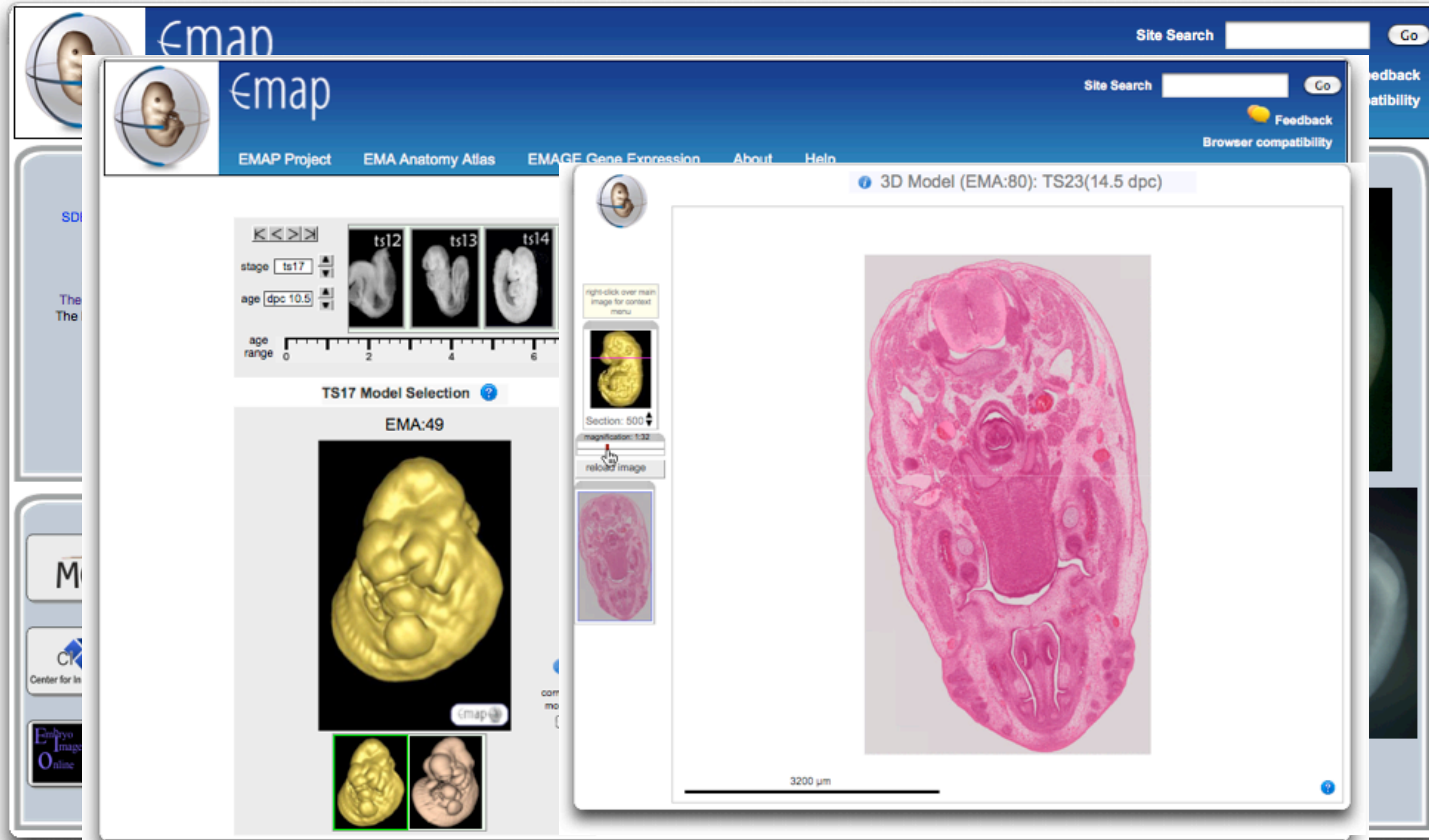
eMouseAtlas



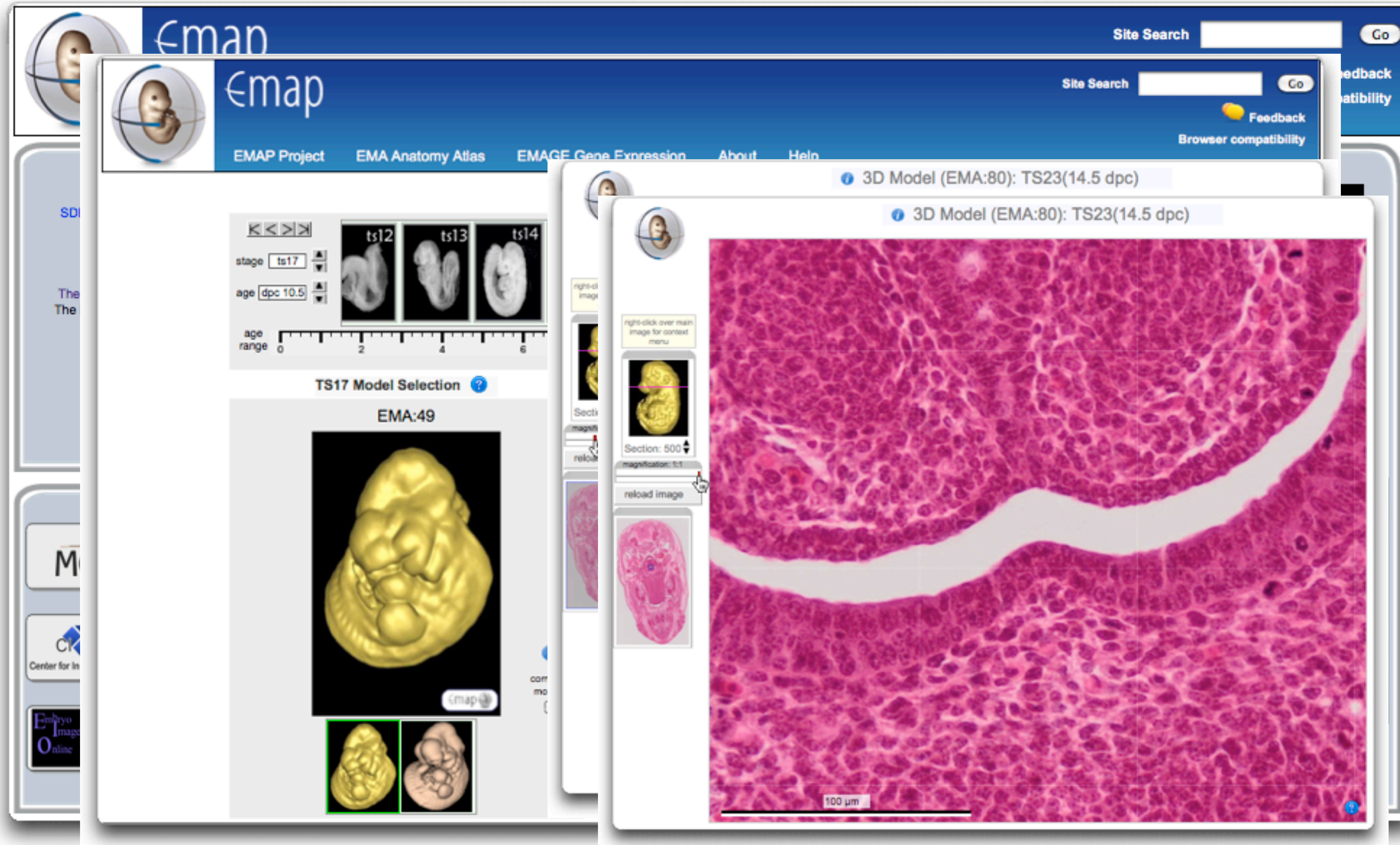
eMouseAtlas



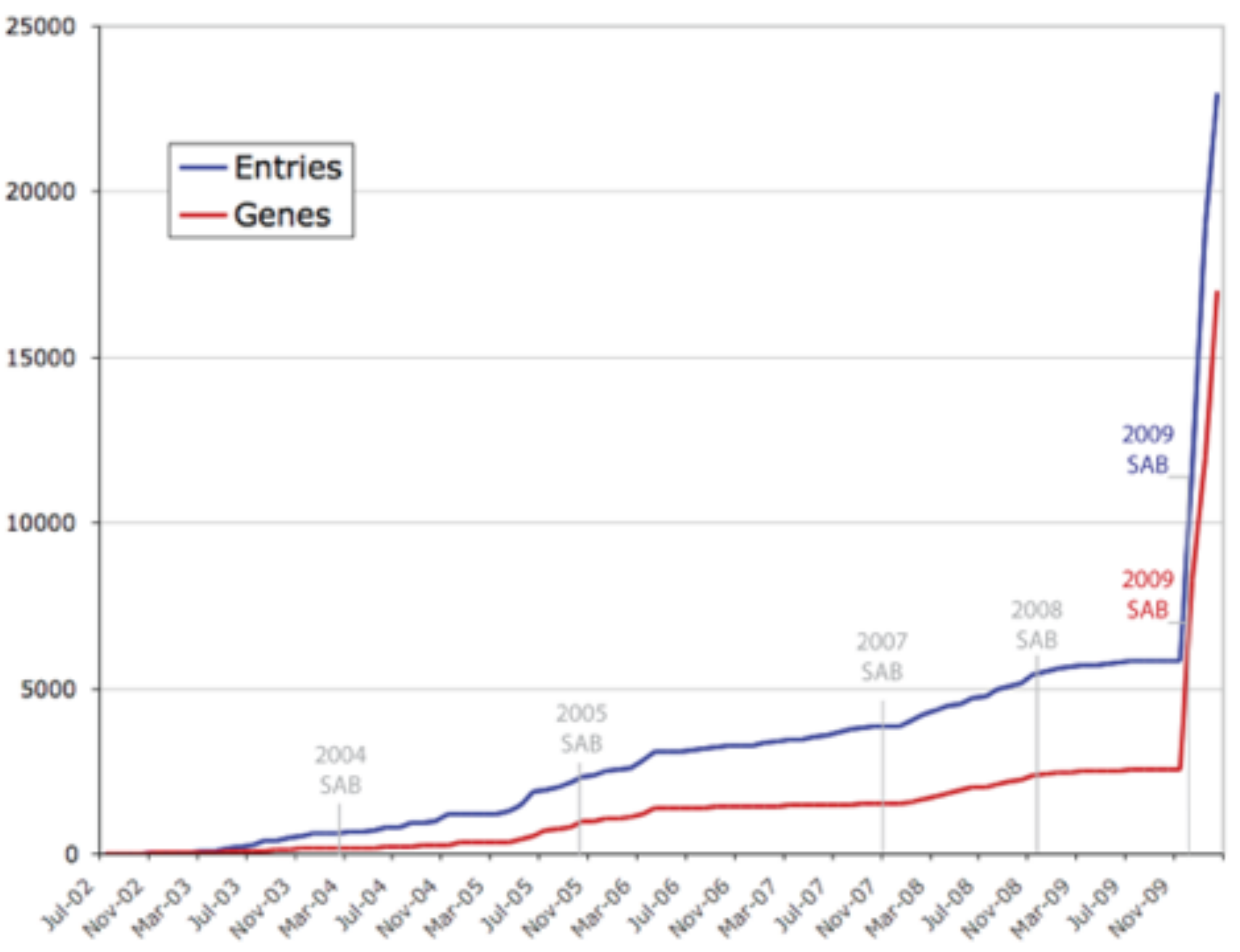
eMouseAtlas

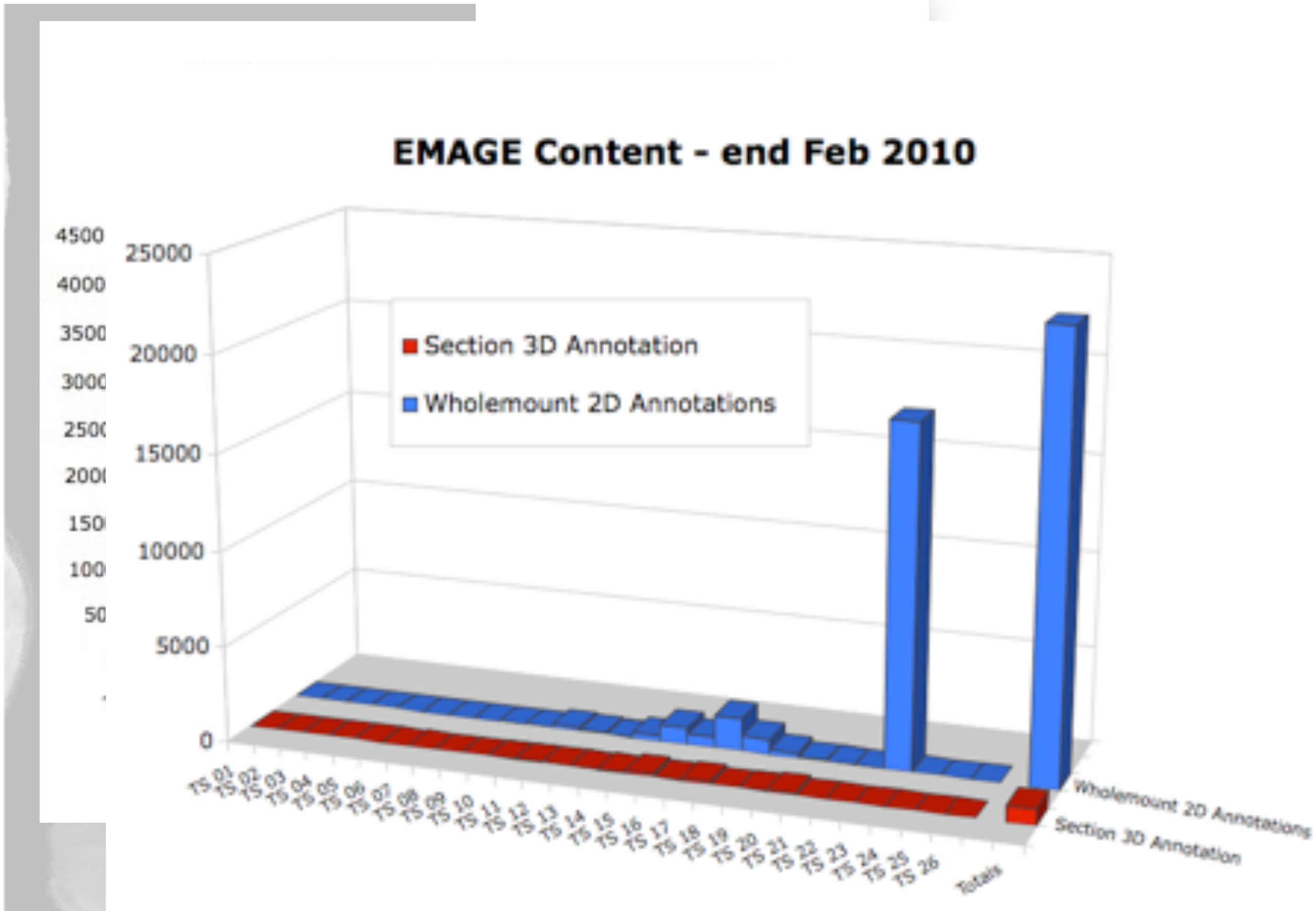


eMouseAtlas



EMAGE - current status

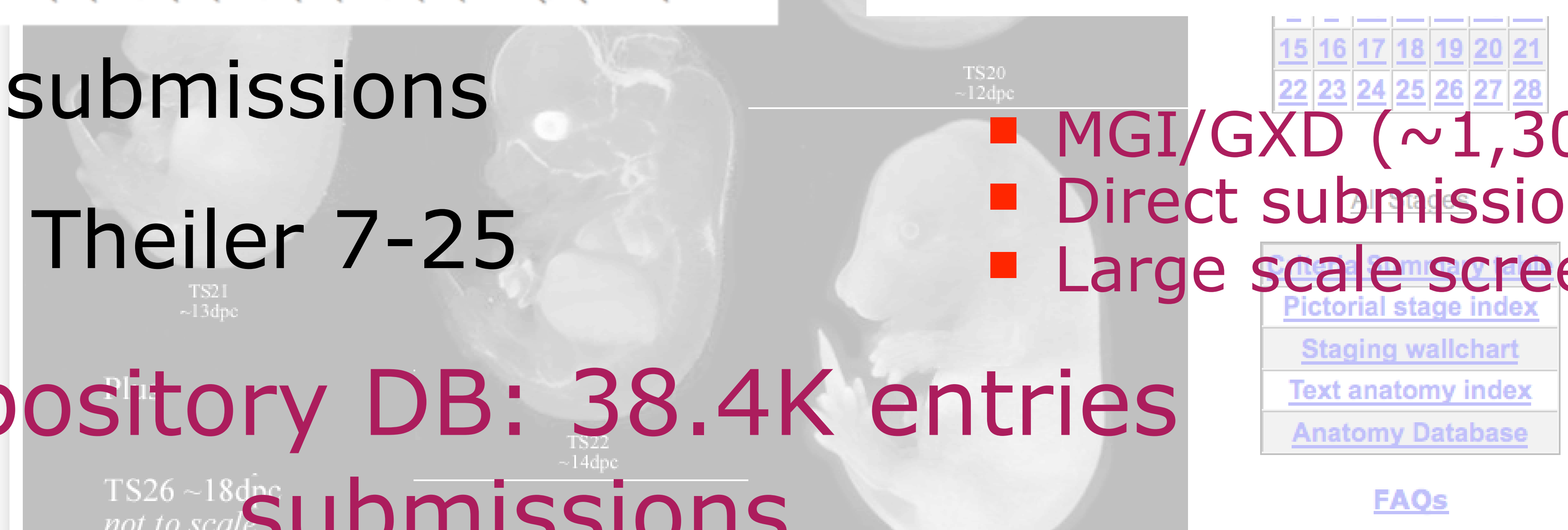




~22K submissions

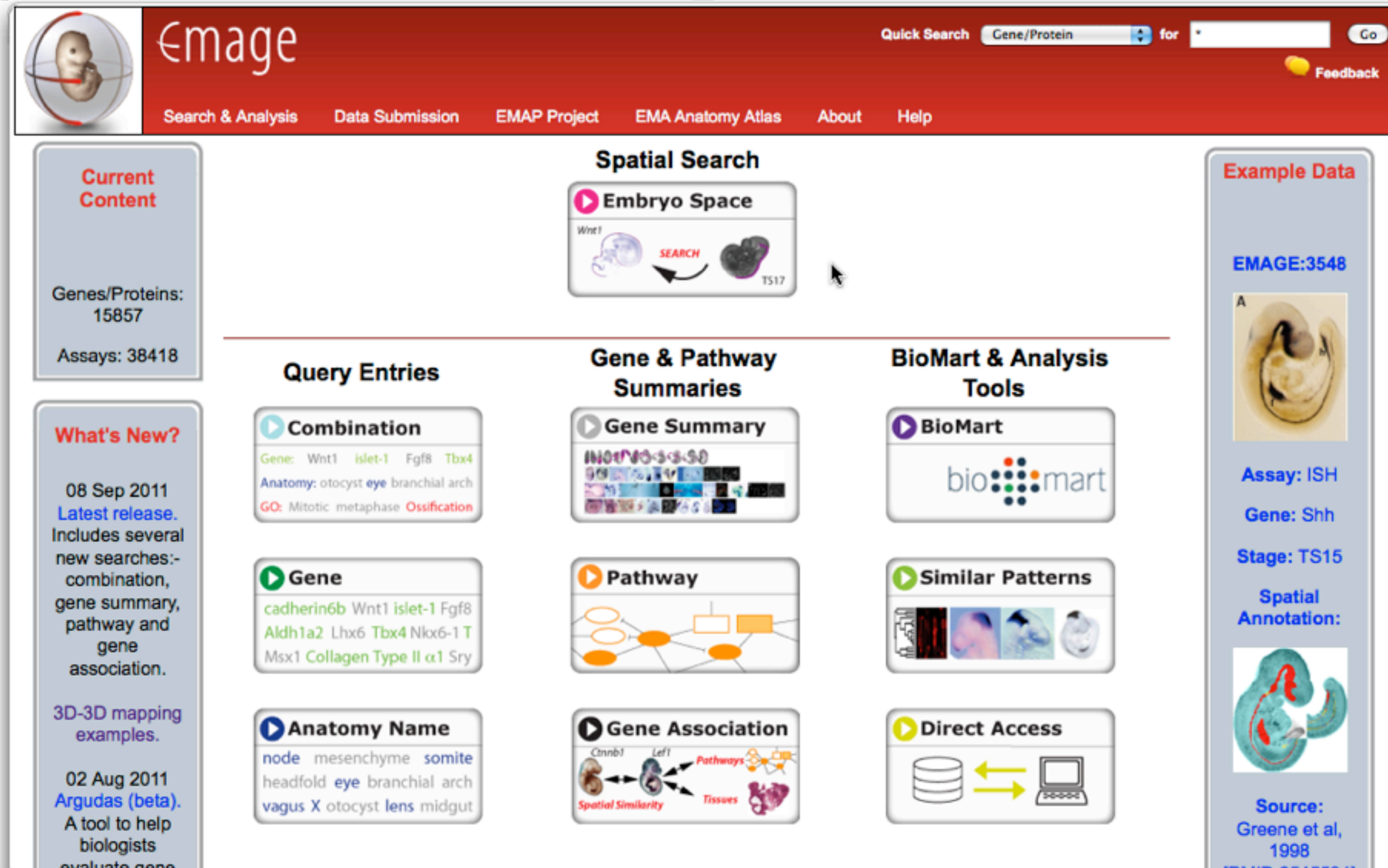
Range Theiler 7-25

- MGI/GXD (~1,300)
- Direct submission (~300)
- Large scale screens (~16K)



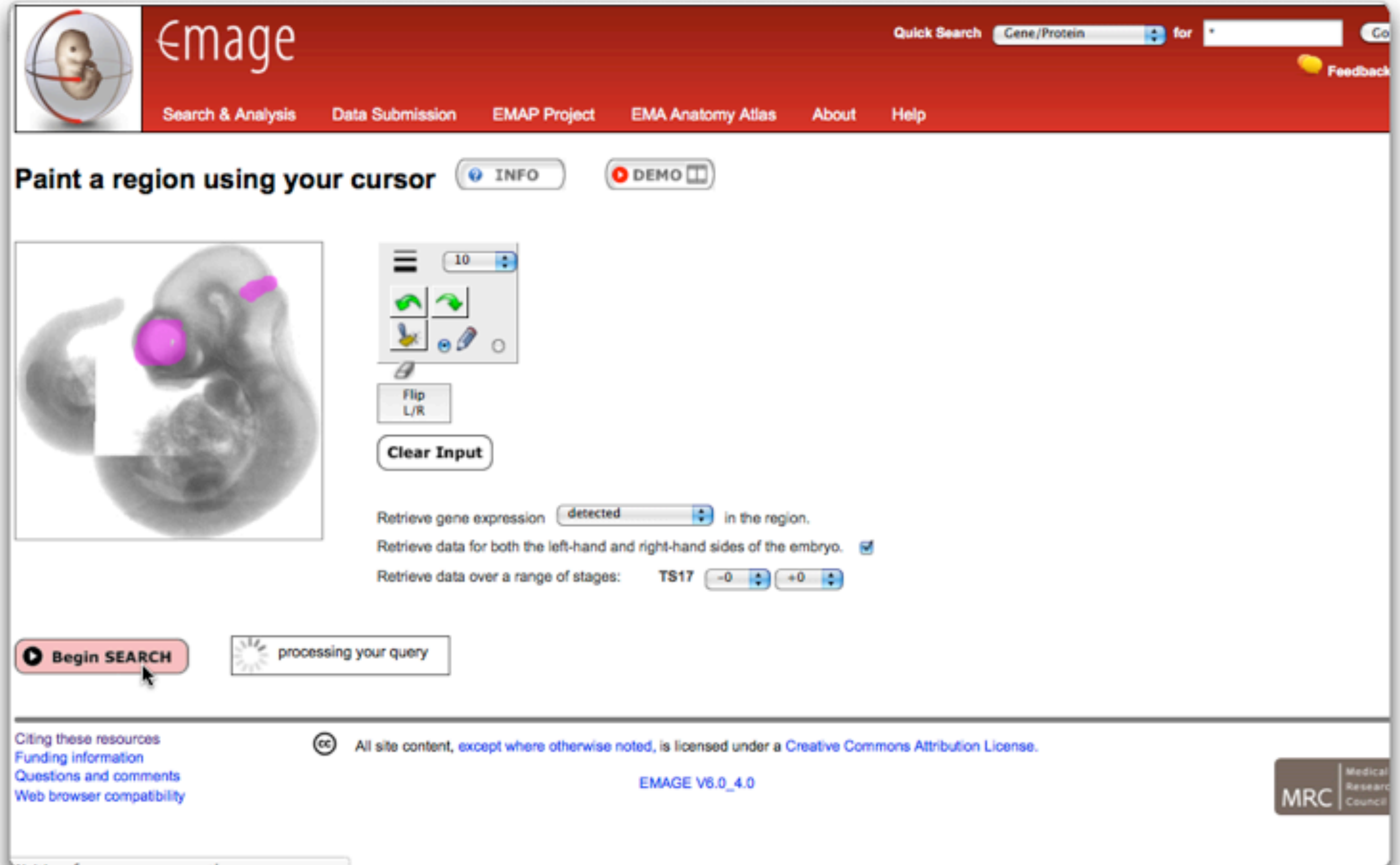
Repository DB: 38.4K entries submissions

EMAGE - current status

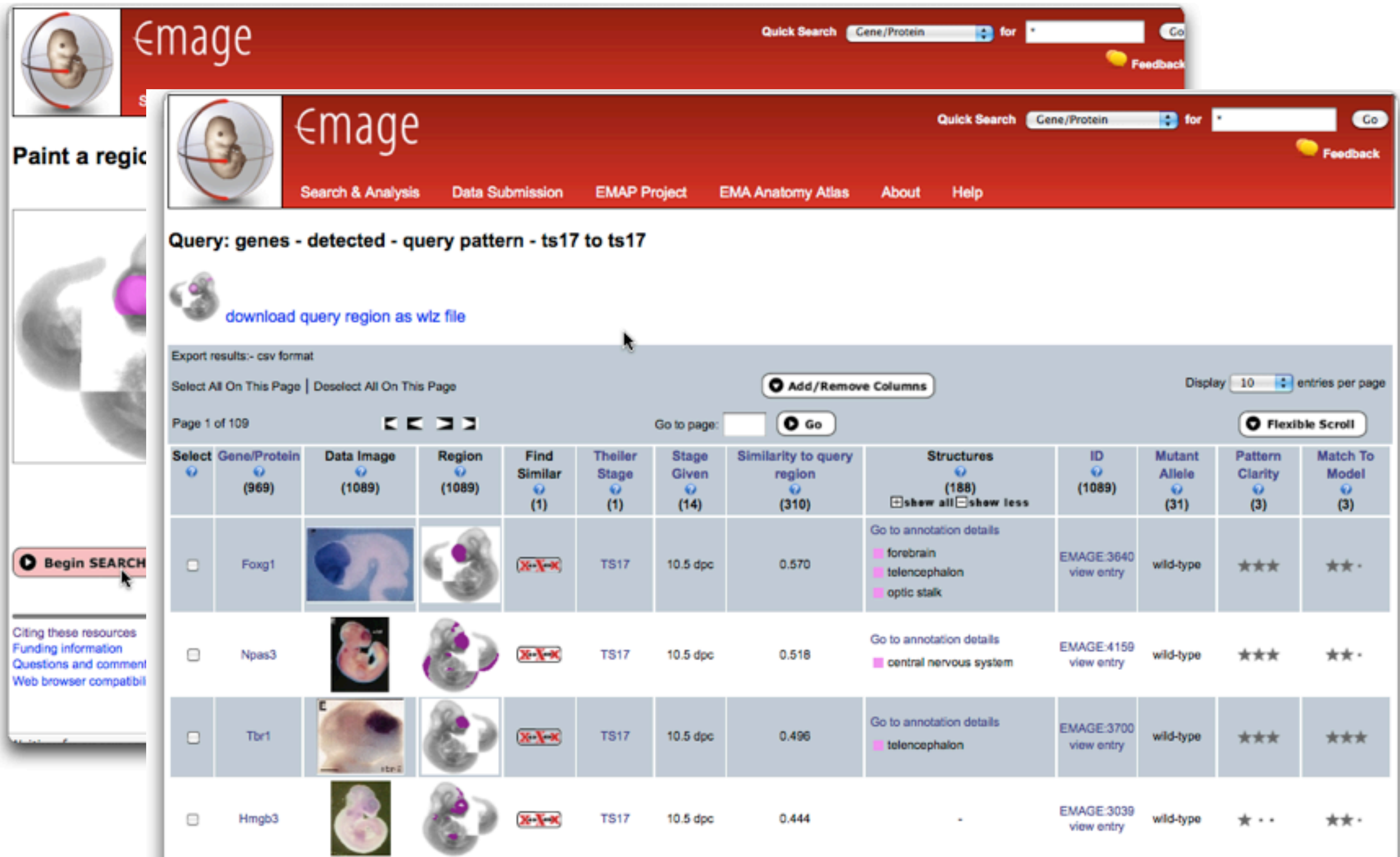


Thursday, 16 February 2012

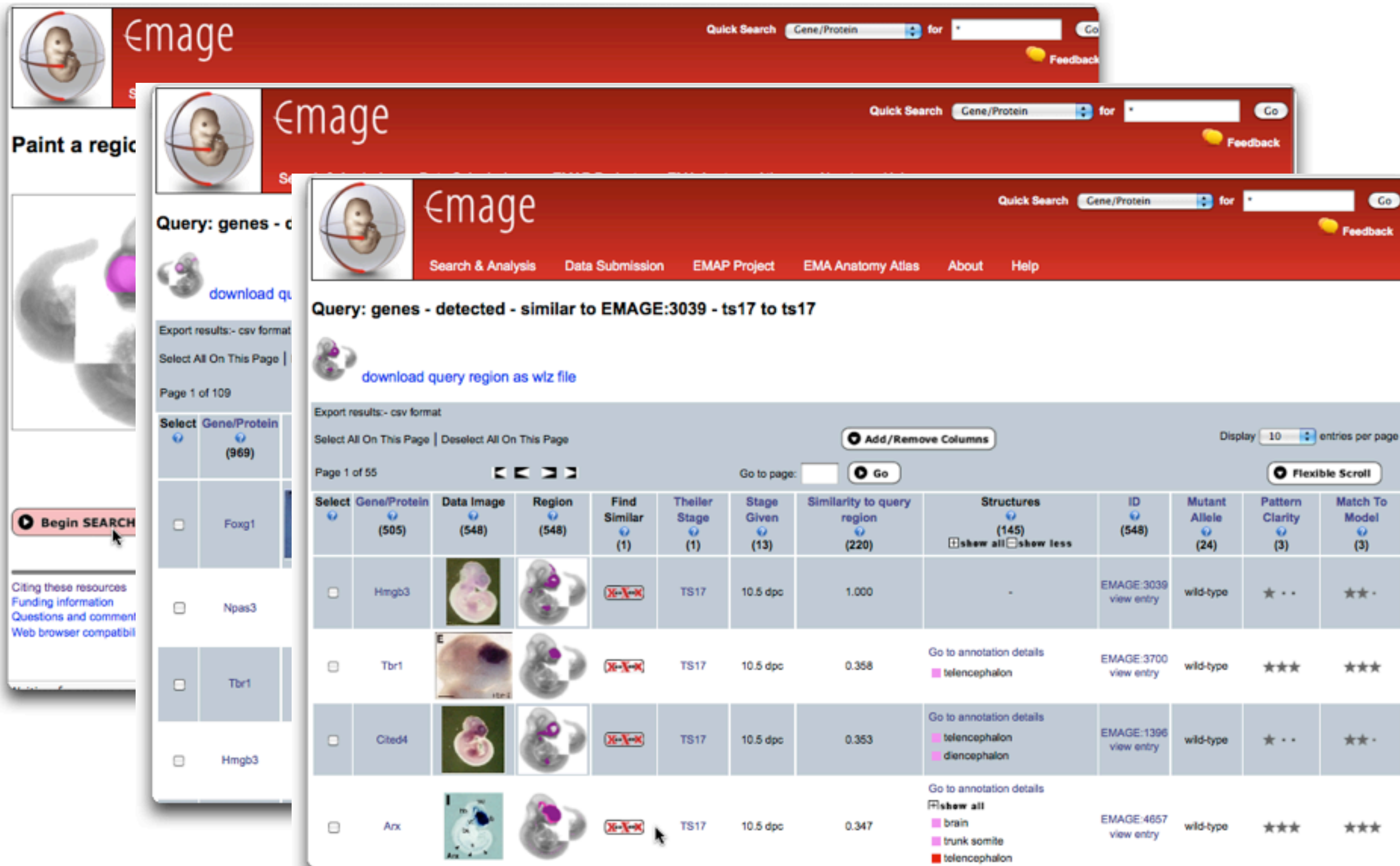
EMAGE Embryo Space



EMAGE Embryo Space



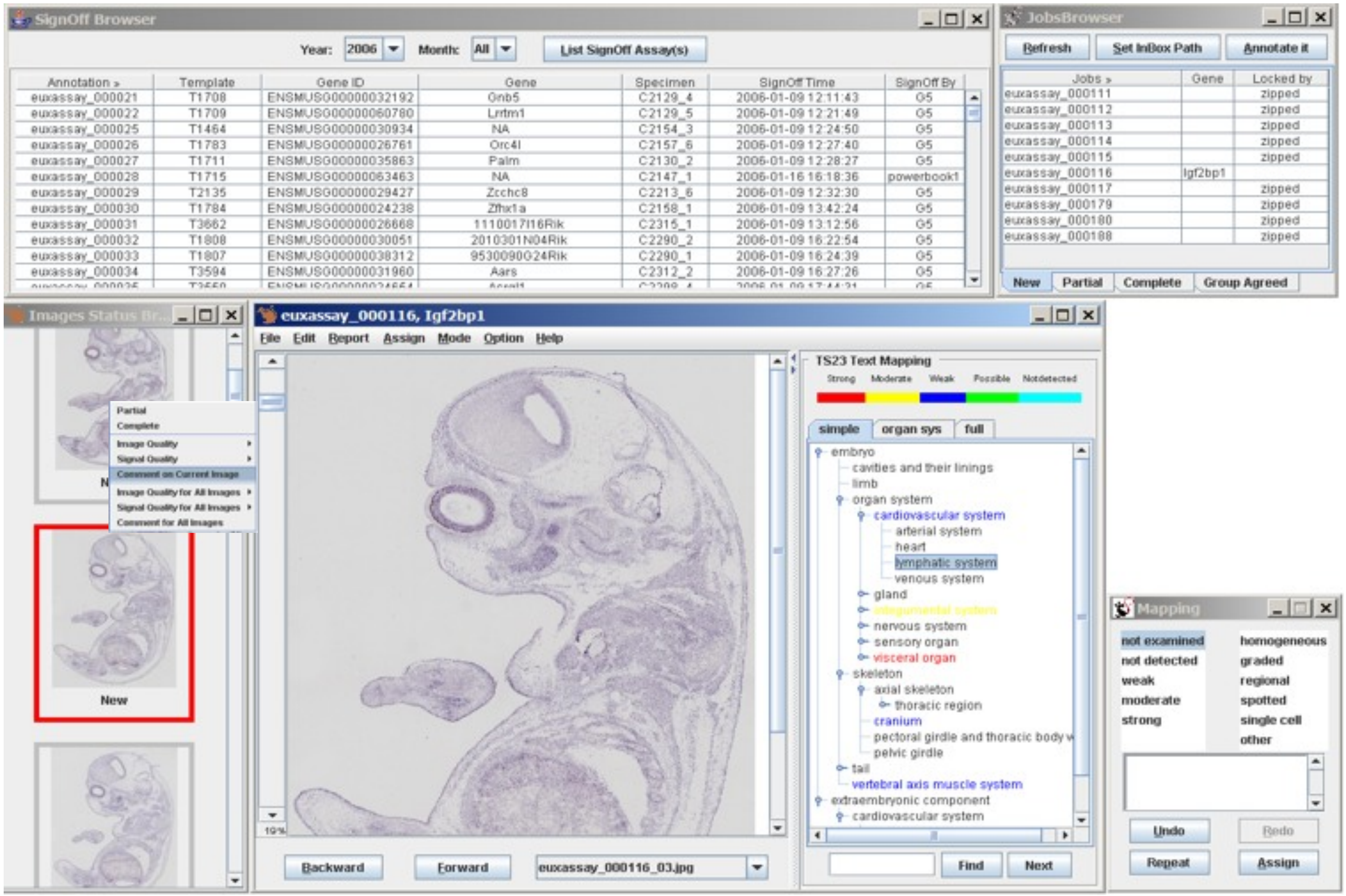
EMAGE Embryo Space



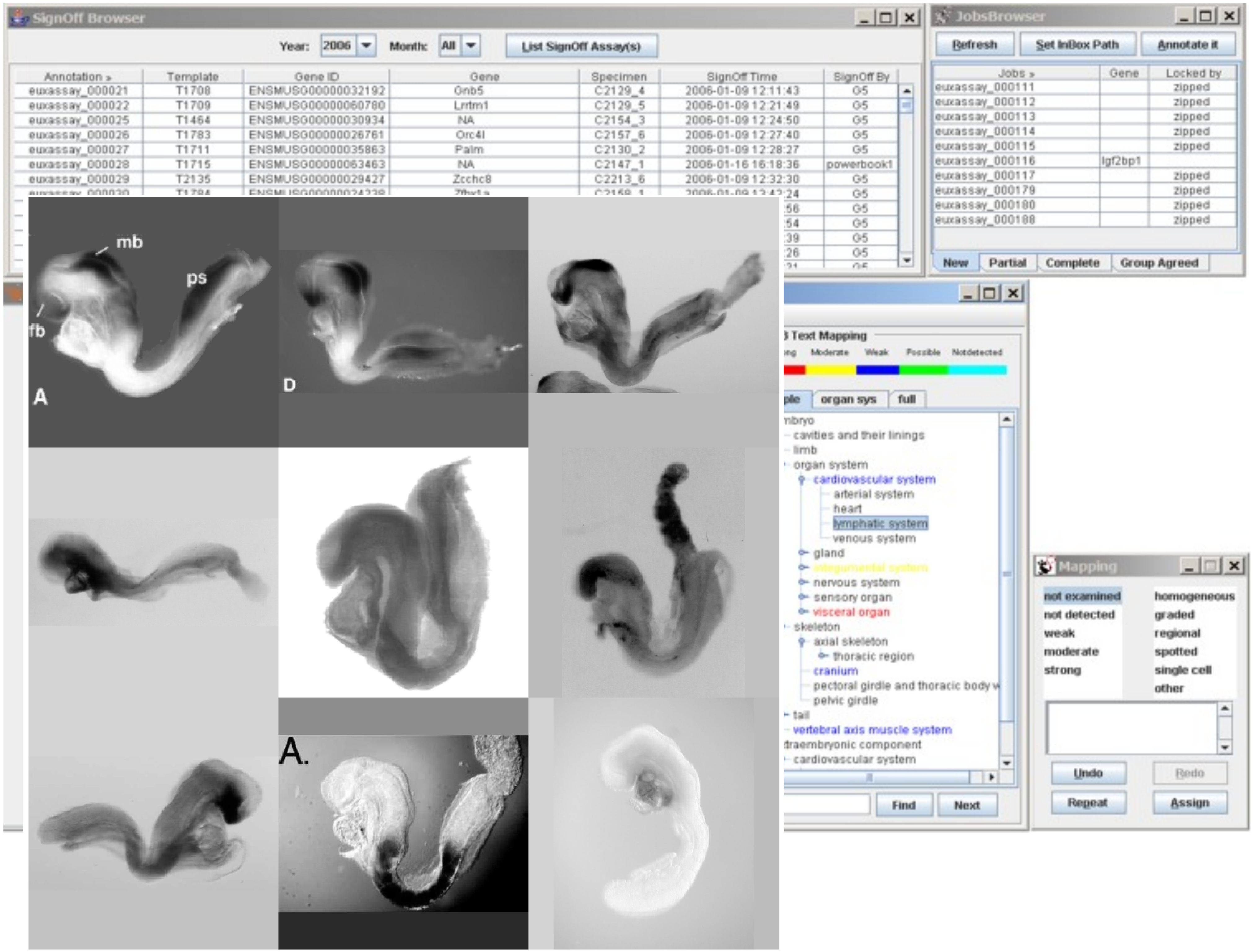
BioAtlas - data mapping

- image collection - no mapping all spatial interpretation left to user
- implicit mapping - data interpreted and annotated with controlled vocabulary or ontology, image requires interpretation but some query and pattern analysis possible - “simple”
- explicit mapping, full spatial delineation of information e.g. expression pattern.

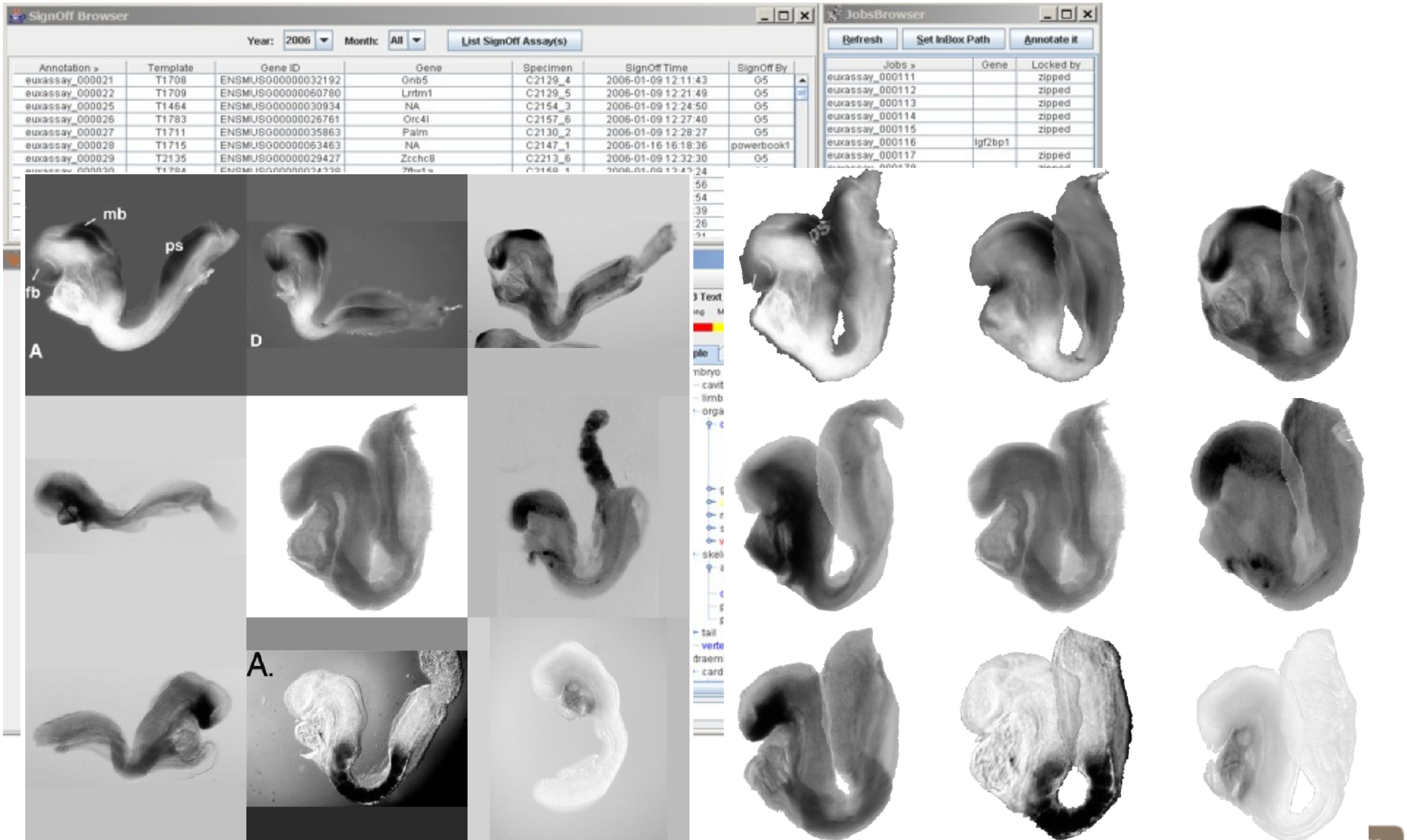
BioAtlas - data mapping



BioAtlas - data mapping



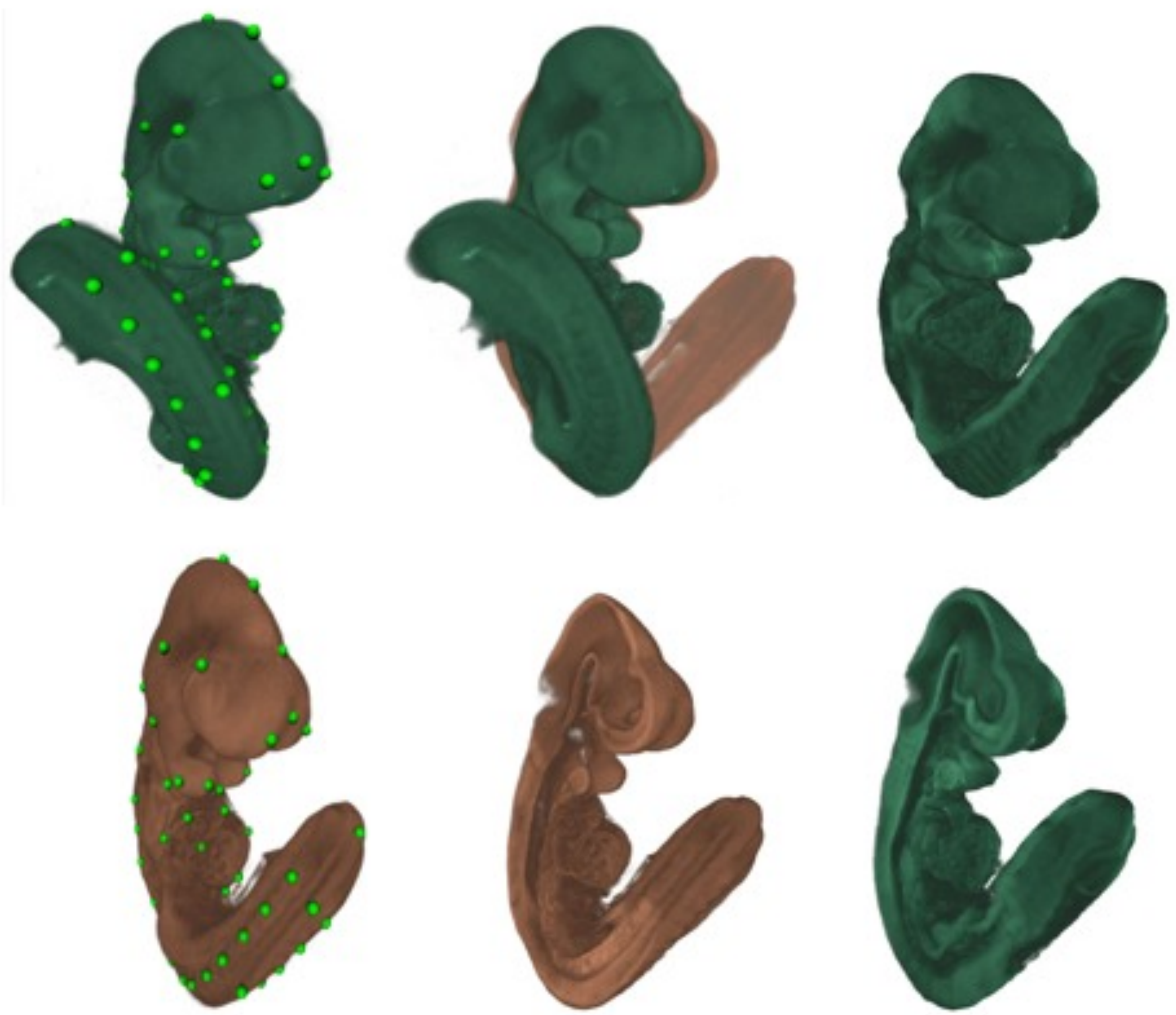
BioAtlas - data mapping



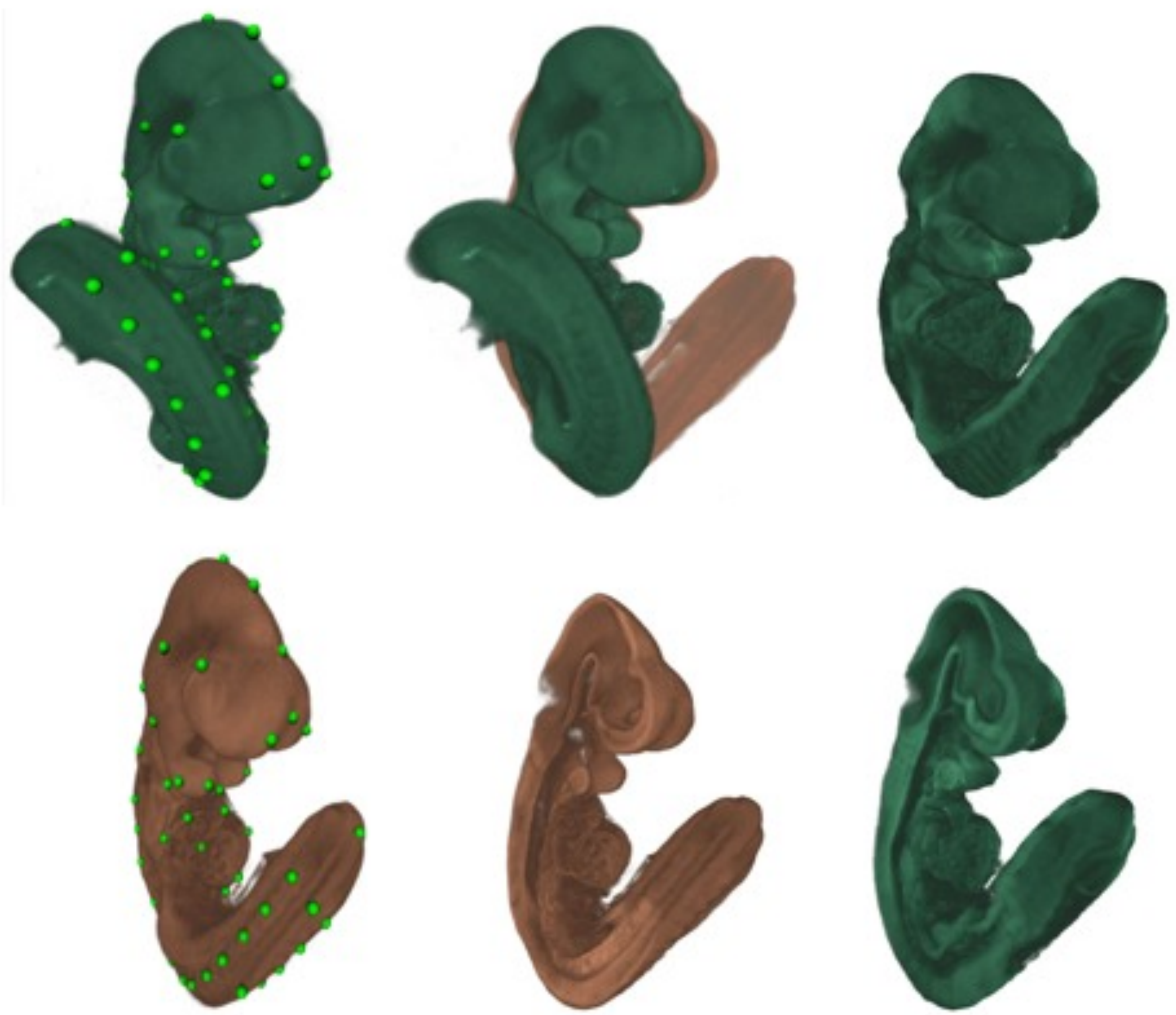
Spatial Data Mapping

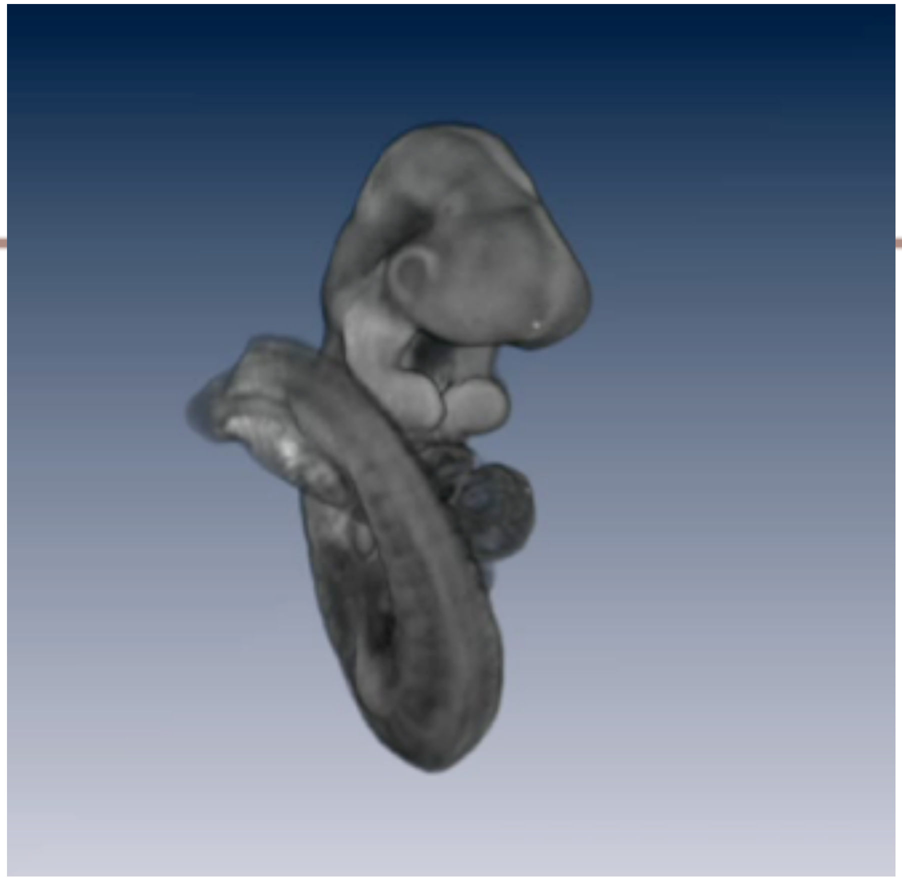
- Manual tie-point alignment (WlzWarp)
  - mesh-based constrained distance transform
  - interactive
  - arbitrary complexity
- Automated fine tuning (ITK/ANTS)
- Editor review

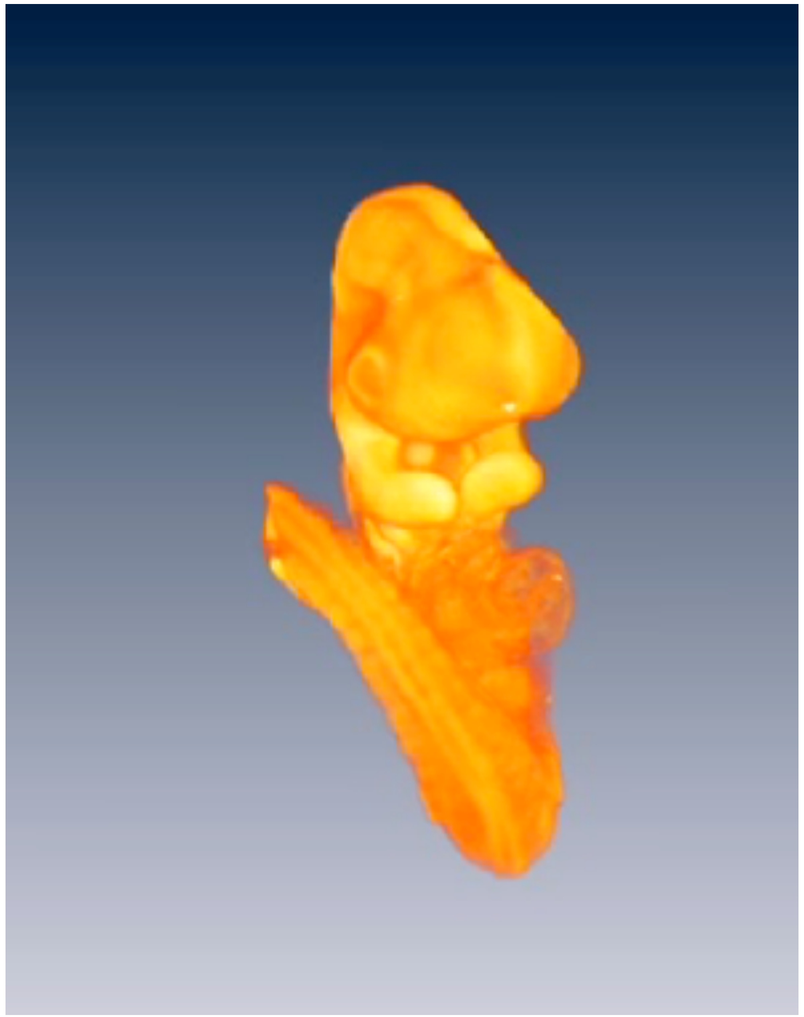
3D Data Mapping - WlzWarp



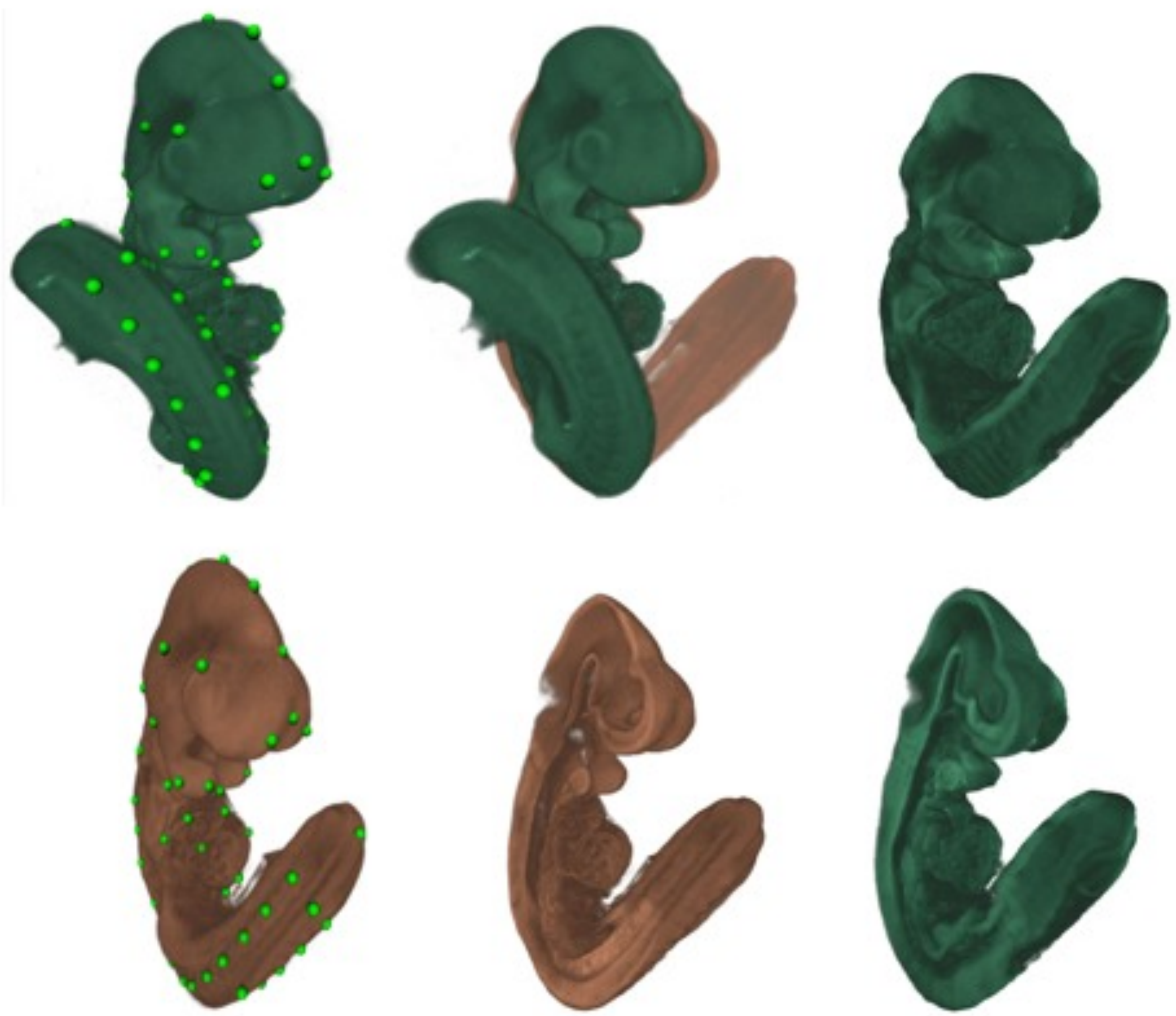
3D Data Mapping - WlzWarp

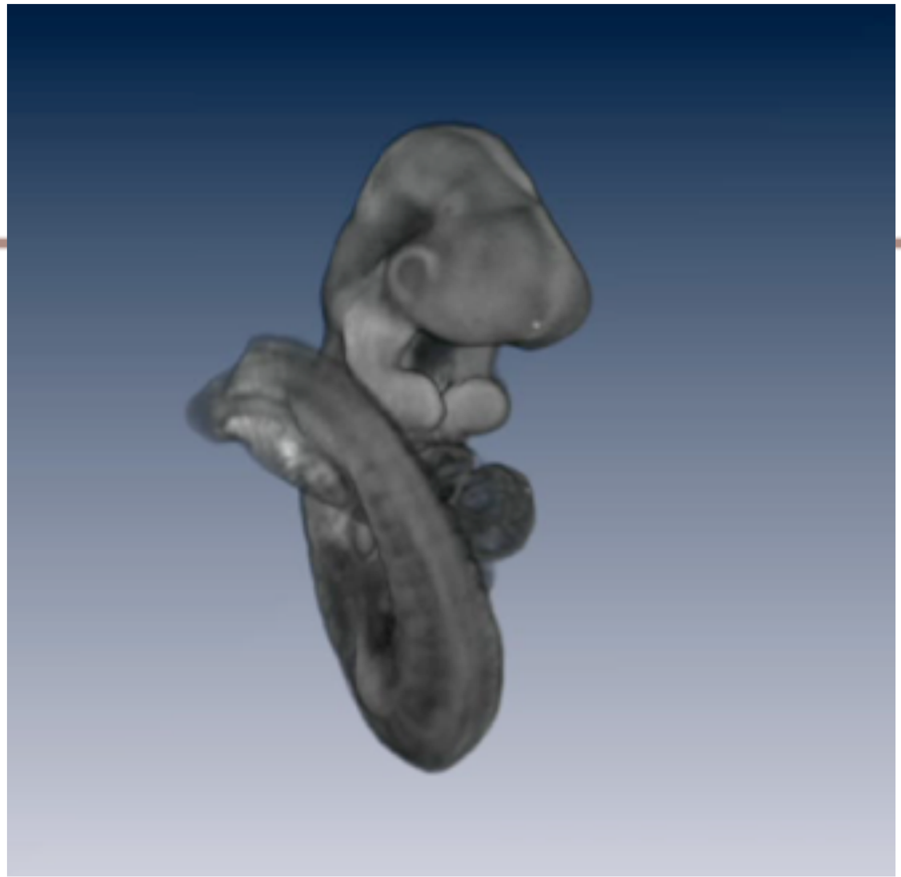


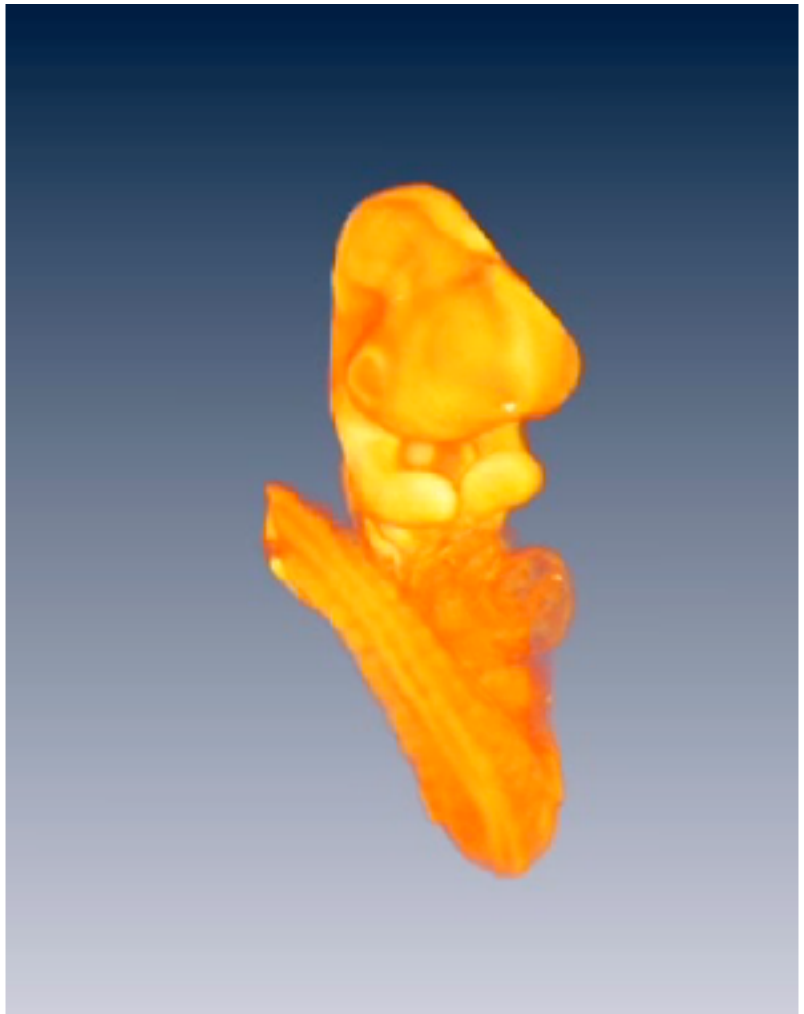




3D Data Mapping - WlzWarp







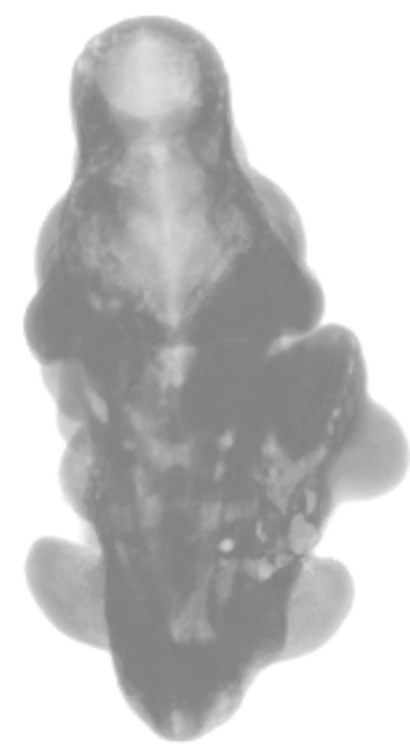
3D Mapping - Wnt signalling pathway

Wnt1		TS17	10.5dpc	3D View	EMAGE:6132
Wnt2		TS17	10.5dpc	3D View	EMAGE:6134
Wnt3		TS17	10.5dpc	3D View	EMAGE:6138
Wnt3A		TS17	10.5dpc	3D View	EMAGE:6141
Wnt4		TS17	10.5dpc	3D View	EMAGE:6142
Wnt5A		TS17	10.5dpc	3D View	EMAGE:6144
Wnt6		TS17	10.5dpc	3D View	EMAGE:6148
Wnt7A		TS17	10.5dpc	3D View	EMAGE:6150

3D Mapping - Wnt signalling pathway

Wnt1		TS17	10.5dpc	3D View	EMAGE:6132
Wnt2		TS17	10.5dpc	3D View	EMAGE:6134
Wnt3		TS17	10.5dpc	3D View	EMAGE:6138
Wnt3A		TS17	10.5dpc	3D View	EMAGE:6141
Wnt4		TS17	10.5dpc	3D View	EMAGE:6142
Wnt5A		TS17	10.5dpc	3D View	EMAGE:6144
Wnt6		TS17	10.5dpc	3D View	EMAGE:6148
Wnt7A		TS17	10.5dpc	3D View	EMAGE:6150

Wnt1



MRC Human Genetics Unit

3D Visualisation

- Applications:
  - SectionBrowser, JAtlasViewer
  - Format conversion -> a.n.other
- Browser-Based
  - canned views & movies
  - Tiled zoom-viewer
    - Extended to 3D protocol (IIP3D)
    - Multi-layer
    - Interactive overlays
    - WebGL

OME Project Objectives

To use and extend OMERO to meet mouse atlas and IGMM requirements:

- Embed woolz images
- Sparse reconstruction & mapping
- large image data
- Annotation overlay and visualisation
- 3D mapping - e.g. OPT images
- IGMM imaging - archiving and analysis

Woolz images

A fast interval processor

G.A. Shippey[a], R.J.H. Bayley[a], A.S.J. Farrow[a], D.R. Rutovitz[a] and J.H. Tucker[a]

[a]MRC Clinical and Population Cytogenetics Unit, Edinburgh, U.K.

Received 22 December 1980. Available online 19 May 2003.

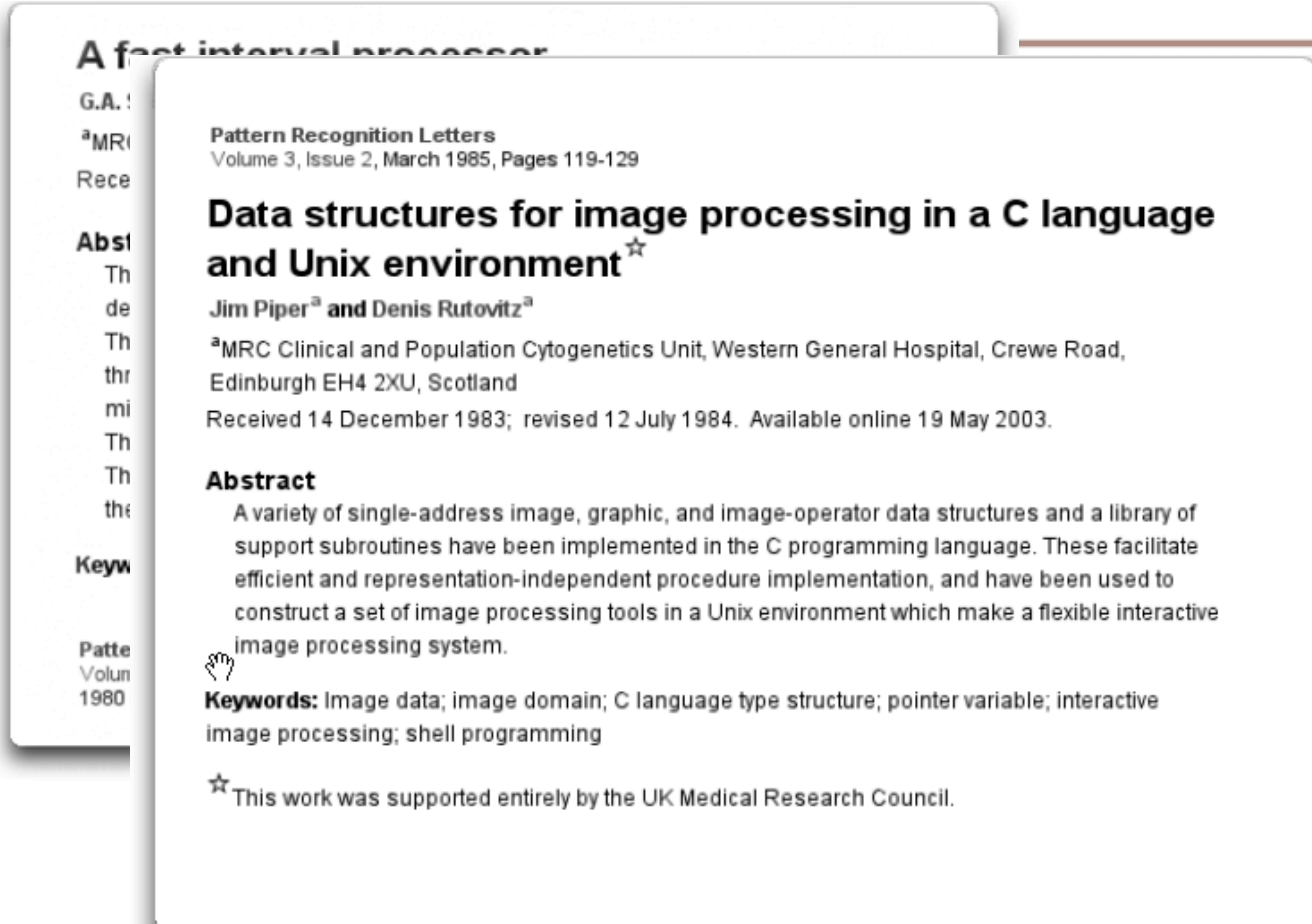
Abstract

The advent of high resolution Linear Image Sensors, and high p.r.f. stepping
development at the MRC Edinburgh is intended to scan a conventional micros
The high pixel data rate (8 MHz peak) easily saturates most computer configur
threshold, pixels (i.e. 'intervals') into a set of interval parameters. These interval
microprocessors to give object parameters from which the cells can then be
The paper describes the hardware and software architecture, with comments
The linkage procedure used to reconstitute contiguous object descriptions is
the order of 1 ms.

Keywords: Interval; Image sensor; Stepping motor; Auto-focus; Metaphase;

Pattern Recognition
Volume 14, Issues 1-6, 1981, Pages 345-356
1980 Conference on Pattern Recognition

Woolz images



Pattern Recognition Letters
Volume 3, Issue 2, March 1985, Pages 119-129

Data structures for image processing in a C language and Unix environment ☆

Jim Piper[a] and Denis Rutovitz[a]

[a]MRC Clinical and Population Cytogenetics Unit, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, Scotland

Received 14 December 1983; revised 12 July 1984. Available online 19 May 2003.

Abstract

A variety of single-address image, graphic, and image-operator data structures and a library of support subroutines have been implemented in the C programming language. These facilitate efficient and representation-independent procedure implementation, and have been used to construct a set of image processing tools in a Unix environment which make a flexible interactive image processing system.

Keywords: Image data; image domain; C language type structure; pointer variable; interactive image processing; shell programming

☆ This work was supported entirely by the UK Medical Research Council.

Emap

Woolz images

A fast interval processor
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Pattern Reco
Volume 3, Issu
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Jim Piper[a] a
[a]MRC Clinic
Edinburgh E
Received 14
Abstract
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image pro
Keywords: I
image proce
☆This work

Cytometry. 1994 May 1;16(1):7-16.

Automatic fluorescence metaphase finder speeds translocation scoring in FISH painted chromosomes.

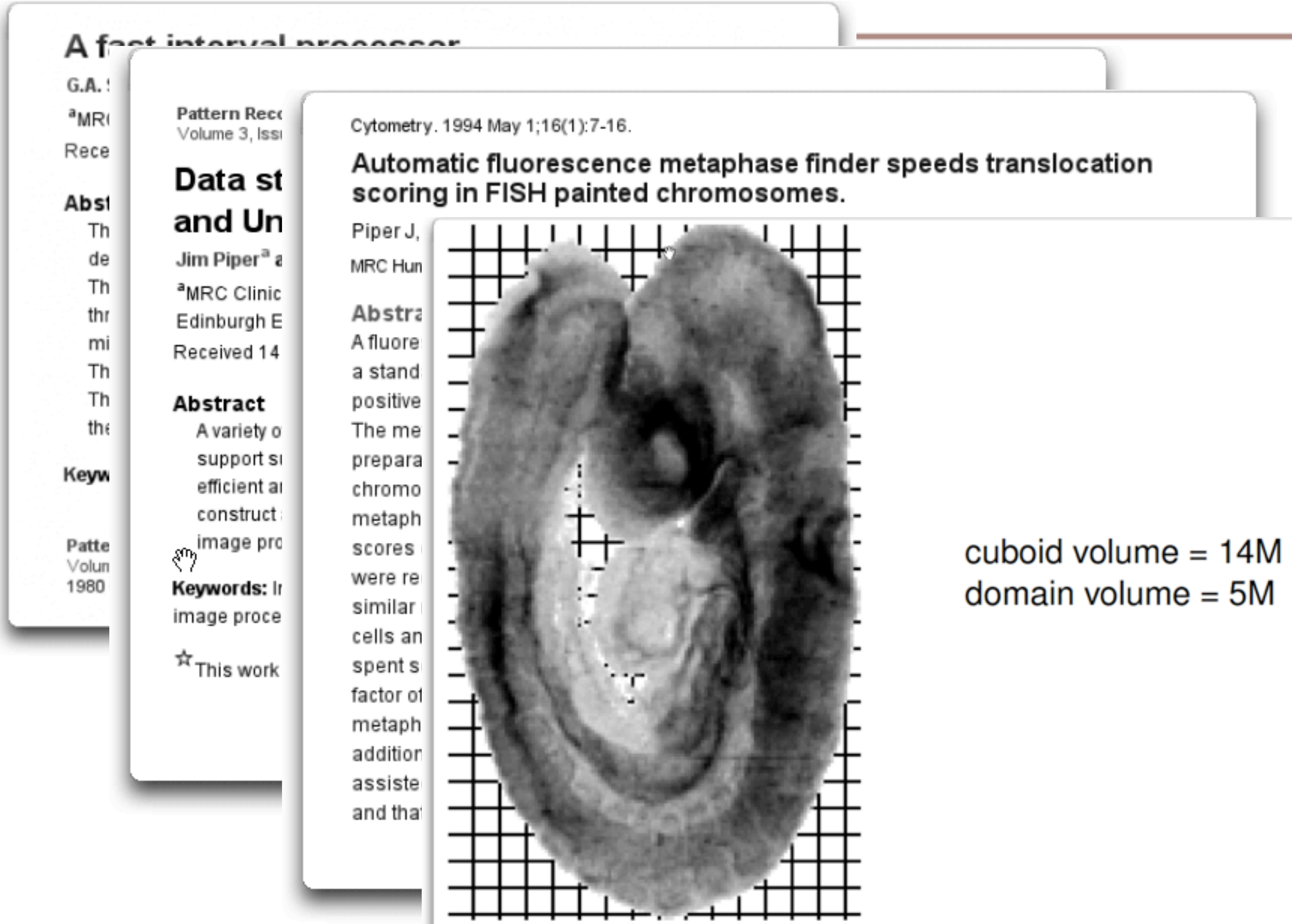
Piper J, Poggensee M, Hill W, Jensen R, Ji L, Poole I, Stark M, Sudar D.

MRC Human Genetics Unit, Edinburgh, Scotland.

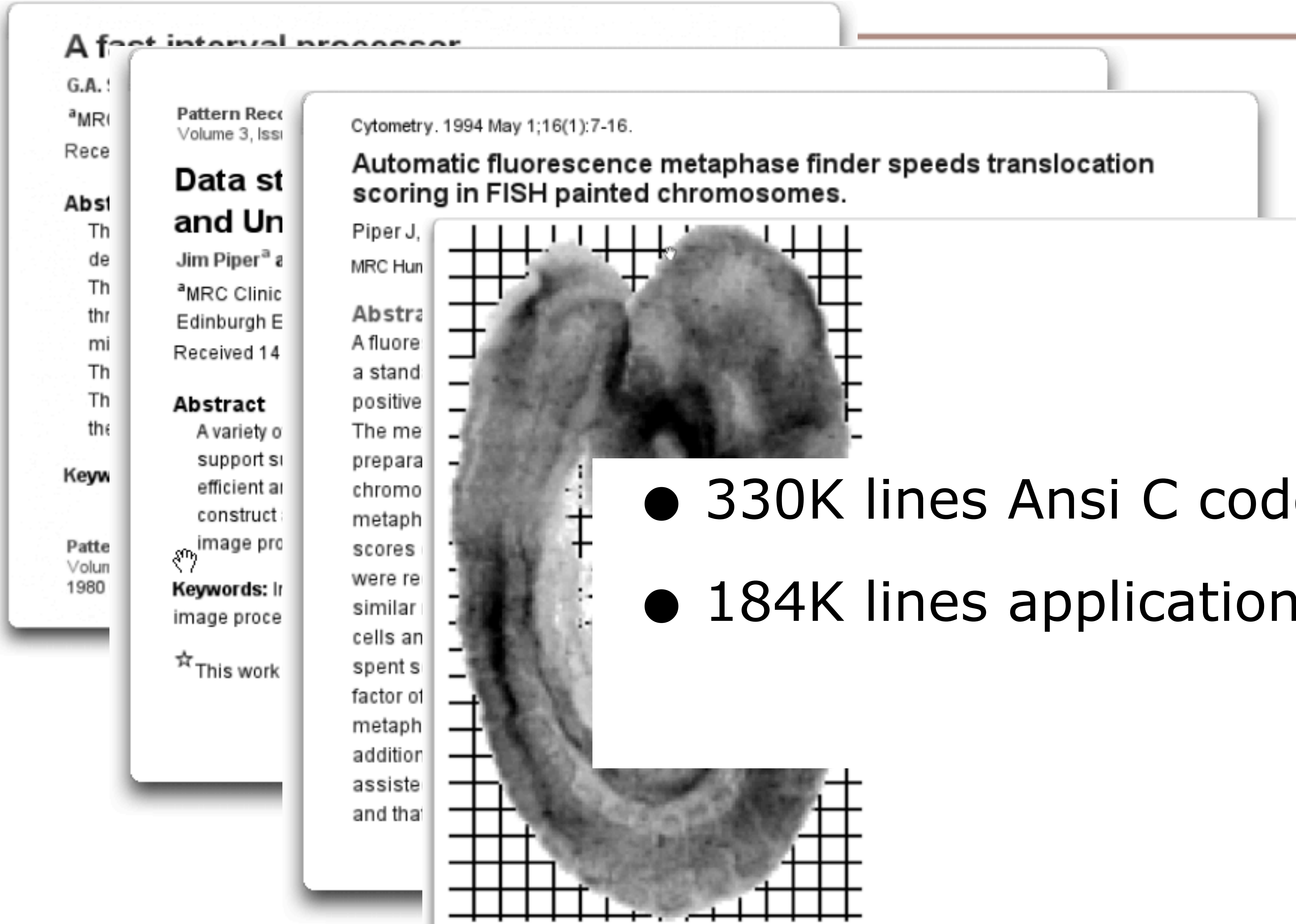
Abstract

A fluorescence metaphase finder was constructed with commercially available hardware and a standard Unix workstation. Its accuracy was measured in terms of the number of false positive and false negative detected metaphases on a variety of different slide preparations. The metaphase finder was used in a translocation scoring experiment in which metaphase preparations of human peripheral blood lymphocytes were hybridized with whole chromosome probes to chromosomes #1, #2, and #4. The automatic finder presented metaphases to the cytogeneticist, centered in the eyepieces at x63. The cytogeneticist's scores of analyzable metaphases and of painted chromosomes involved in rearrangements were recorded. The time for the analysis was recorded and compared to the time to analyze a similar number of cells in a purely visual experiment in which the cytogeneticist scanned for cells and analyzed them, both at x63. The results showed that, neglecting the machine time spent scanning unattended, the amount of time required for the analysis was reduced by a factor of three. Furthermore, in this experiment the metaphase finder found more scorable metaphases than the cytogeneticist found by visual scanning. Machine-assisted scoring had additional, less quantifiable, benefits; notably that digital images of metaphases sometimes assisted the analysis of chromosome rearrangements, that cells could be revisited easily, and that the analysis was much less fatiguing.

Woolz images



Woolz images



- 330K lines Ansi C code
- 184K lines application code

Woolz Images

- Domain
  - Rectangle based
  - Interval based
  - 3D planewise domains
- Values
  - Rectangle based
  - Raged and interval based
  - Tiled

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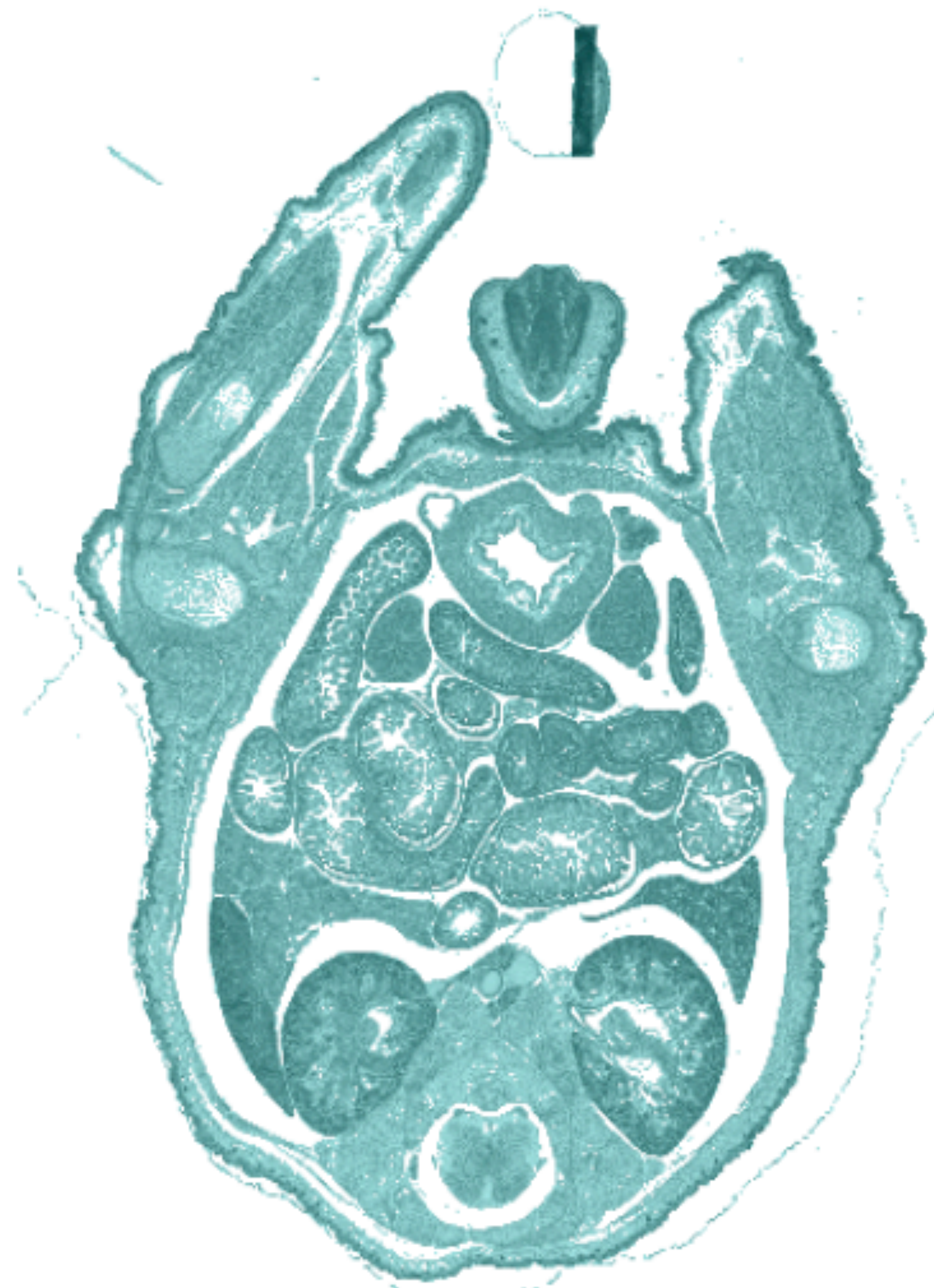

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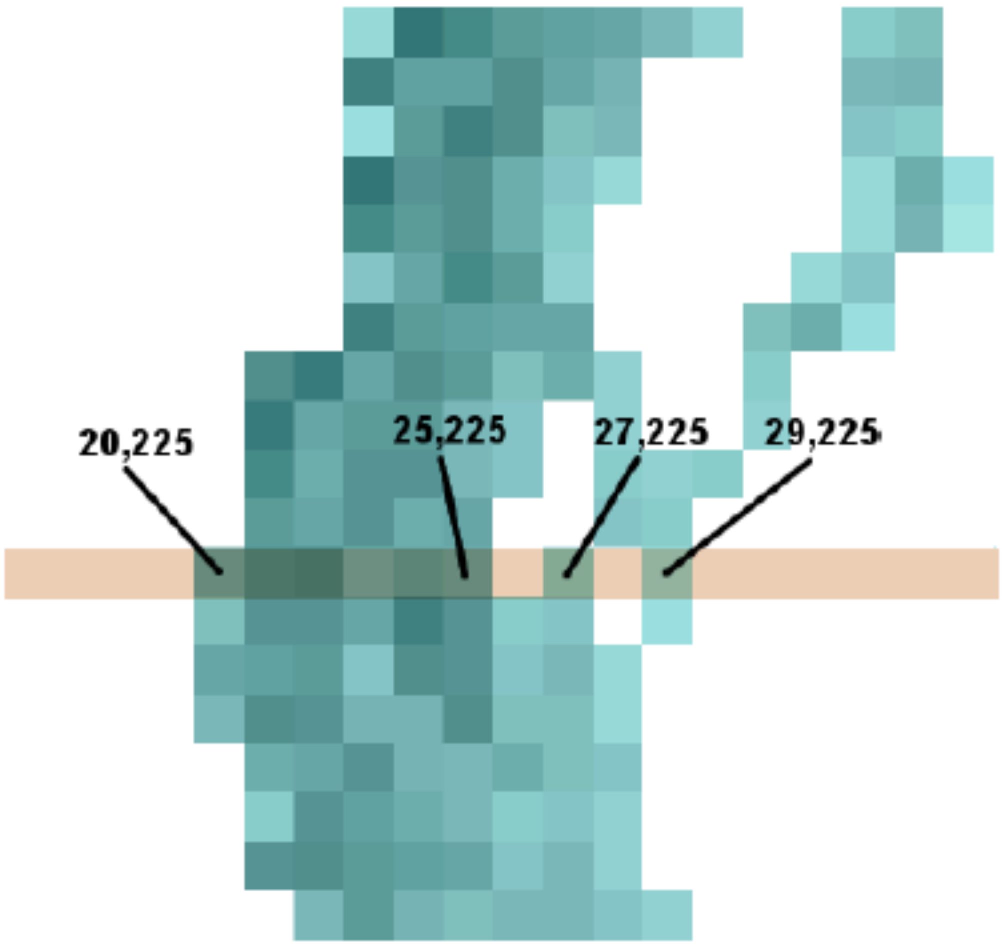

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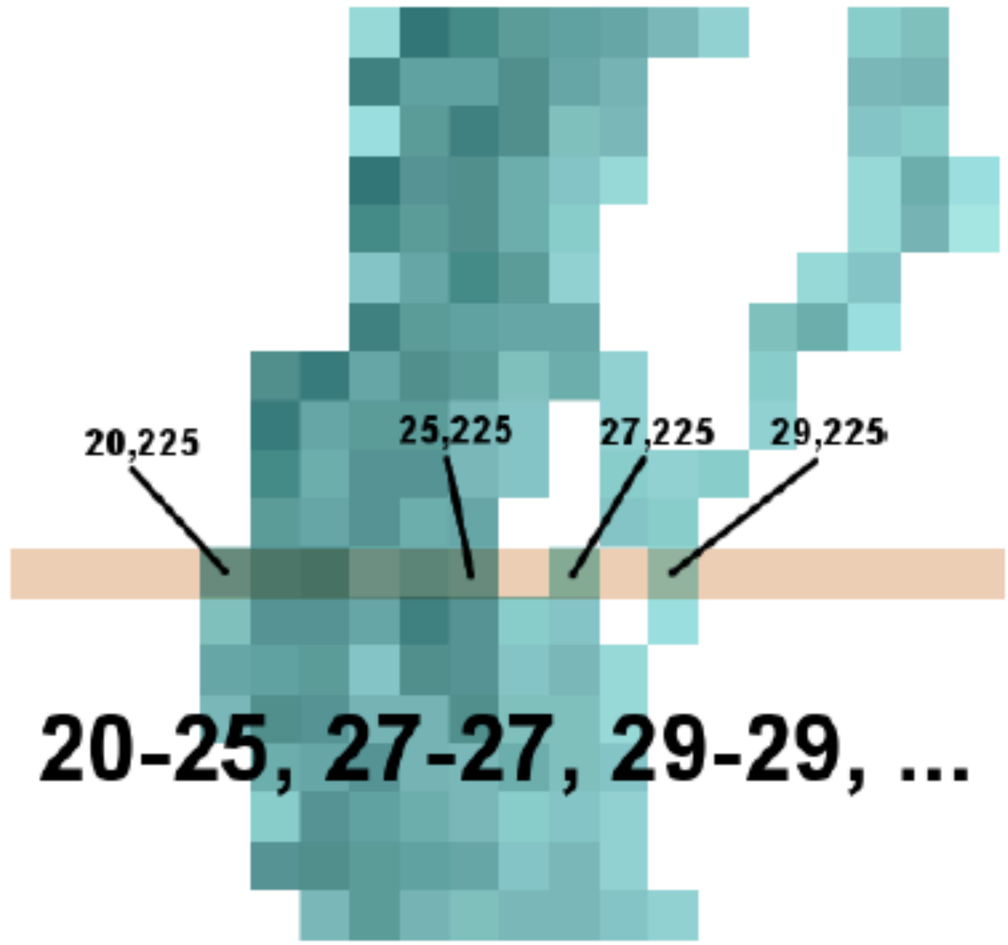

MRC Human Genetics Unit

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    based
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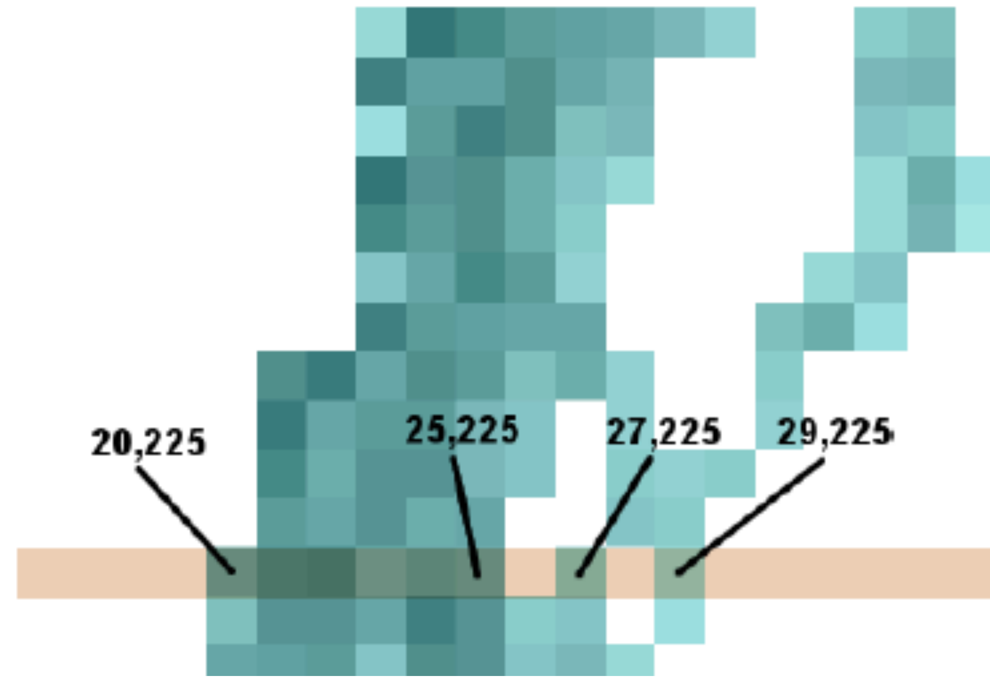

- Arbitrary bounding box
- Interval coding - compact
- Fast binary & morphological operations
- Separation of domain from values enables value data sharing

Woolz Images

- Domain
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- Values
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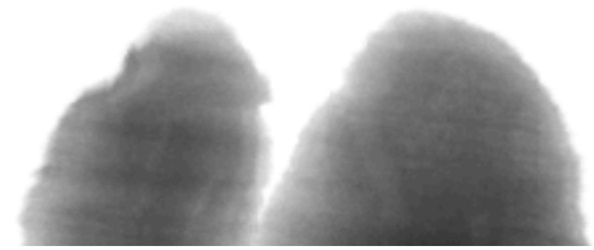
Woolz Images

- Domain
  - Rect
  - Inter
  - 3D p
- Values
  - Rect
  - Rage base
  - Tiled



- value types: ubyte, short, int, float, double, rgba, bitmap
- Value table can be shared by many objects
- Compact coding without compression
- Iterators to navigate data
- Tiled data can be memory mapped for very fast access - minimal coding change

Woolz Images

- Domain
  - Rect
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  - 3D p
- Values
  - Rect
  - Rage base
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Woolz image objects

- Polylines, boundary lists
- histograms
- meshes - 2D & 3D
- transforms
  - affine
  - basis function
  - mesh
  - conforming mesh

Woolz image objects

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- histograms
- meshes - 2D & 3D
- transforms
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  - basis function
  - mesh
  - conforming mesh

$$\begin{pmatrix} t_{00} & t_{01} & t_{02} & t_{03} \\ t_{10} & t_{11} & t_{12} & t_{13} \\ t_{20} & t_{21} & t_{22} & t_{23} \\ 0 & 0 & 0 & t_{33} \end{pmatrix}$$

Woolz image objects

- Polylines, boundary lists
- histograms
- meshes - 2D & 3D
- transforms
  - affine
  - basis function
  - mesh
  - conforming mesh

$$\Delta u = u - x$$

$$\Delta u = P_u(x, y) + \sum_{i=1}^{i=N} \lambda_i b(r_i)$$

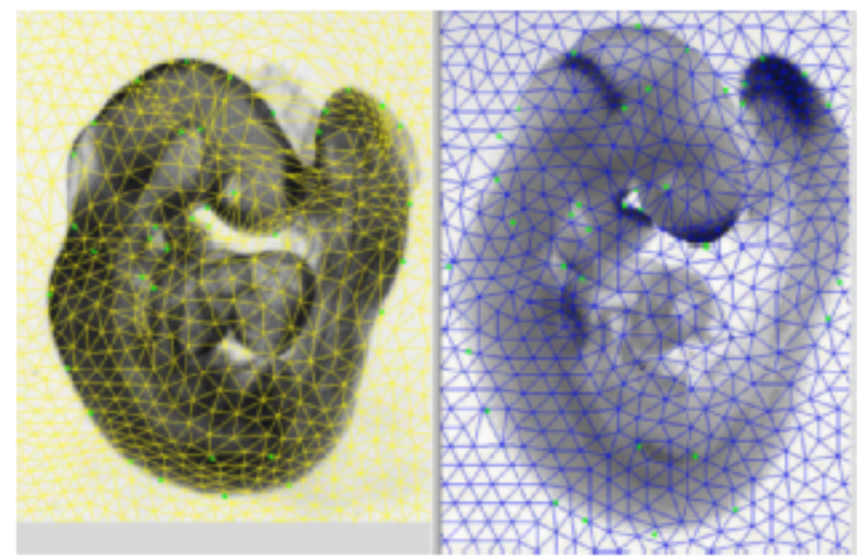
$$b_{TPS}(r) = r^2 ln(r^2)$$

$$b_{MQ}(r) = \sqrt{r^2 + \delta^2}$$

$$b_{IMQ}(r) = \frac{1}{\sqrt{r^2 + \delta^2}}$$

Woolz image objects

- Polylines, boundary lists
- histograms
- meshes - 2D & 3D
- transforms
  - affine
  - basis function
  - mesh
  - conforming mesh



Woolz image objects

- Polylines, boundary lists
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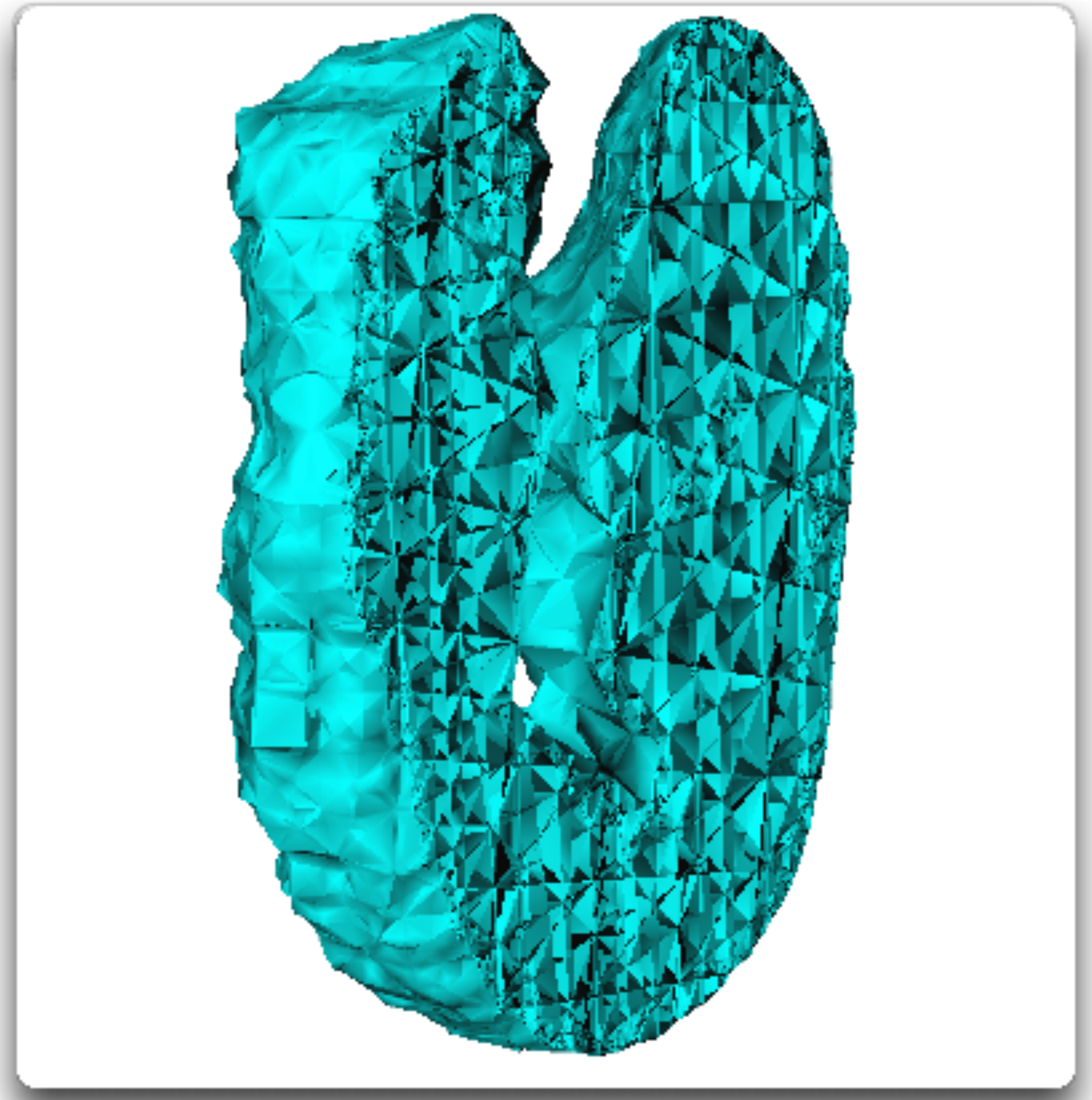
- meshes - 2D & 3D
- transforms
  - affine
  - basis function
  - mesh
  - conforming mesh



Sparse Image Reconstruction & Mapping

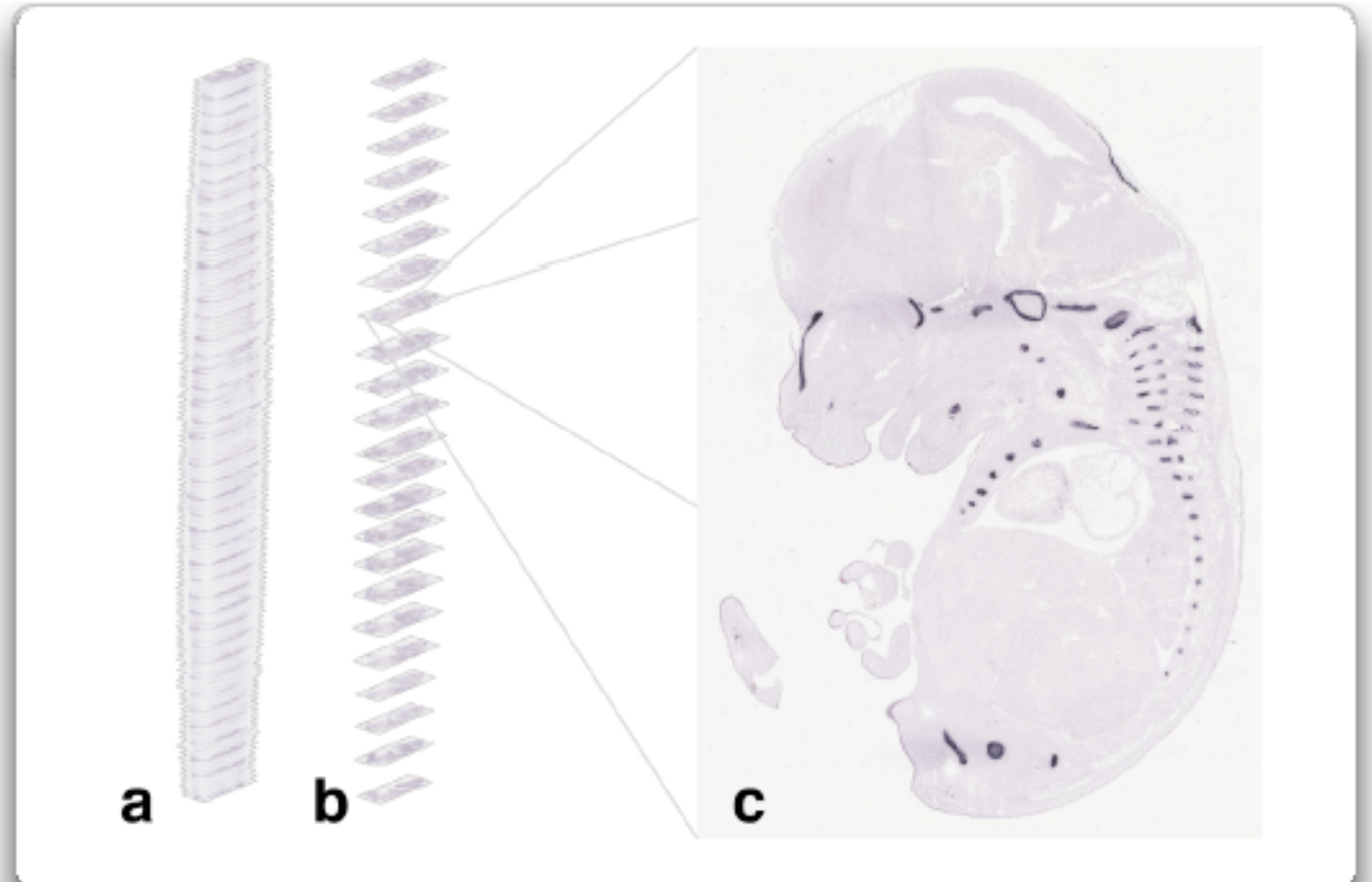
- EurExpress project
    - 19.5K in situ probes, 350K images
    - ~24 images per in situ probe
    - ~0.5 micron resolution in plane
    - 150 micron plane separation
- EmbryoExpress - 20K images
- Allen Brain Atlas - 200K images
- Require automation - Advanced Normalisation Tool (ANTs)
    - sparse image, matching mask
    - Full 3D affine then non-linear warping.

Pseudo Wholemount Mapping to Emap - done

- Semi-automatic reconstruction
- Automated segmentation
- Manual mapping
- 2D pseudo wholemount
- full 3D in progress

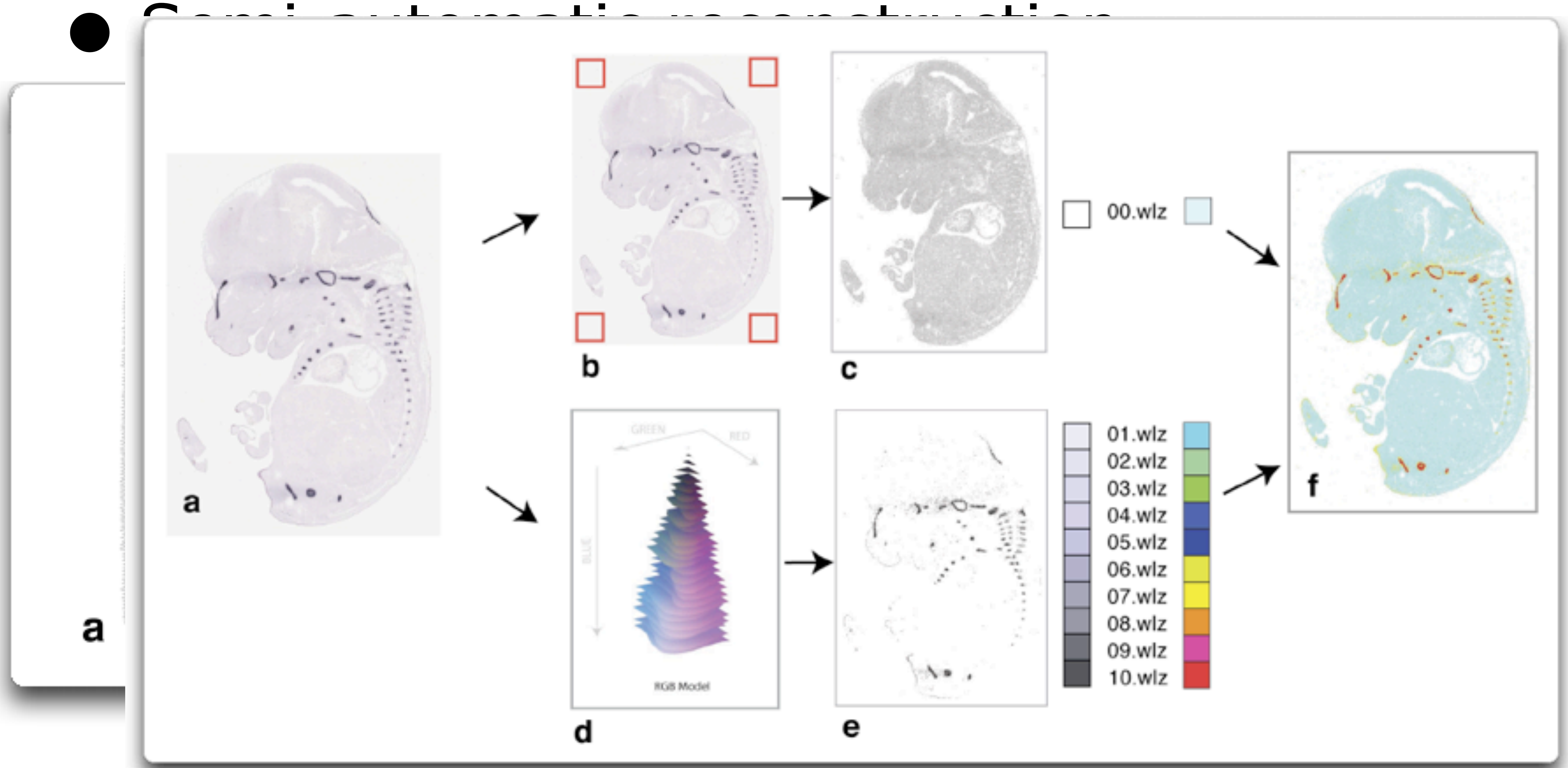
Pseudo Wholemount Mapping to Emap - done

- Semi-automatic reconstruction



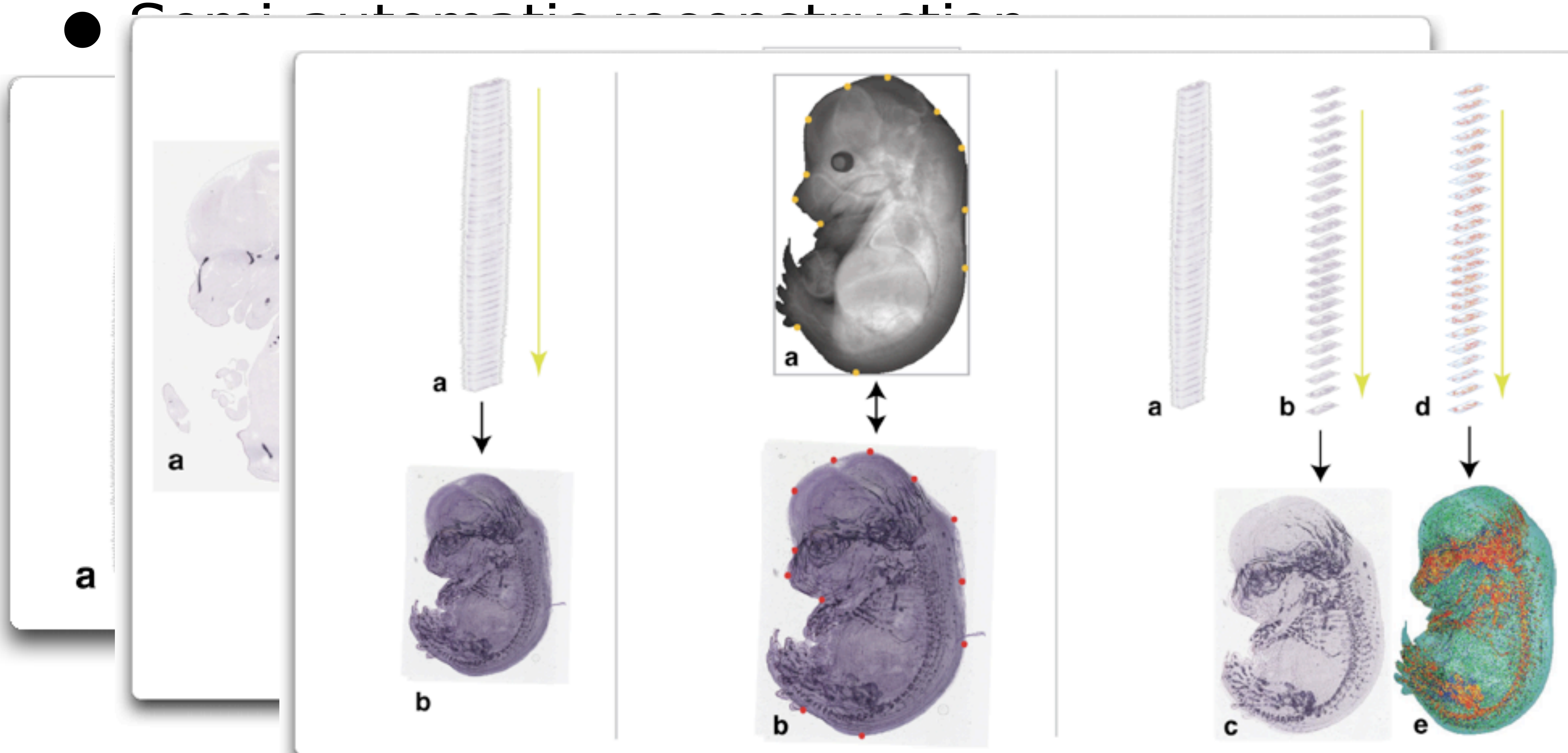
Pseudo Wholemount Mapping to Emap - done

- Semi-automatic reconstruction

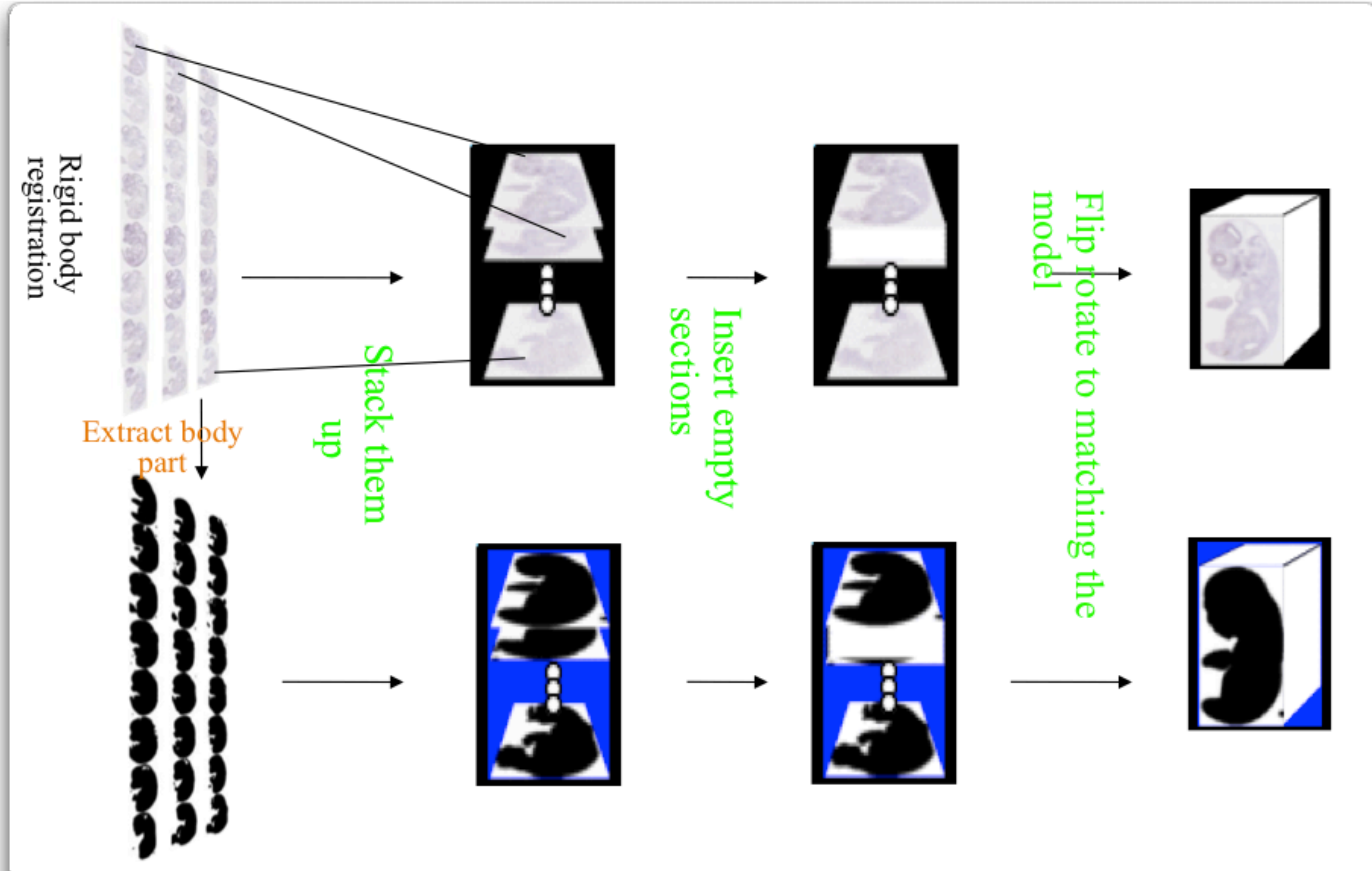


Pseudo Wholemount Mapping to Emap - done

- Semi-automatic reconstruction

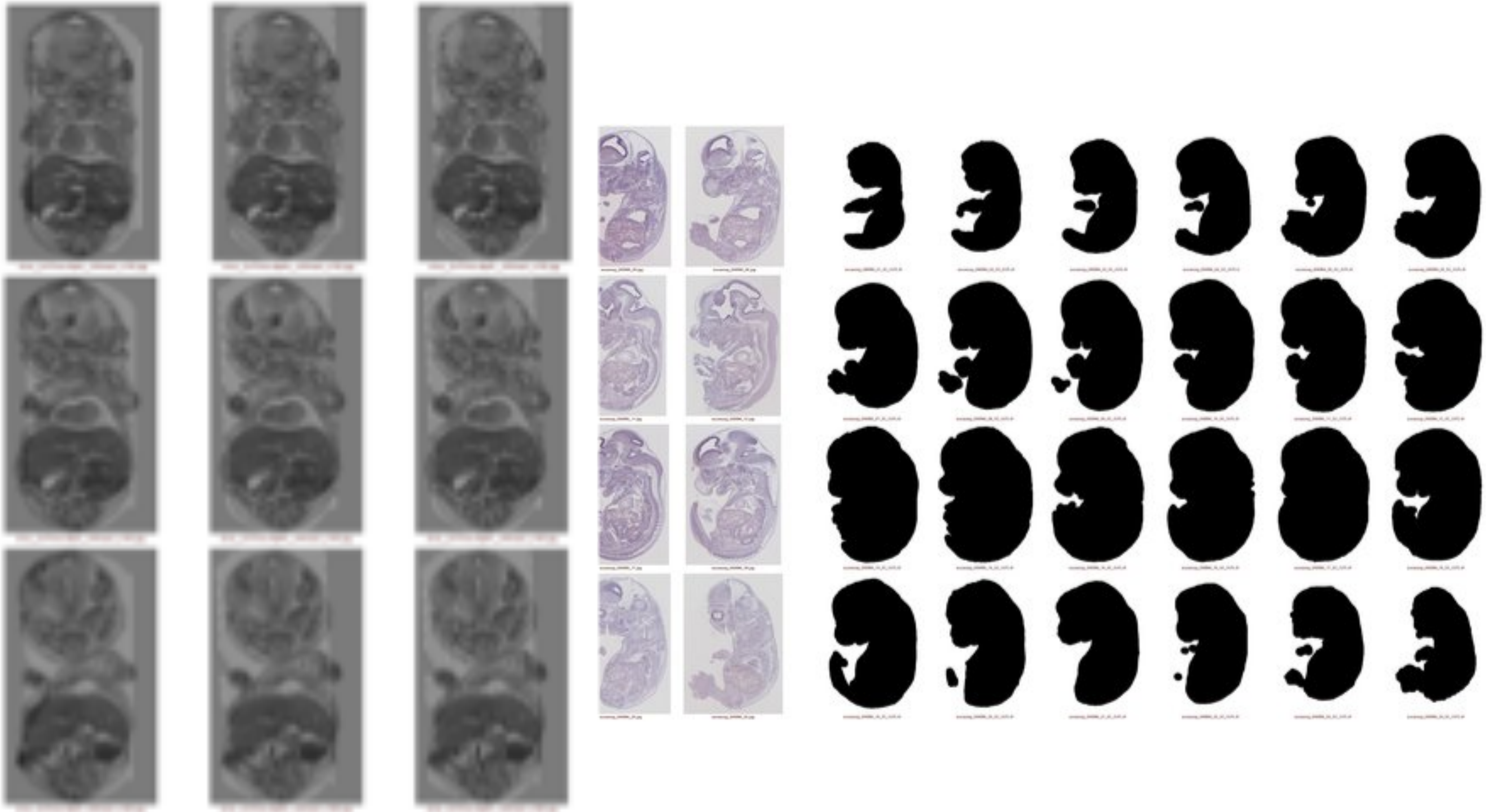


3D Mapping to emap

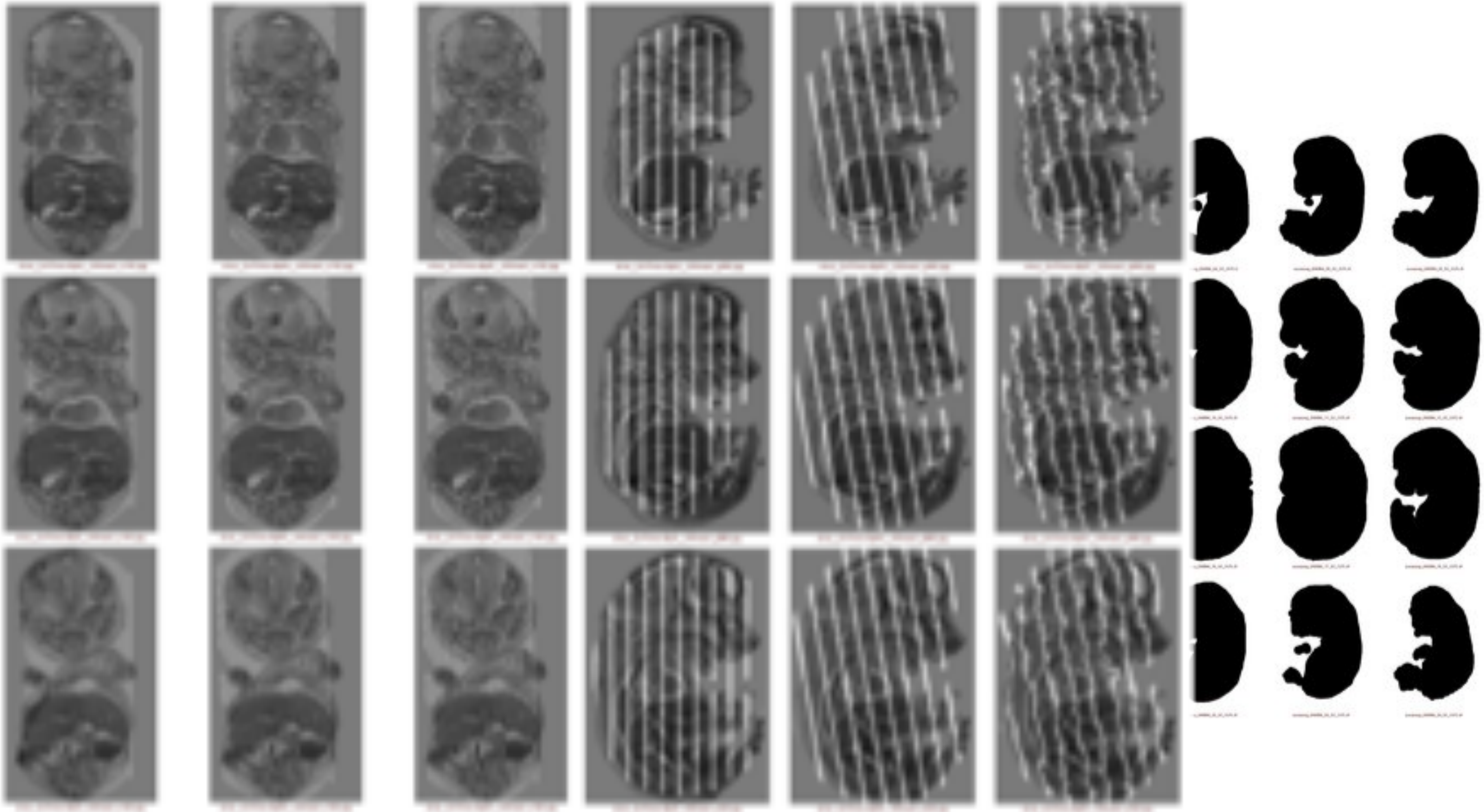


3D Mapping to emap

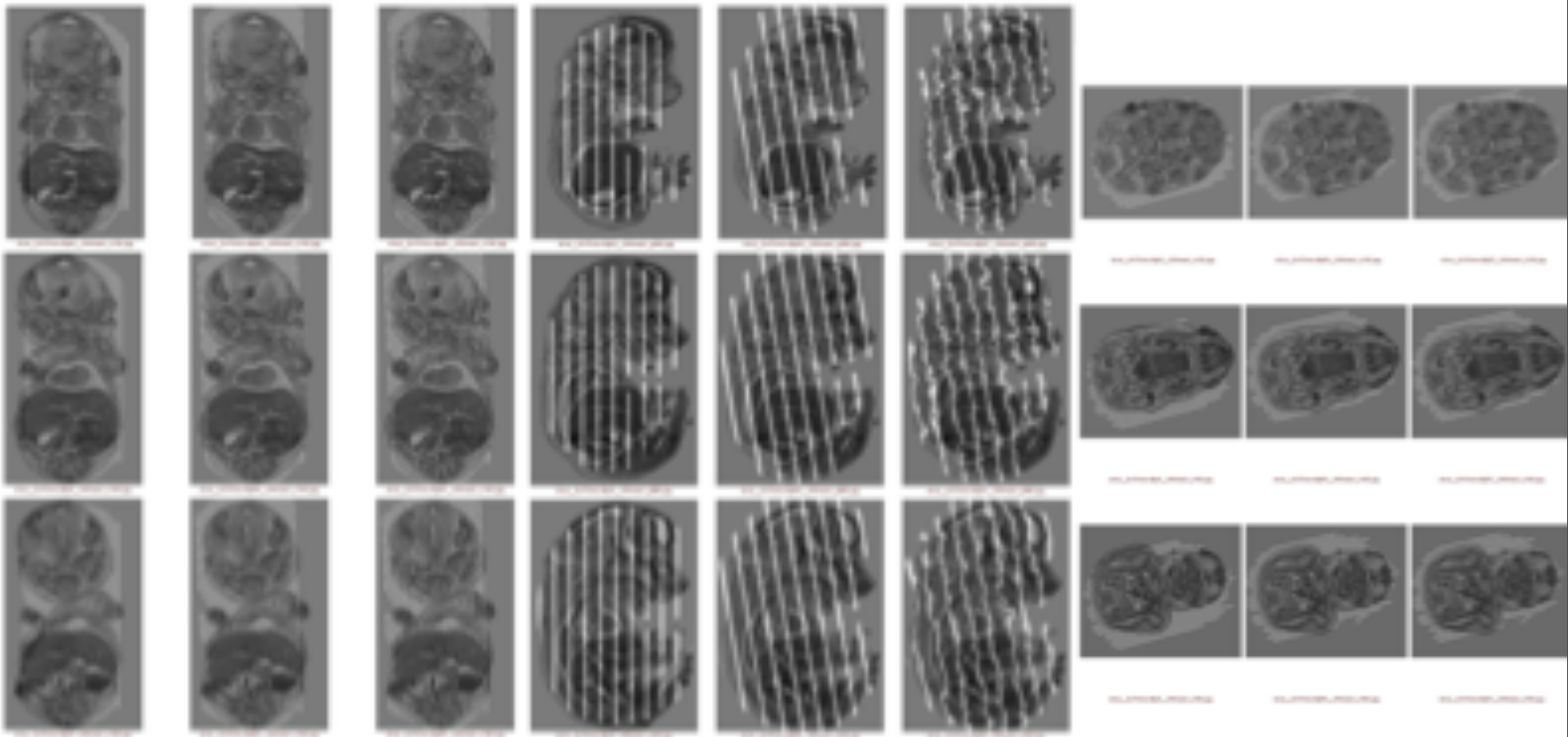
3D Mapping to emap



3D Mapping to emap



3D Mapping to emap



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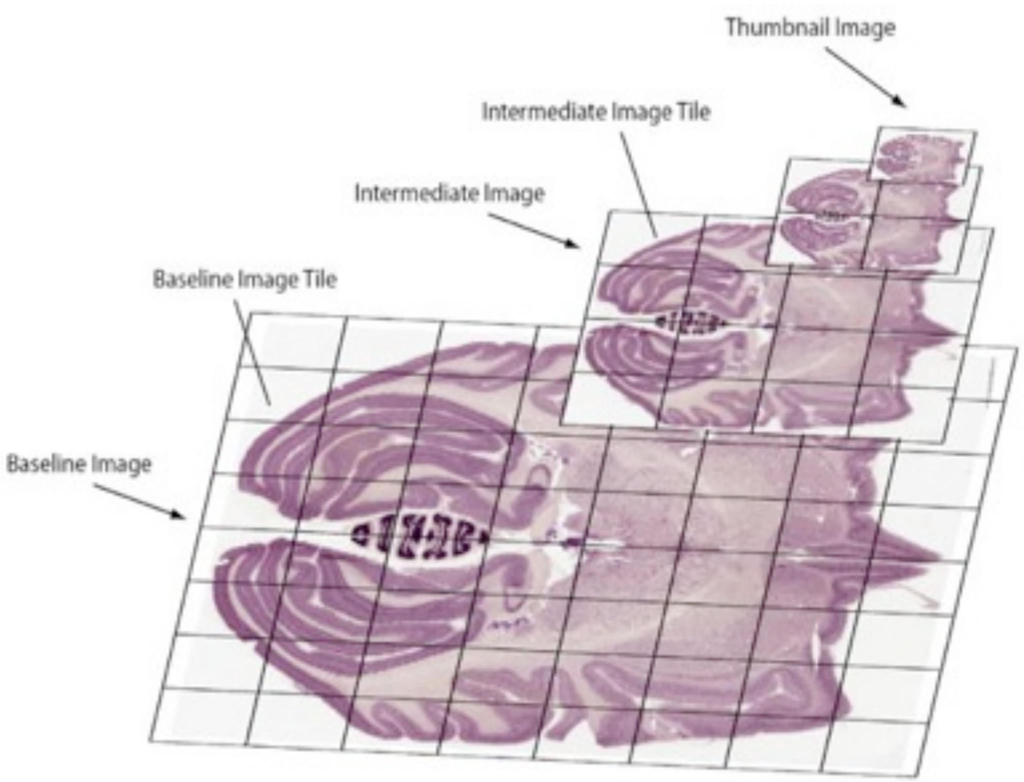
Large Image Data

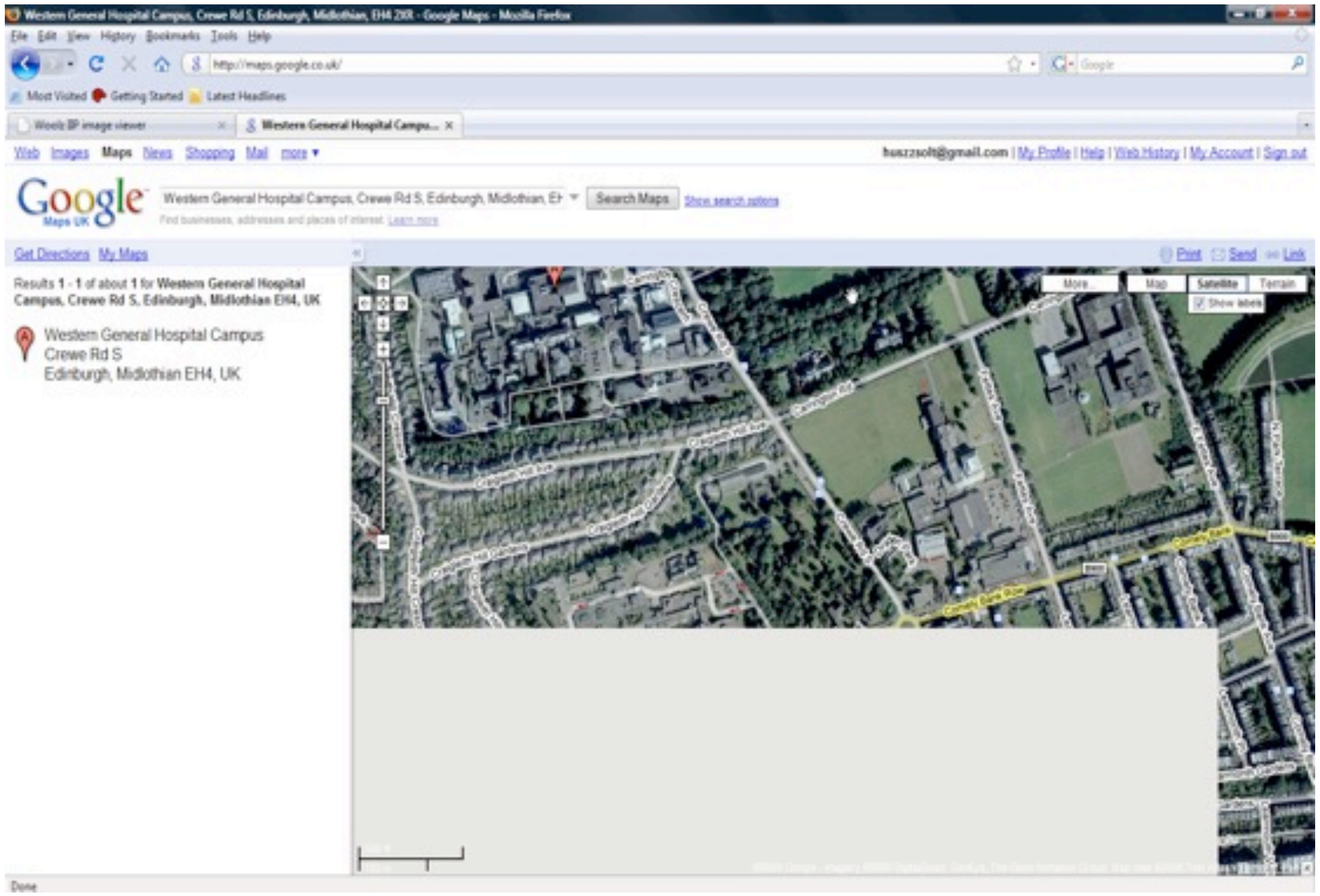
- Single reconstructions already 30+GB
- New EM embryo data ~0.5TB
- OPT data - small (200MB) but many - 5K
- Typical requirement to browse as sections
- Require arbitrary angle re-sectioning

- BLB - want to browse online using no more that a web-browser

Tiled Image Servers



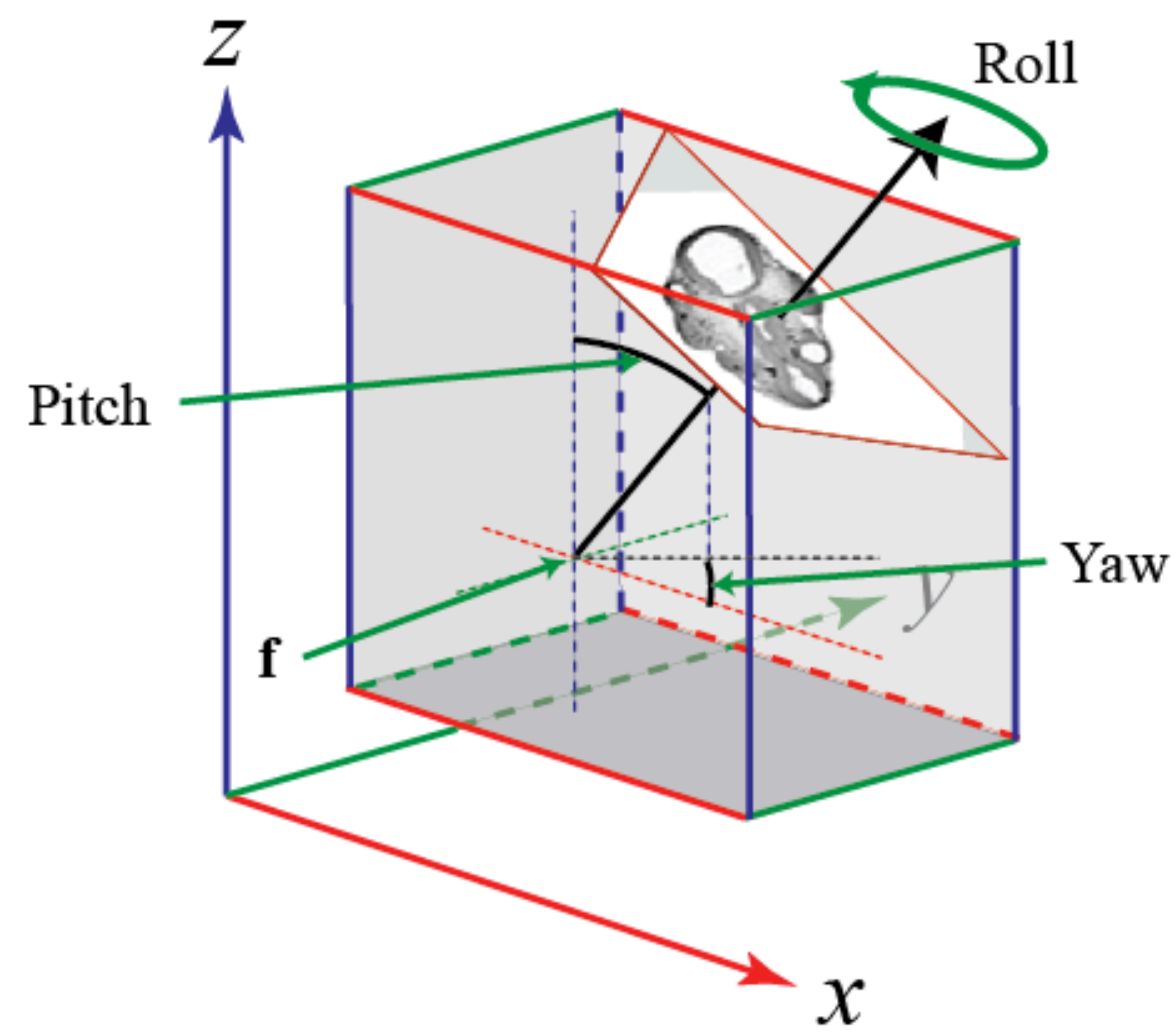
[Shawn Mikula, Issac Trotts, James M. Stone, and Edward G. Jones,Internet-Enabled High-Resolution Brain Mapping and Virtual Microscopy, Neuroimage, vol 35(1), p. 11, 2007]



[maps.google.com]

Sectioning Parameters

- Angles:
  - Pitch, Yaw, Roll
- Position:
  - Fixed point (f) & distance
- Scale
- Tiling depends on orientation & scale



Emap

IIP3D - Extensions

Command	Purpose	Syntax
WLZ	Specify the Woolz object	WLZ=*path*
DST	Specify the distance of the sectioning plane	DST=*dis*
FXP	Specify the fixed point of the viewing section rotation	FXP=*X,Y,Z*
FXT	Specify the second fixed point of the viewing section rotation	FXT=*X,Y,Z*
MOD	Specify the projection mode	MOD=*mode*
PIT	Specify the pitch angle of the sectioning rotation	PIT=*angle*
PAB	Specify the 3D query point absolute in the object coordinate	PAB=*X,Y,Z*
PRL	Specify the 2D query point relative in tile or display or tile coordinate	PRL=*T,X,Y*
ROL	Specify the roll angle of the sectioning rotation	ROL=*angle*
SCL	Specify the scale used in the sectioning transformation	SCL=*scale*
UPV	Specify the up vector for the **UP_IS_UP** mode	UPV=*X,Y,Z*
YAW	Specify the yaw angle of the sectioning rotation	YAW=*angle*

Table 1: Extended command overview

Object	Purpose
IIP-server	Identify if WLZ-IIP is running
Max-size	The size of the section
Tile-size	The size of a tile
Wlz-true-voxel-size	The voxel size of the object
Wlz-volume	The volume of the object
Wlz-distance-range	The range of the sectioning plane distance
Wlz-sectioning-angles	The pitch, yaw and roll angles of of the sectioning plane
Wlz-3d-bounding-box	The first and last plane, line and column number of the object
Wlz-coordinate-3D	The 3D coordinates defined in 2D by the **PRL** command
Wlz-grey-value	The grey or RGB value of a point specified either the **PRL** or the **PAB** commands

Table 2: Extended object overview

R A Baldock

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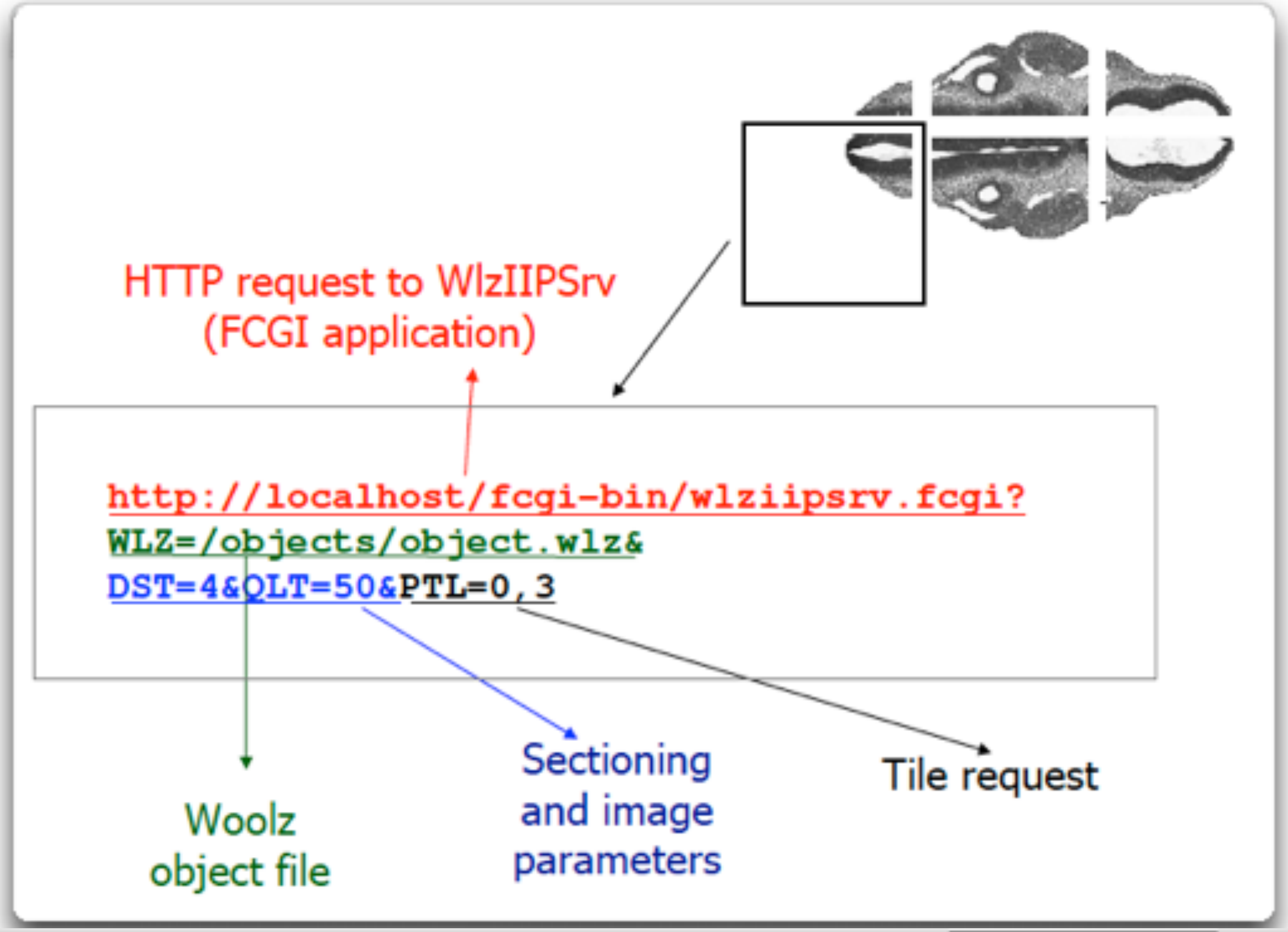
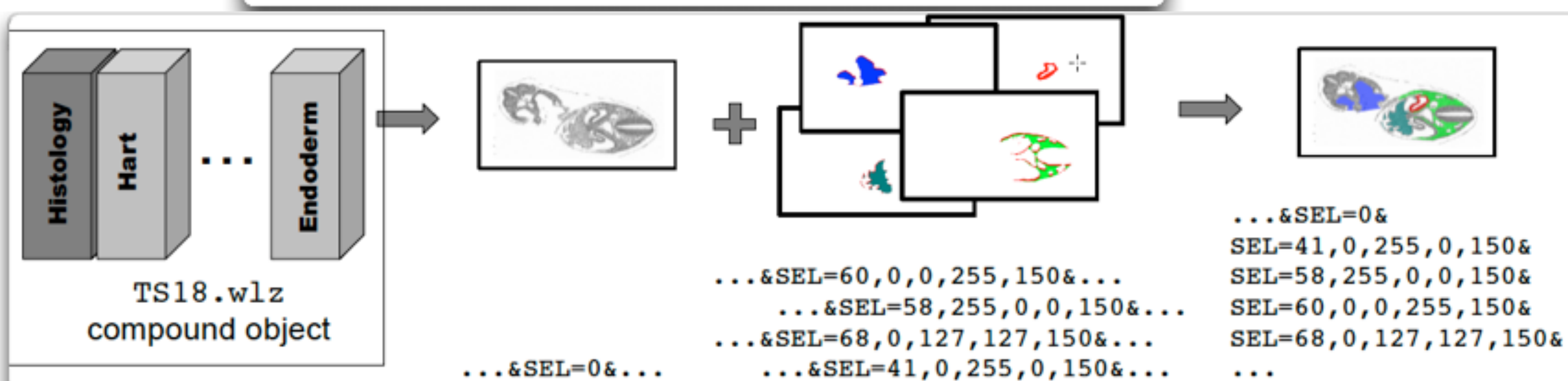
IIP3D


HTTP request to WlzIIPSrv
(FCGI application)
http://localhost/fcgi-bin/wlziipsrv.fcgi?
WLZ=/objects/object.wlz&
DST=4&QLT=50&PTL=0,3
Woolz
object file
Sectioning
and image
parameters
Tile request


Histology
Hart
...
Endoderm
TS18.wlz
compound object
...&SEL=0&...
...&SEL=60,0,0,255,150&...
...&SEL=58,255,0,0,150&...
...&SEL=68,0,127,127,150&...
...&SEL=41,0,255,0,150&...
...&SEL=0&
SEL=41,0,255,0,150&
SEL=58,255,0,0,150&
SEL=60,0,0,255,150&
SEL=68,0,127,127,150&
...

IIP3D Web-App Architecture

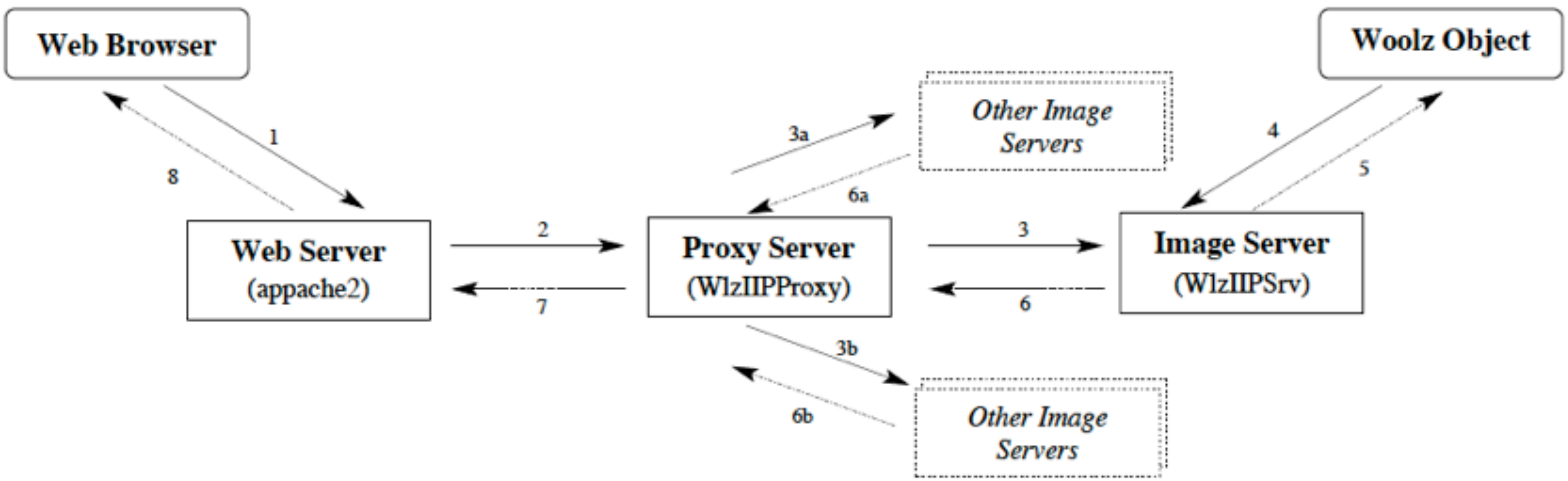


Figure 4: Architecture of IIP3D server using a proxy server. The web server passes the user requests to the proxy, which forwards them to individual IIP servers. These servers have direct access to the Woolz Object and return the requested data. The numbered lines show the order of the requests (continuous lines) and the replies (dotted lines).

IIP3D Web-App Architecture

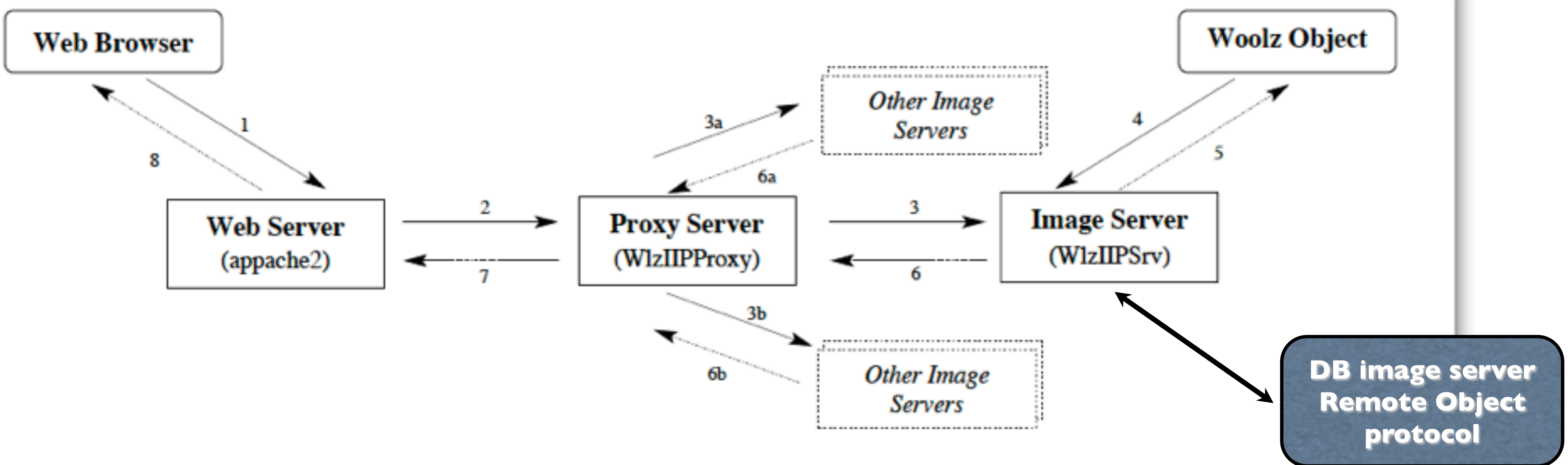
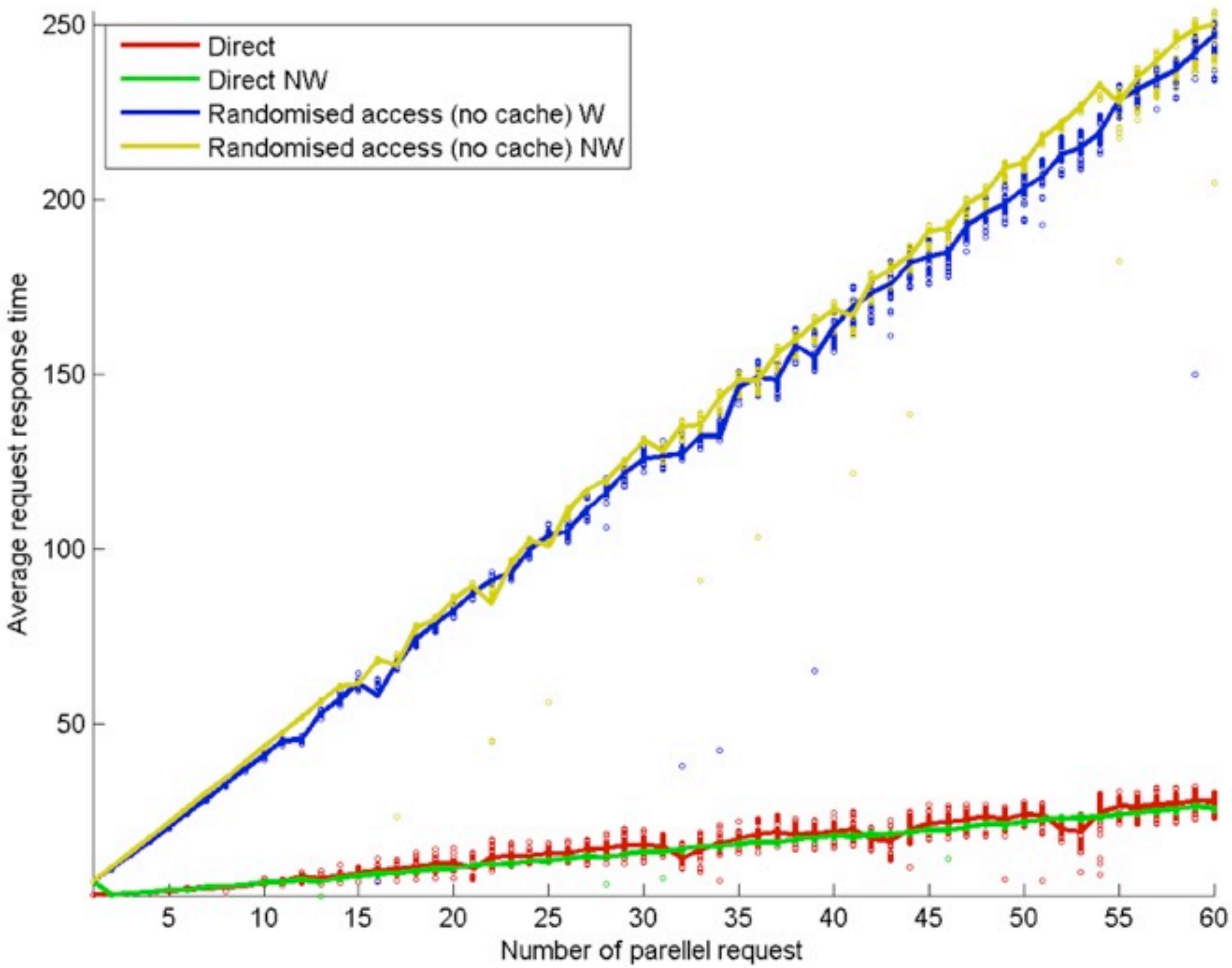


Figure 4: Architecture of IIP3D server using a proxy server. The web server passes the user requests to the proxy, which forwards them to individual IIP servers. These servers have direct access to the Woolz Object and return the requested data. The numbered lines show the order of the requests (continuous lines) and the replies (dotted lines).

Performance



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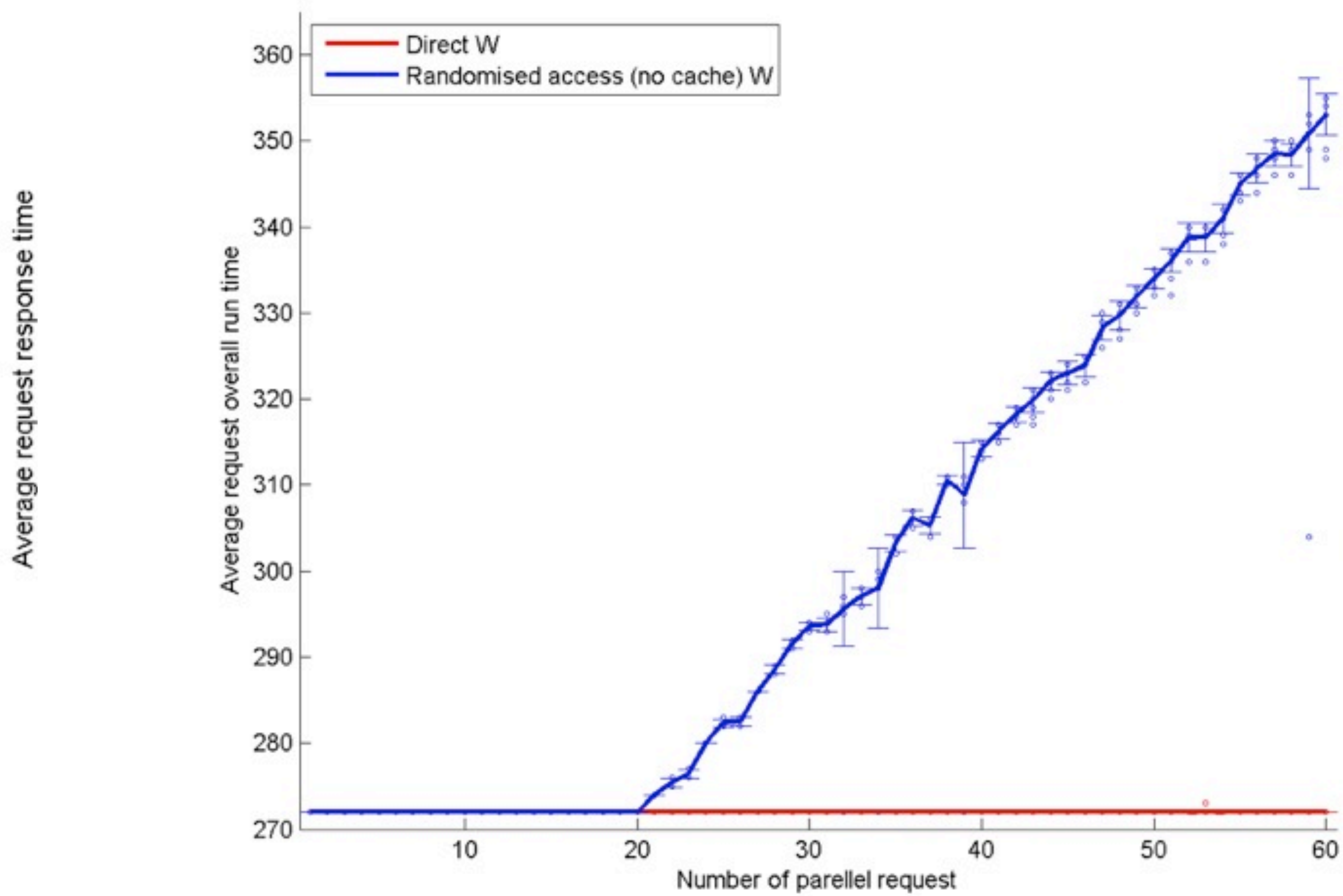
Performance



IIP3D Clients

- Javascript
  - Ajax
  - MVC design, uses MooTools & Yahoo Widgets
- Multi-section at high resolution
- Volume overlays
- Anatomy & gene-expression overlays
- Controls
  - viewing angles - virtual sections
  - zoom
  - distance, fixed point
  - section locator & view angle feedback
  - distance measurement, query by image value
  - ......

Annotation Overlay & Visualisation

- Atlas models include ontology and domains - image regions for anatomical terms. Typically exclusive
- Gene-expression data, open ended, multiple overlapping patterns

Layers, Overlays & Indexed Objects

- Multiple layers via html image overlay including opacity
  - currently layers constrained to identical domains
- Regional overlays using an indexed object
  - currently using “compound object” - regions can overlap
  - TBD - standard indexed volume - regions spatially exclusive

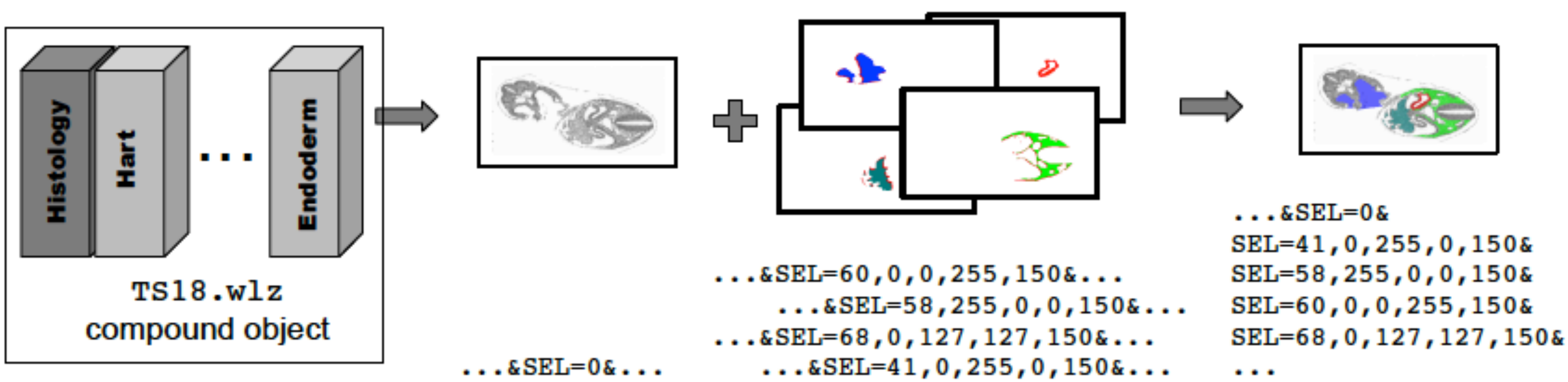


Image Processing IIP3D extensions

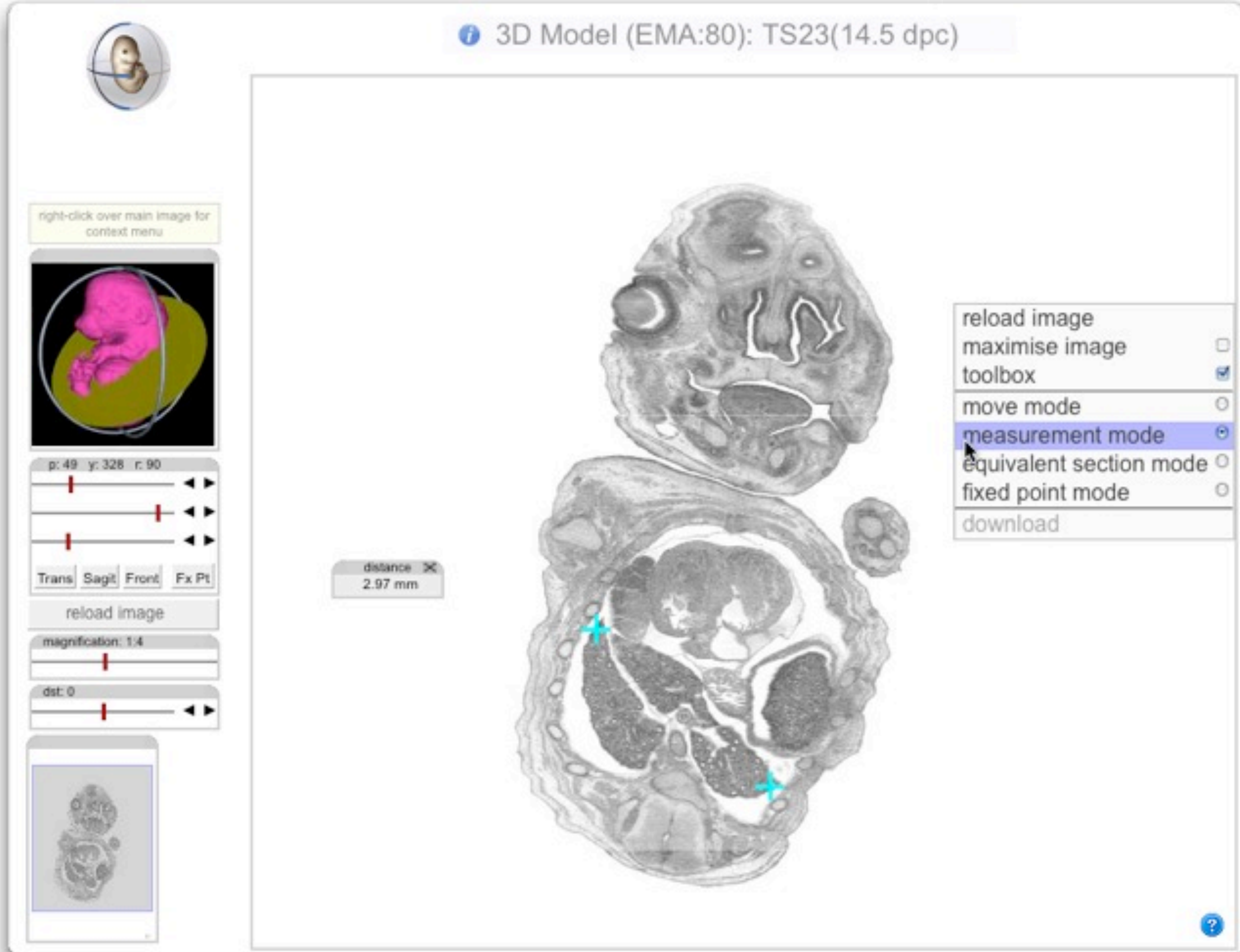
Operator	Description
diff(*exp*,*exp*)	The difference between the two given domains.
dilation(*exp*,*radius*)	The dilation of the domain by *radius* voxels.
domain(*exp*)	The domain of an object.
erosion(*exp*,*radius*)	The erosion of the domain by *radius* voxels.
intersect(*exp list*)	The intersection of the domains in the given lists.
threshold(*exp*,*value*,*comparison*)	Creates an object where the image values satisfy the given *value* and *comparison*. Here the value is floating point and valid comparisons are `lt` (less than), `le` (less than or equal), `eq` (equal), `ge` (greater than or equal) and `gt`) (greater than).
union(*exp list*)	The union of the domains in the given lists.

Table 4: Descriptions of morphological operators

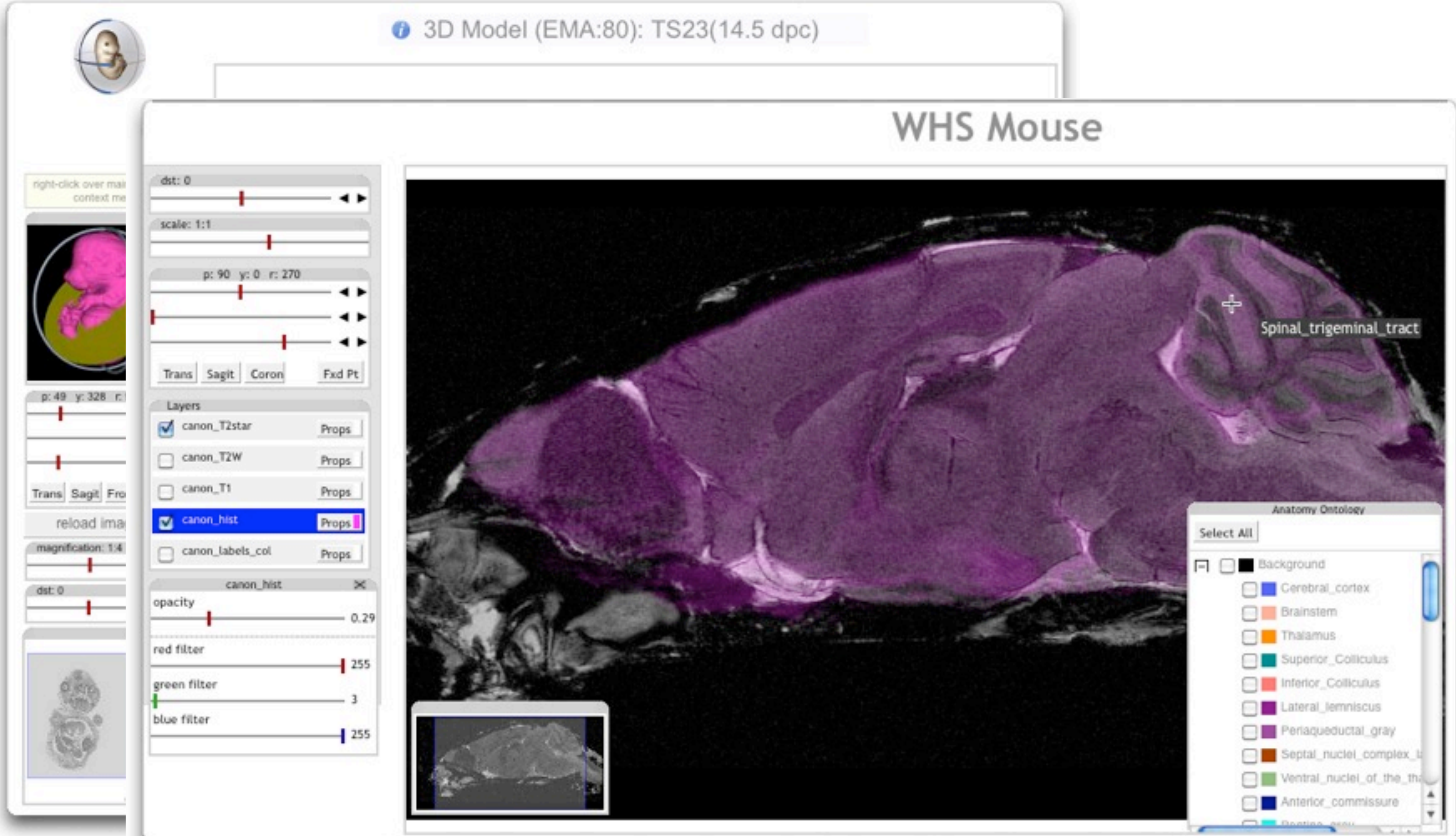
exp list	:=	(*exp* | *idx list*)(,*exp list*)
idx list	:=	(*idx* | (*idx*-) | (*idx*-*idx*) | (-*idx*))(,*idx list*)
exp	:=	*idx*) |
		diff(*exp*,*exp*) |
		dilation(*exp*,*uint*) |
		domain(*exp*) |
		erosion(*exp*,*uint*) |
		intersect(*exp list*,*exp list*) |
		threshold(*exp*,*val*,*cmp*)
		union(*exp list*,*exp list*) |
idx	:=	`[0-9]+`
uint	:=	`[1-9][0-9]*`
val	:=	`[-+]?[0-9]*.?[0-9]+([eE][-+]?[0-9]+)?`
cmp	:=	`(lt)|(le)|(eq)|(ge)|(gt)`

Table 3: Syntax for morphological expressions.

IIP3D Examples



IIP3D Examples



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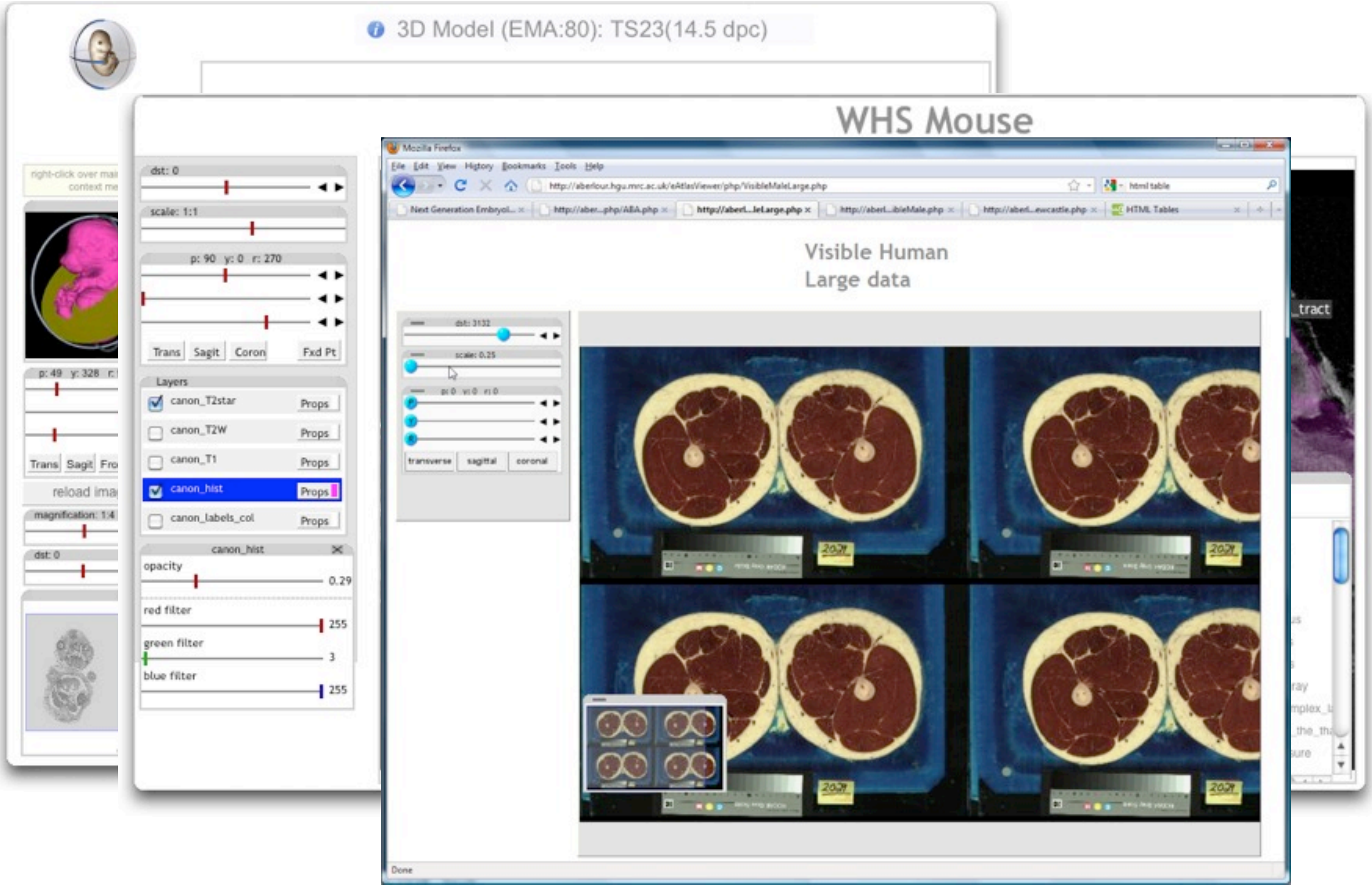
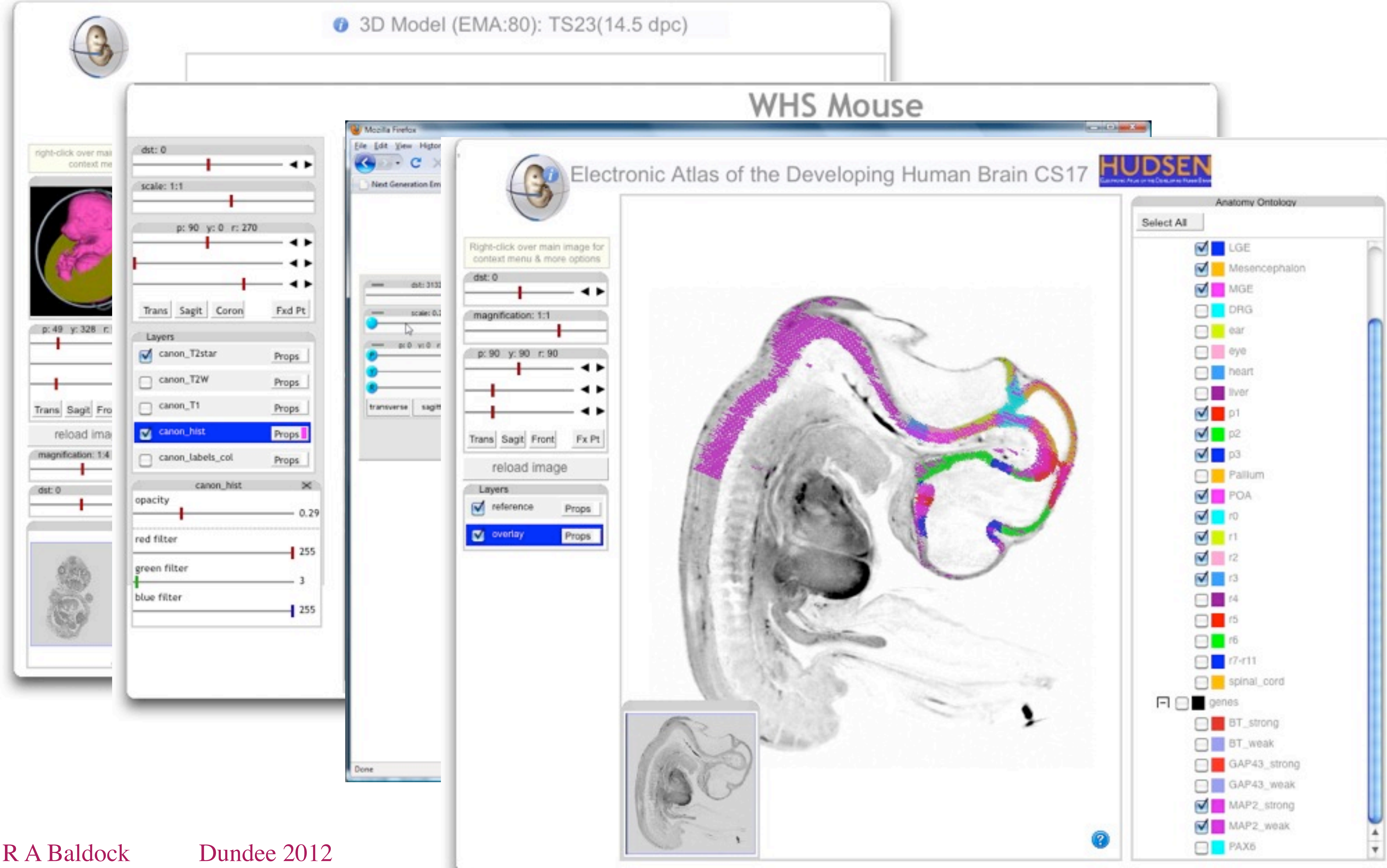
IIP3D Examples



IIP3D Examples



WebGL

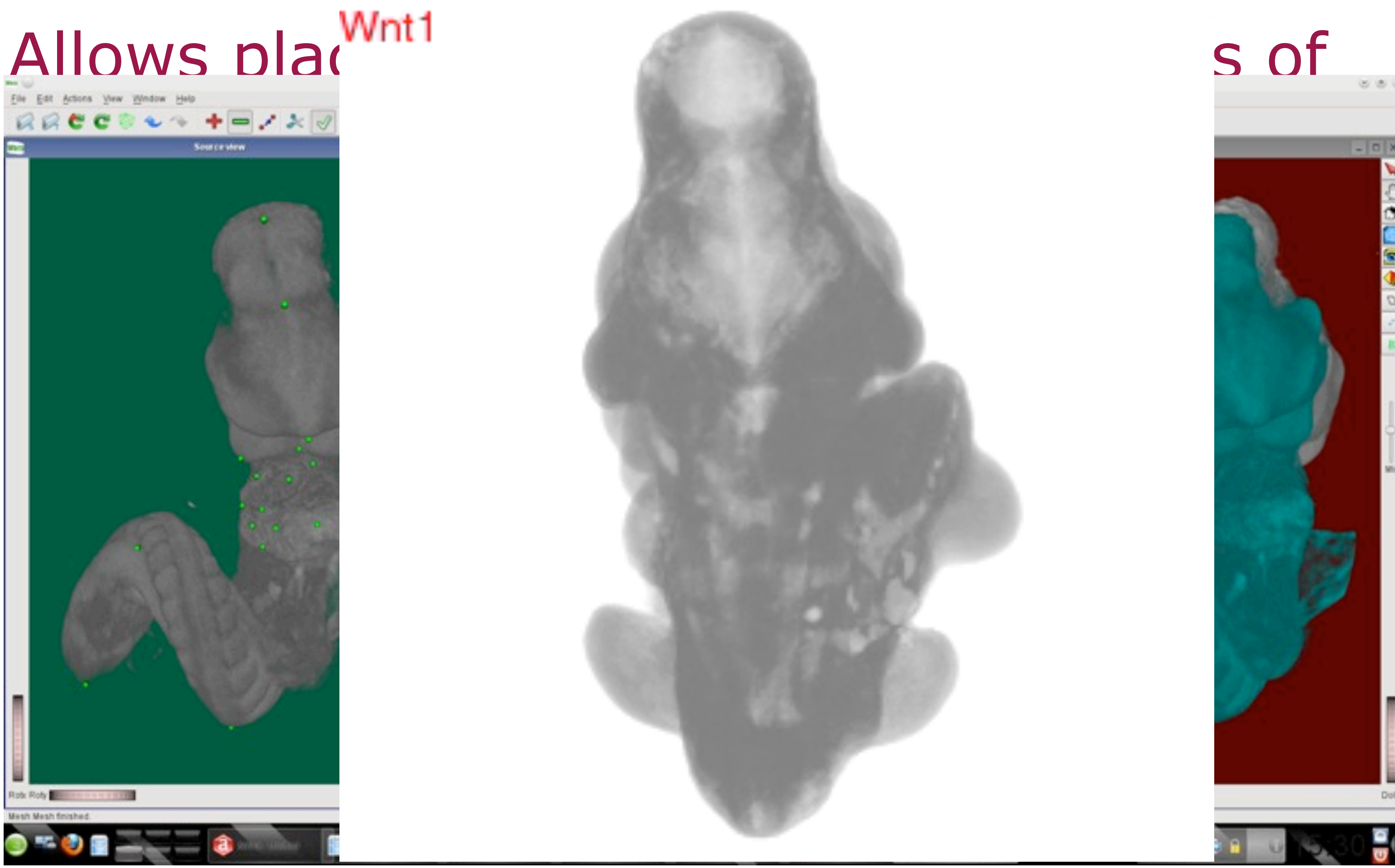
- IIP3D viewer extension to 3D visualisation
  - Use X3Dom - Javascript binding to X3D
- navigation feedback
- Anatomy visualisation
  - see demo
- Extend to 4D

3D mapping - WlzWarp

- Allows placement of landmarks (points of equivalence) on source and target on volume renders instead of isosurfaces
- On-the-fly feedback of warping progress
- Uses constrained distance transform (CDT) in warping
- Woolz, Qt, Coin3D(+SIMVoleon)
- Linux, OS X, Windoes
- Open Source (Free!)

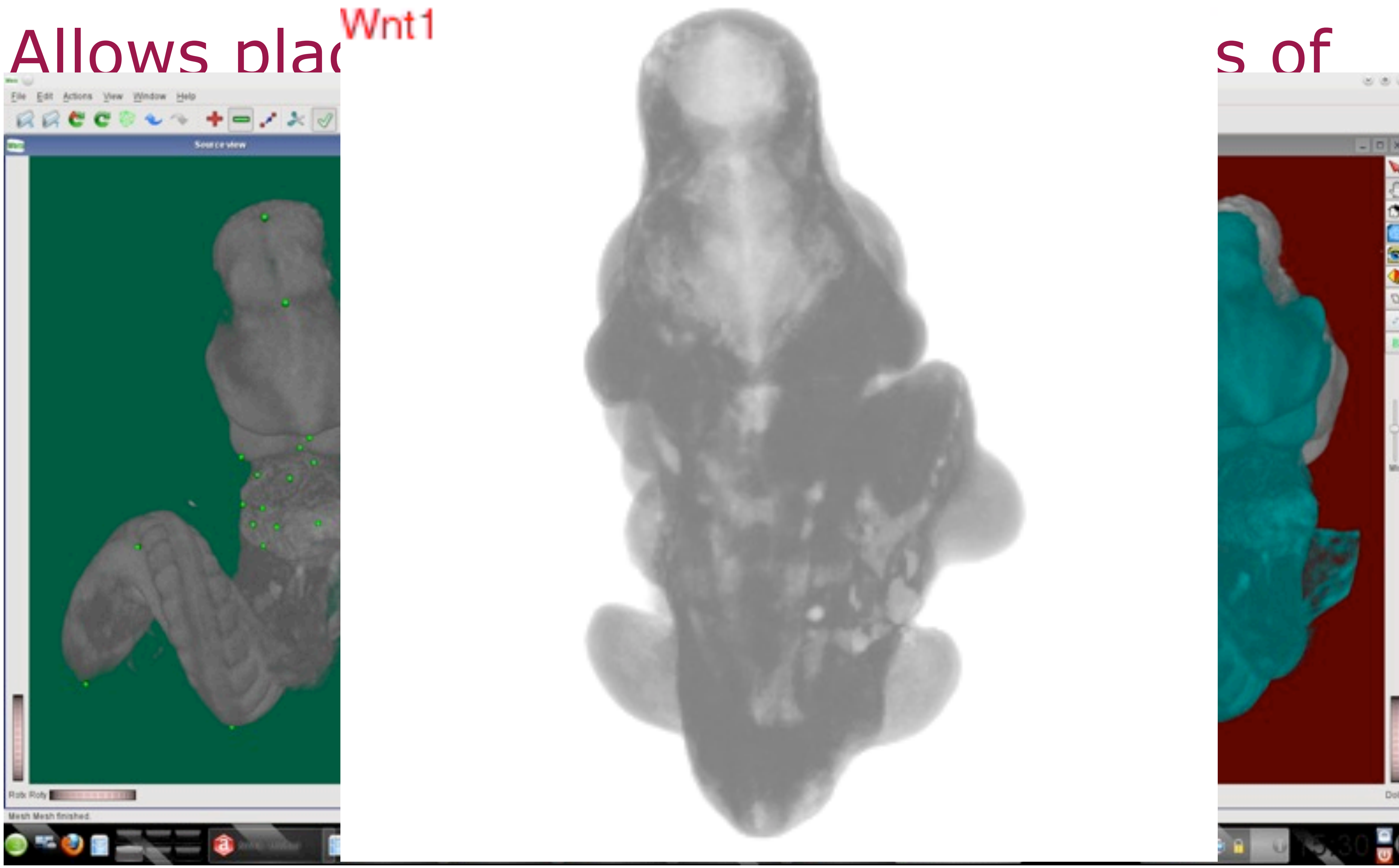
3D mapping - WlzWarp

- Allows plac s of e in



3D mapping - WlzWarp

- Allows plac s of
- e
- in



Lineage & the Brain

- Embryo development 7-5-8.5 dpc
- 11-fold growth of ectoderm cell layer
- complex folding
- lineage clones via HRP cell labelling (iontophoresis)
- pattern recognition very difficult
- conformal transform of ectodermal surface to “flat-map”

Lineage & the Brain

A Camus, K Lawson, W Hill et al
Development 2011

Lineage & the Brain

A Camus, K Lawson, W Hill et al
Development 2011

eMouseAtlas

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Mike Wicks

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