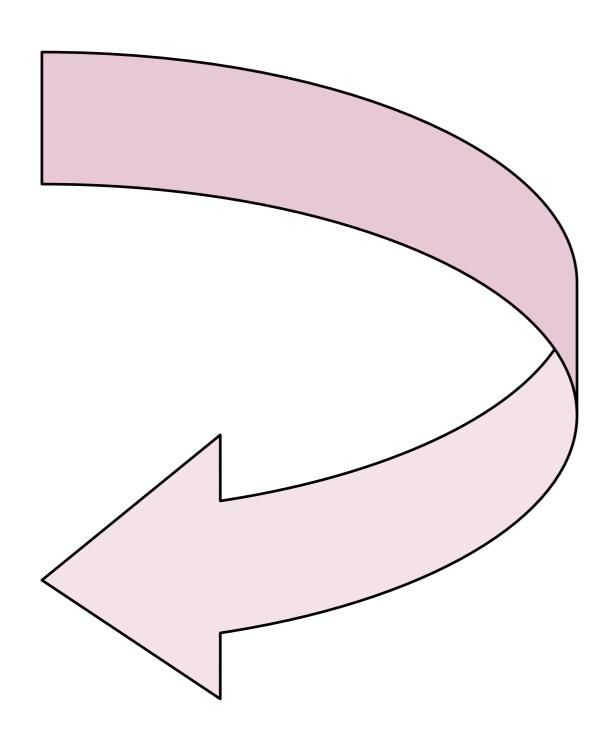


Atlas-Based Bioinformatics

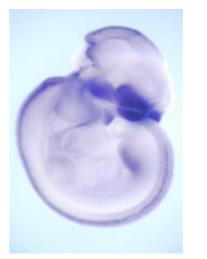
Richard Baldock

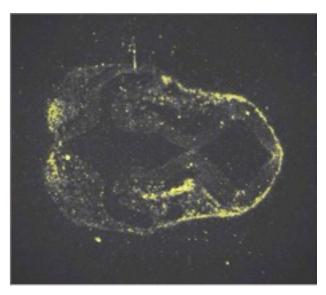
MRC Human Genetics Unit Institute of Genetics and Molecular Medicine Edinburgh, UK



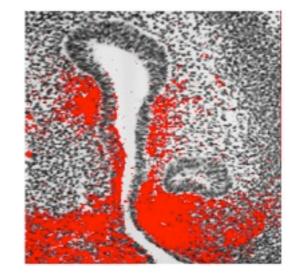


GENE EXPRESSION



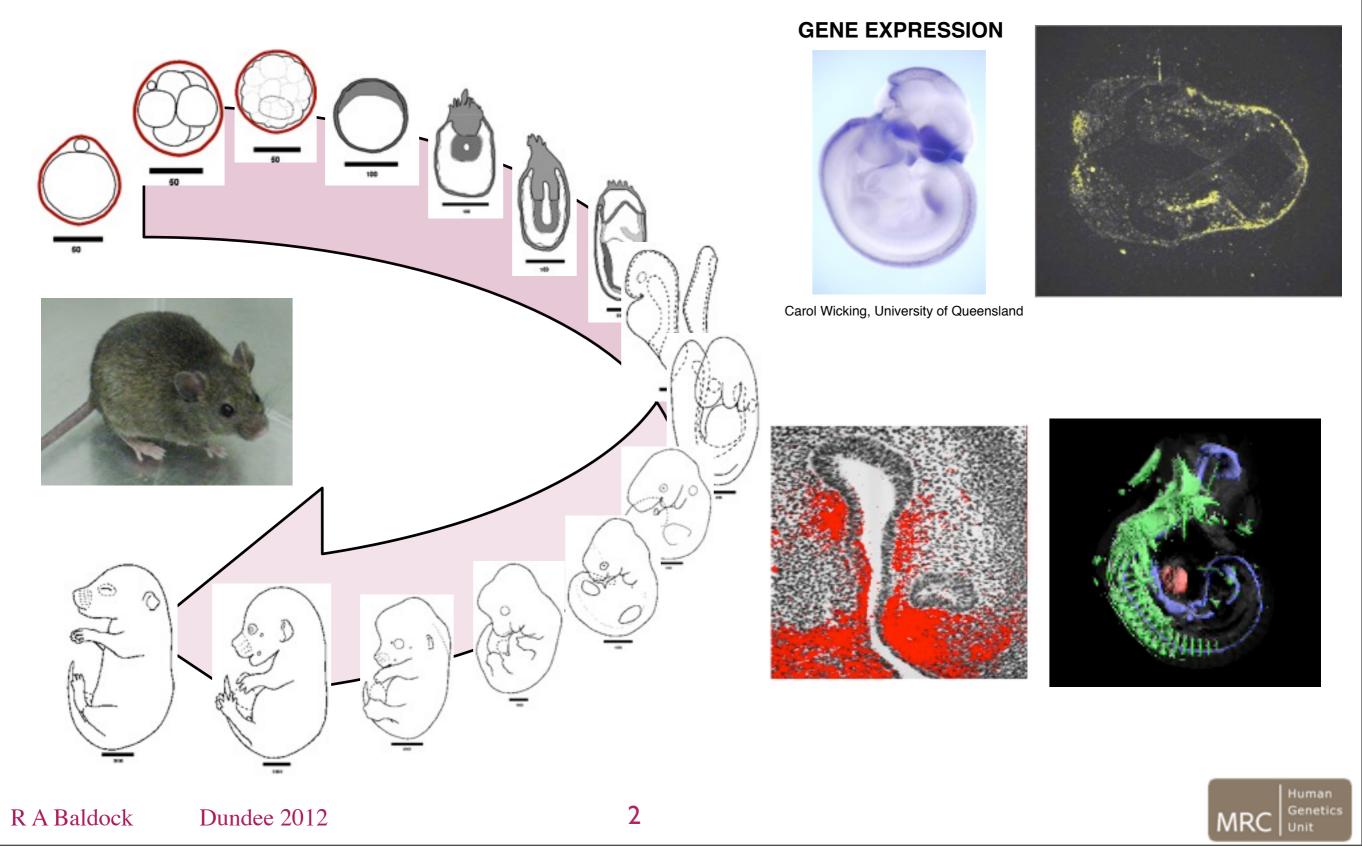


Carol Wicking, University of Queensland

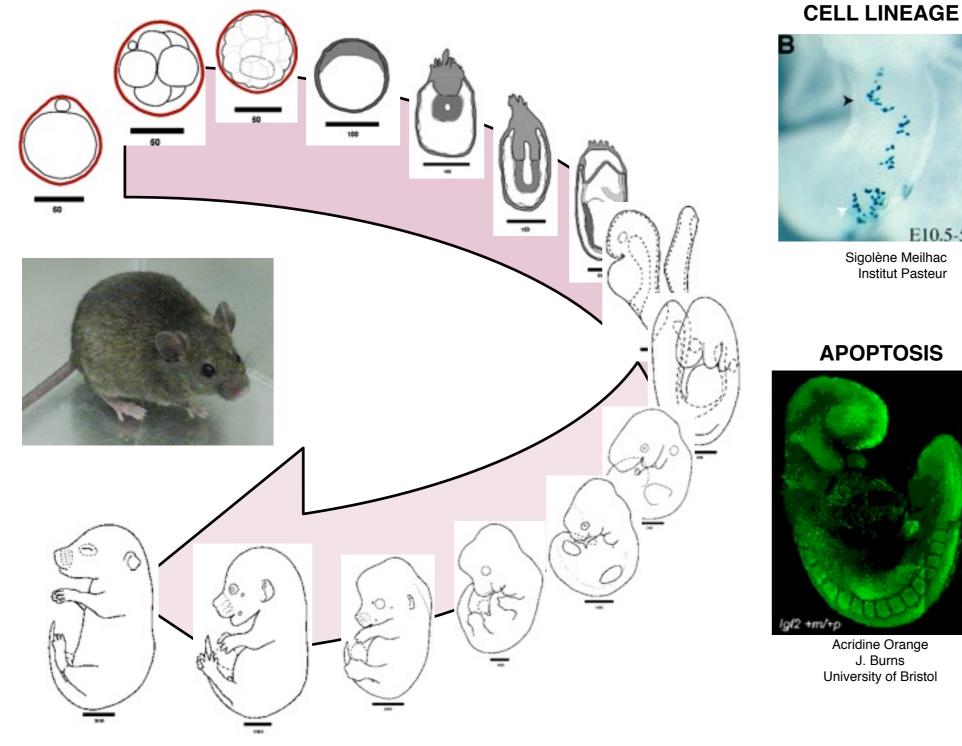






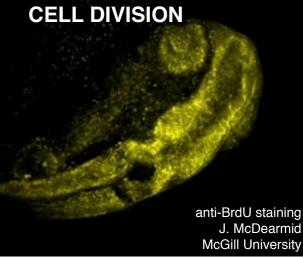






E10.5-540

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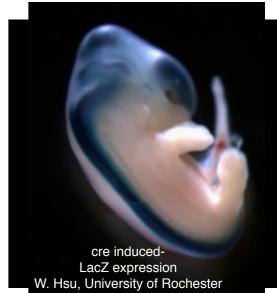


APOPTOSIS



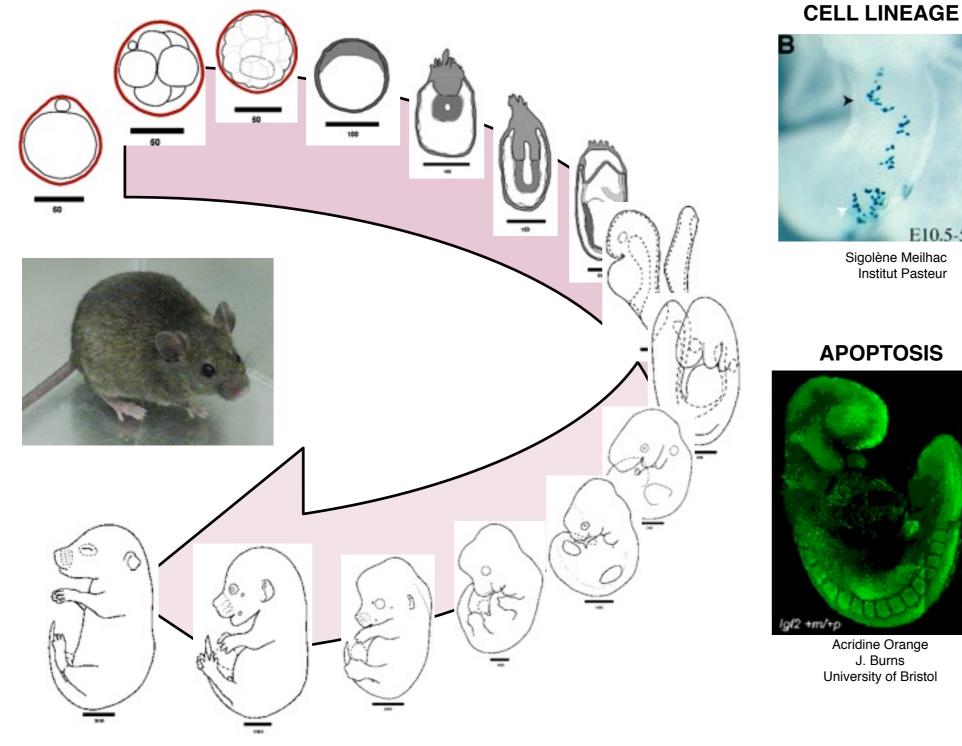
Acridine Orange J. Burns University of Bristol

TRANSGENICS



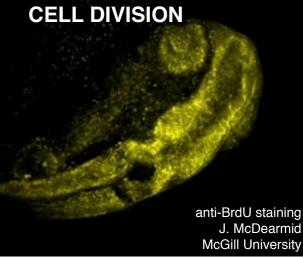






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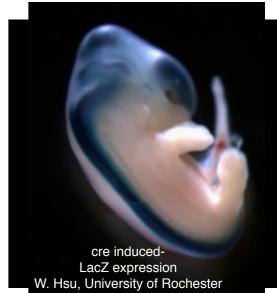


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Acridine Orange J. Burns University of Bristol

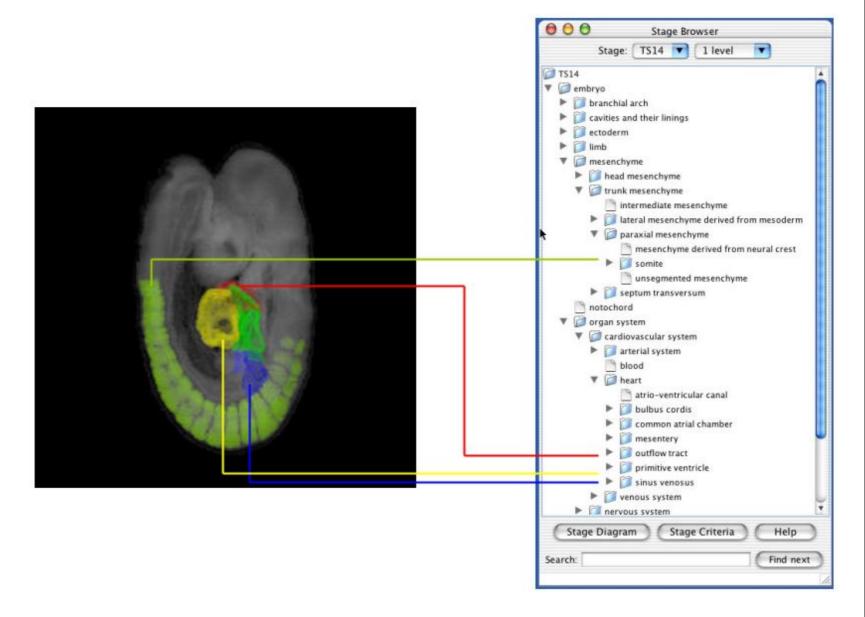
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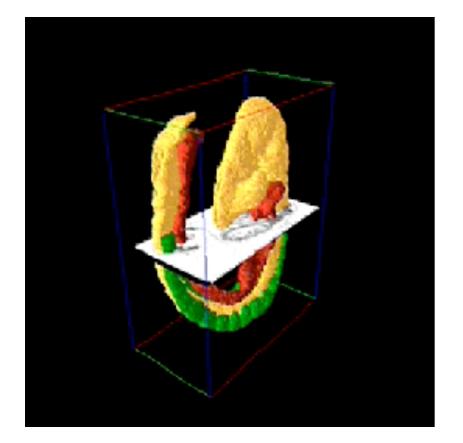
eMouseAtlas Framework

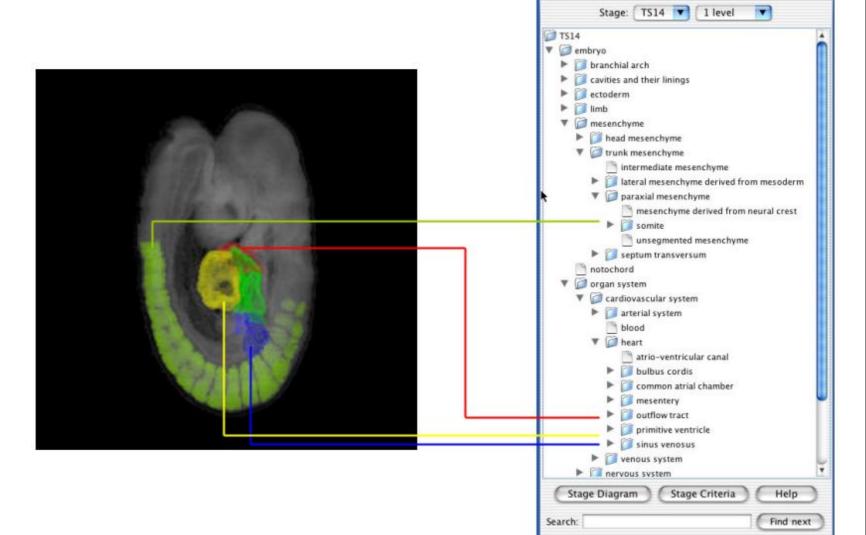






eMouseAtlas Framework





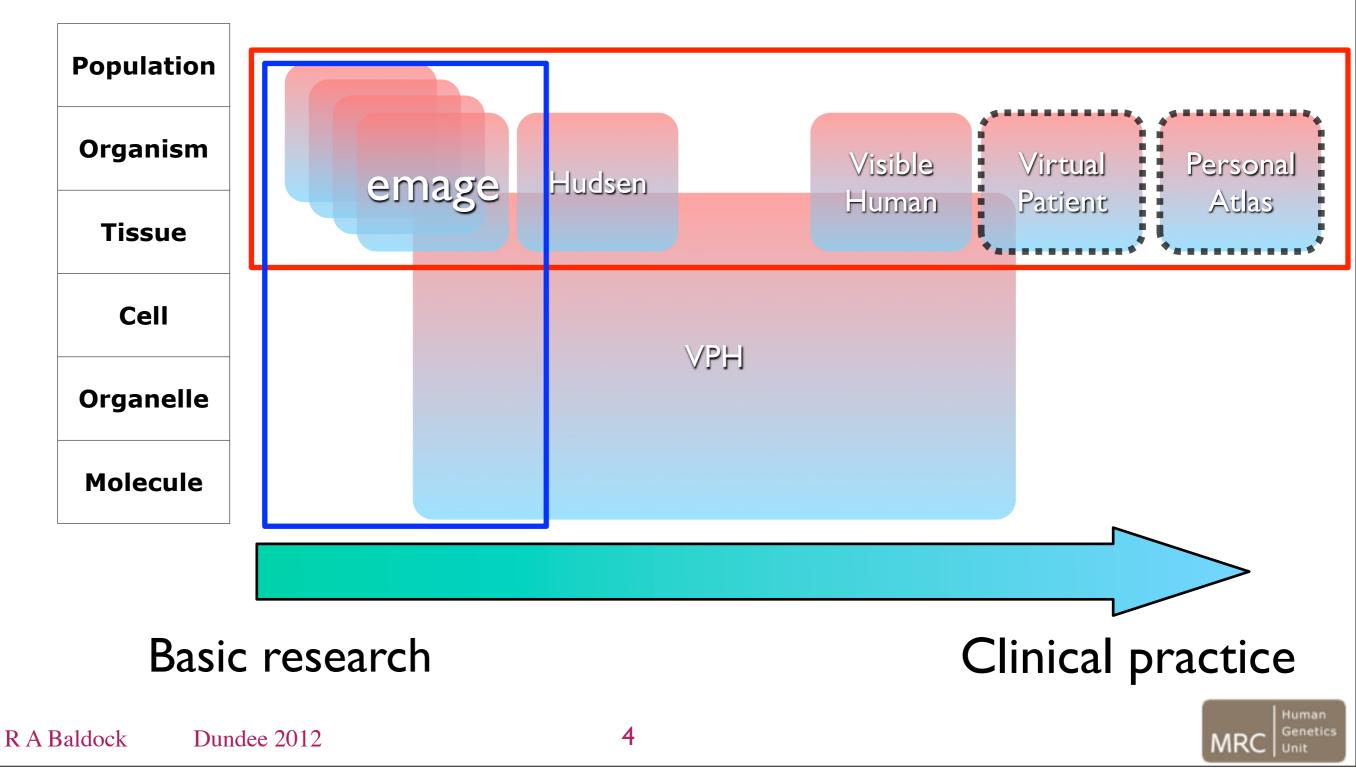
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Stage Browser

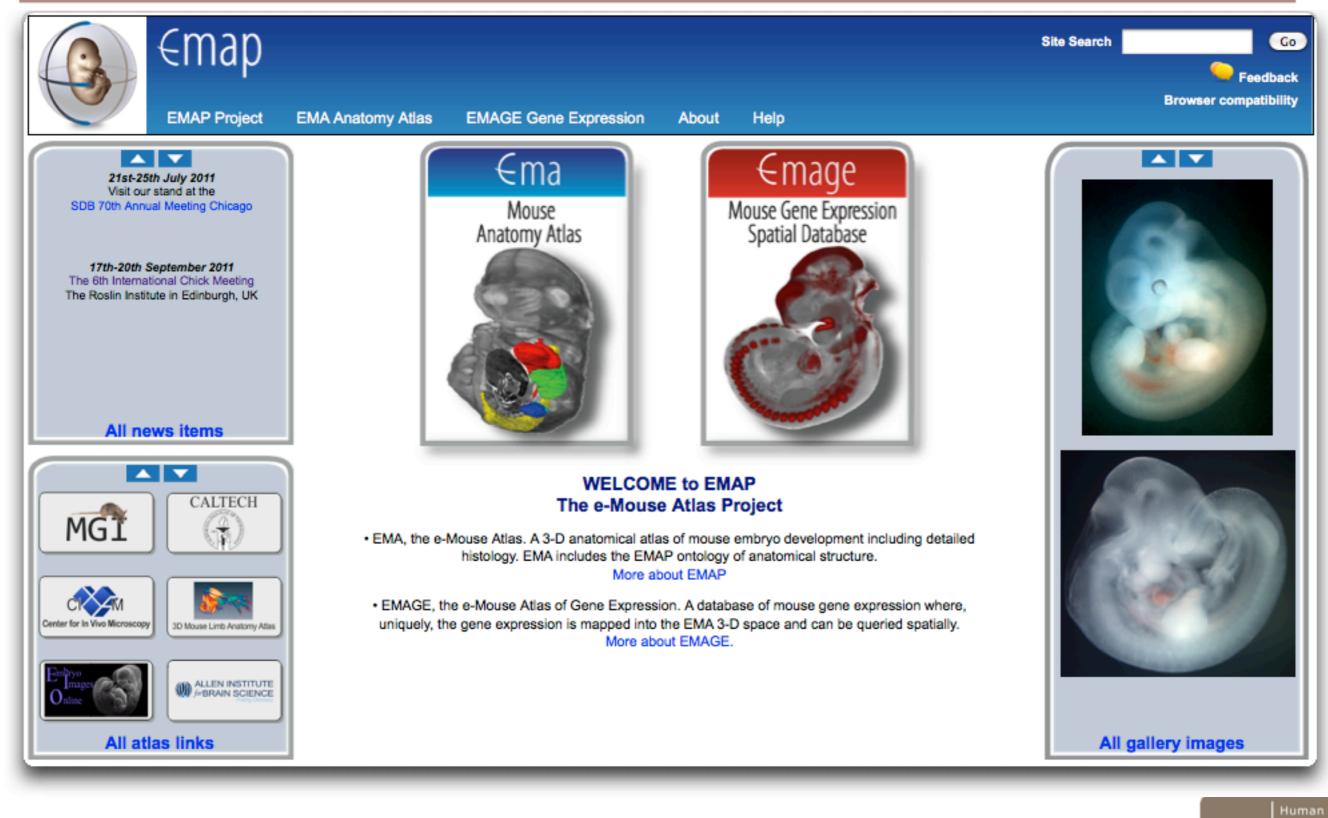


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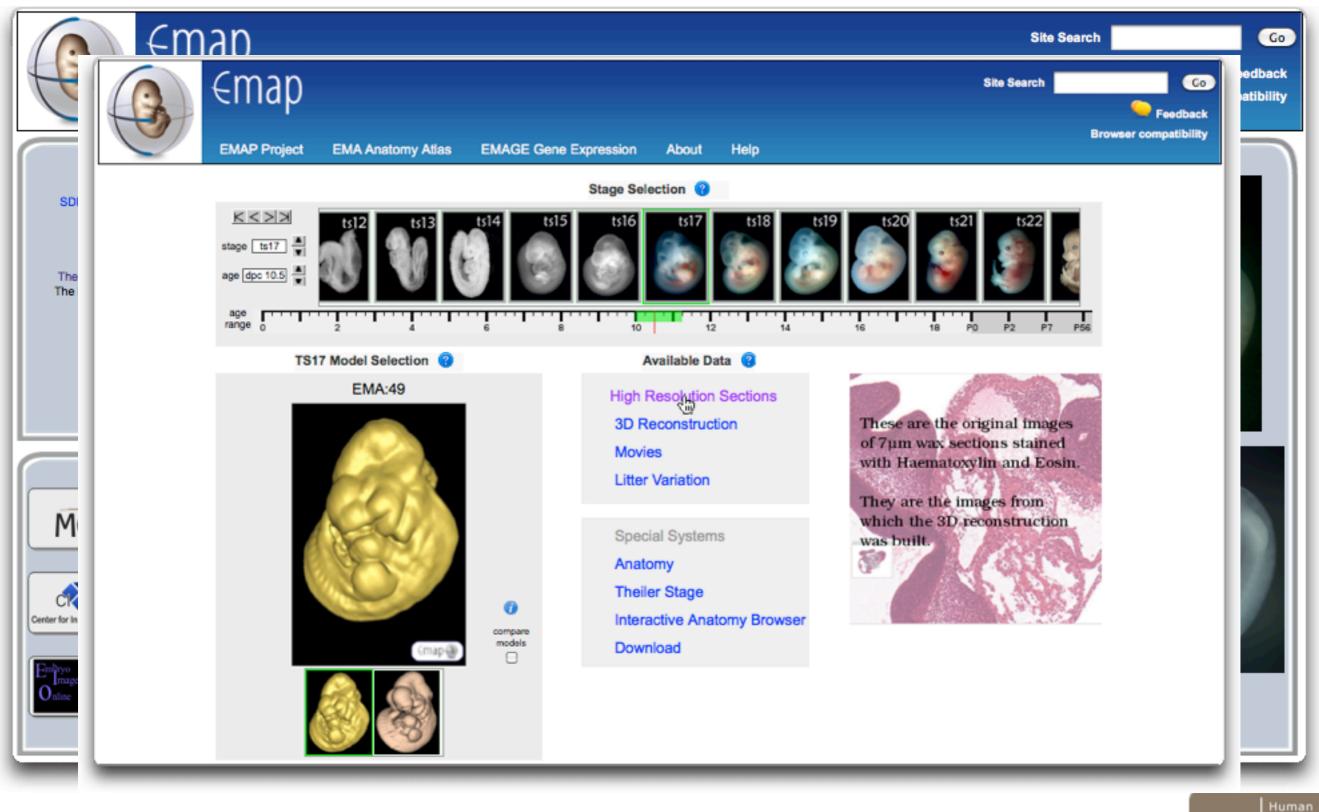
Thursday, 16 February 2012

Dundee 2012

R A Baldock

MRC





Dundee 2012

R A Baldock

MRC







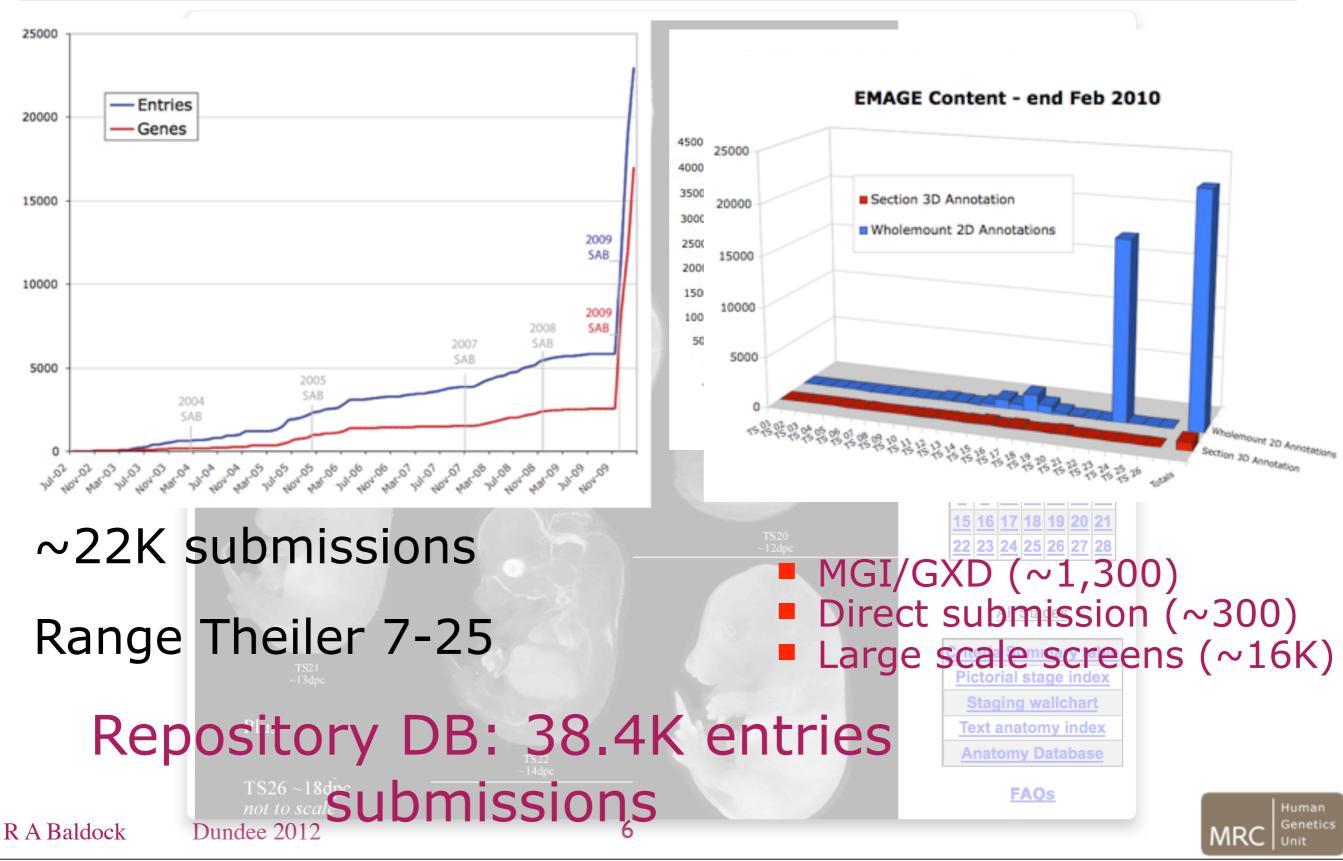


R A Baldock Dundee 2012



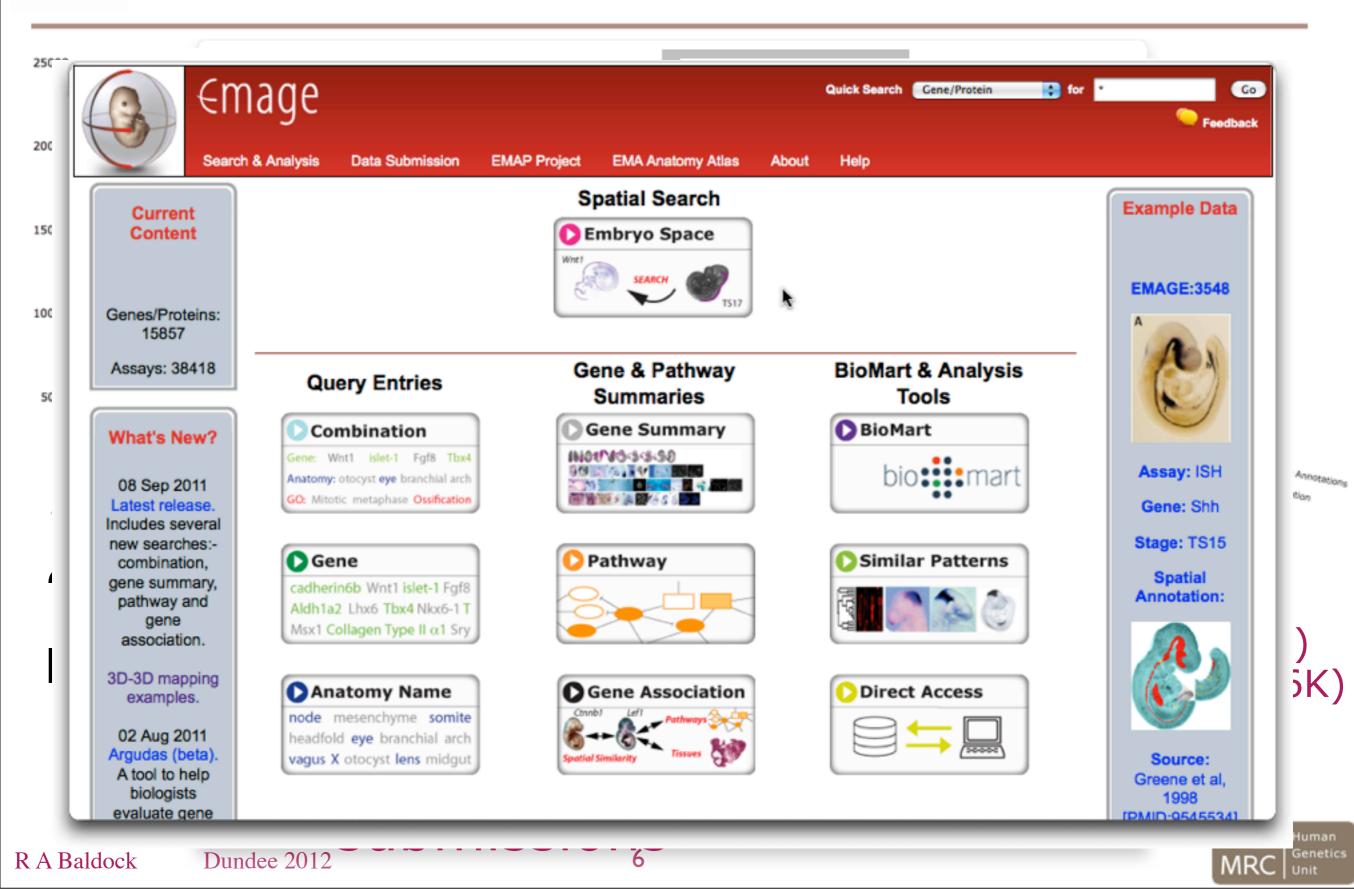
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EMAGE - current status



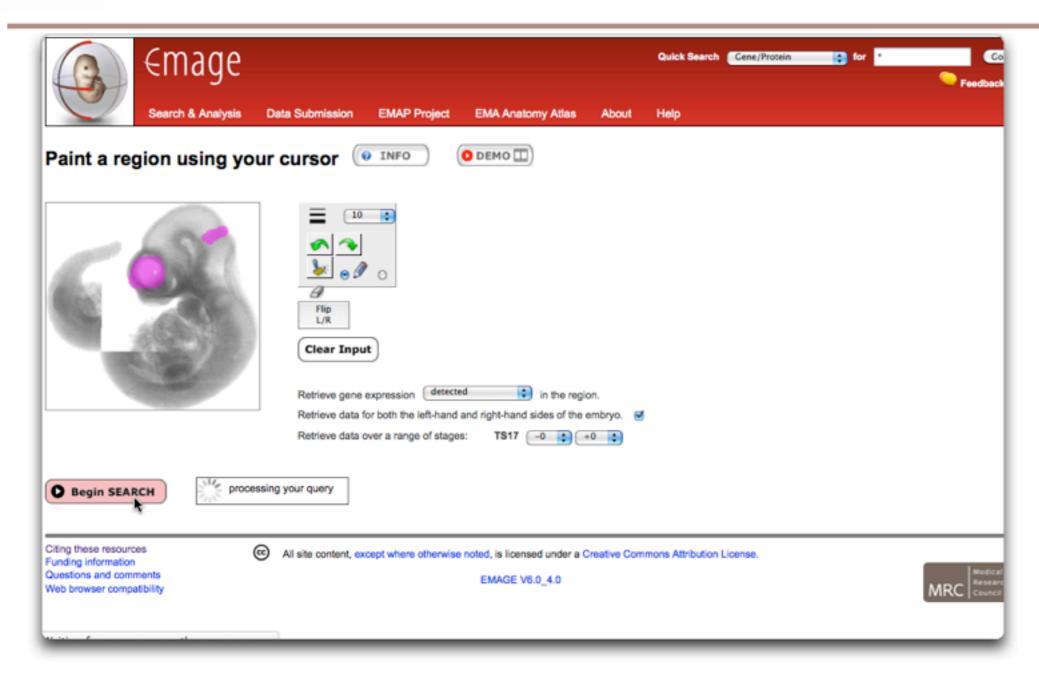


EMAGE - current status





EMAGE Embryo Space





EMAGE Embryo Space

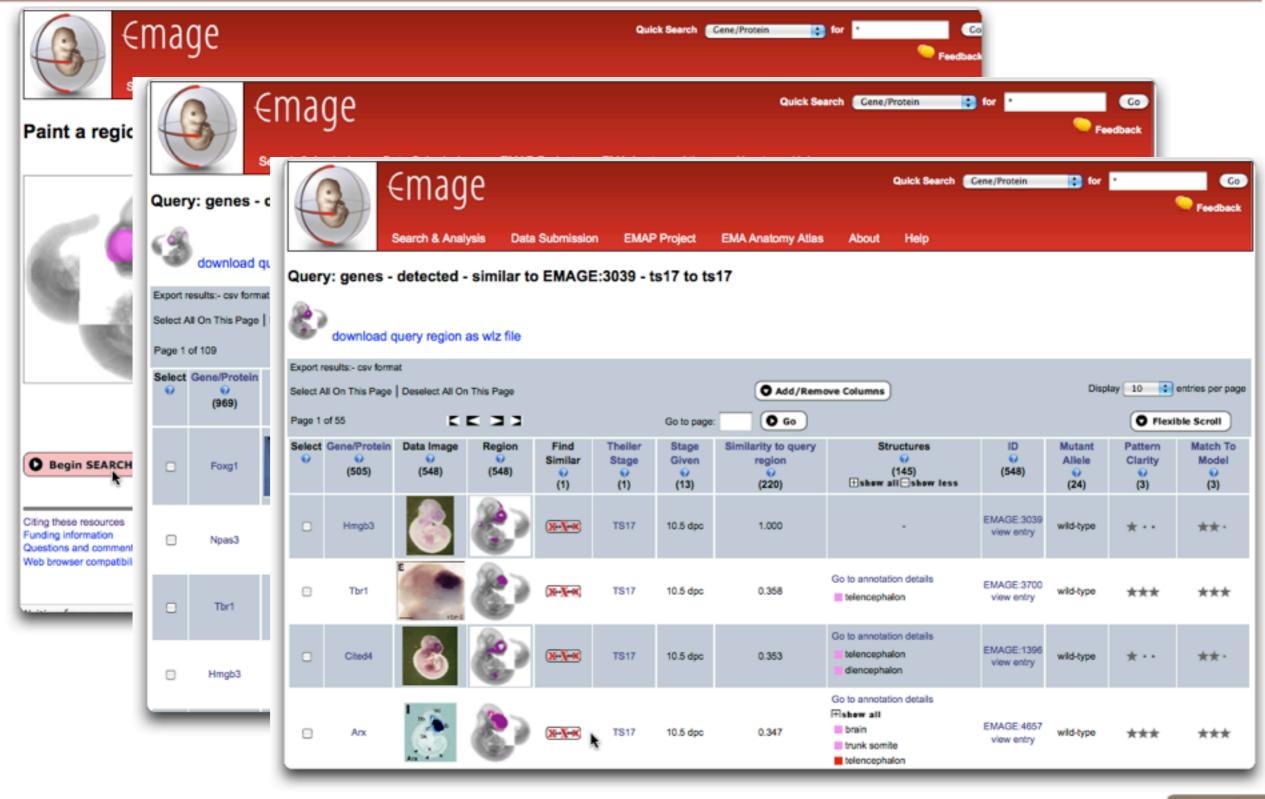
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EMAGE Embryo Space



R A Baldock Dun

Dundee 2012





- 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

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BioAtlas - data mapping

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BioAtlas - data mapping

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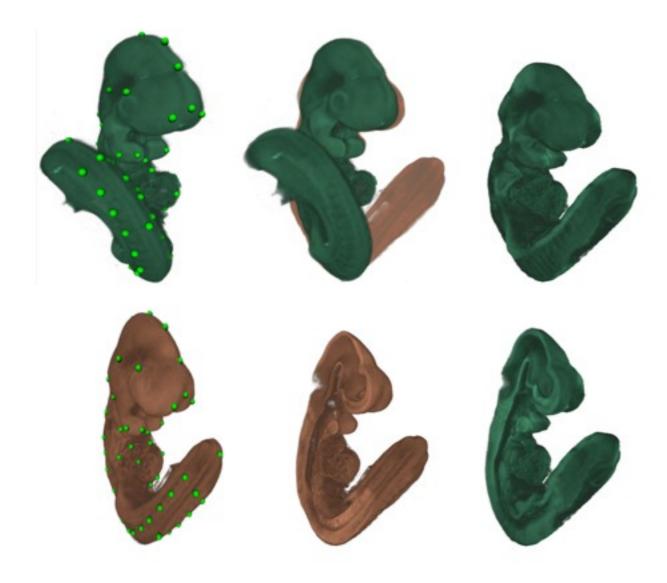
MRC Genetics



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





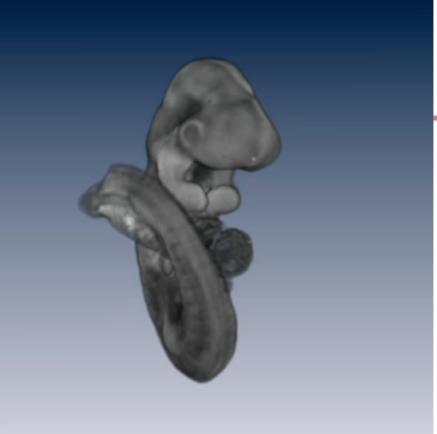


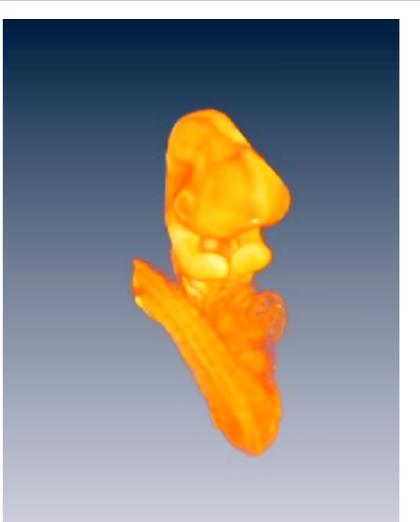




3D Data Mapping - WlzWarp





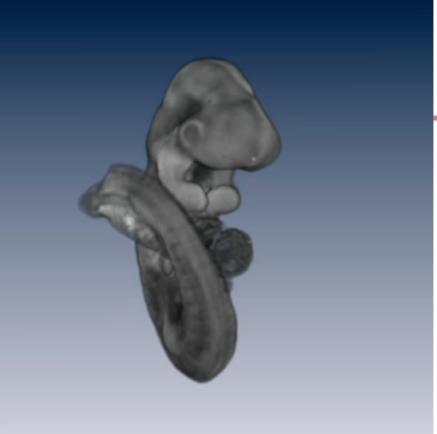


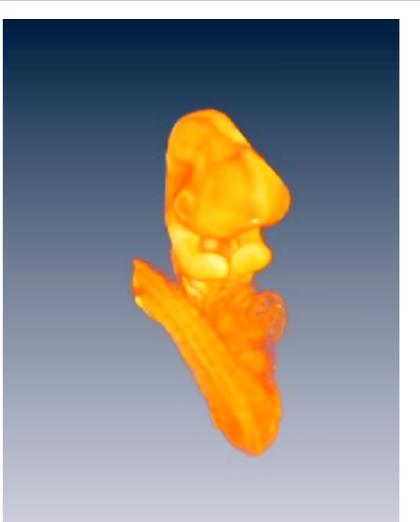




3D Data Mapping - WlzWarp











3D Mapping - Wnt signalling pathway

Wnt1	C.	TS17	10.5dpc	3D View	EMAGE:6132
Wnt2	C.	TS17	10.5dpc	3D View	EMAGE:6134
Wnt3	C.S.	TS17	10.5dpc	3D View	EMAGE:6138
Wnt3A	C.S.	TS17	10.5dpc	3D View	EMAGE:6141
Wnt4	Constant of the second	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

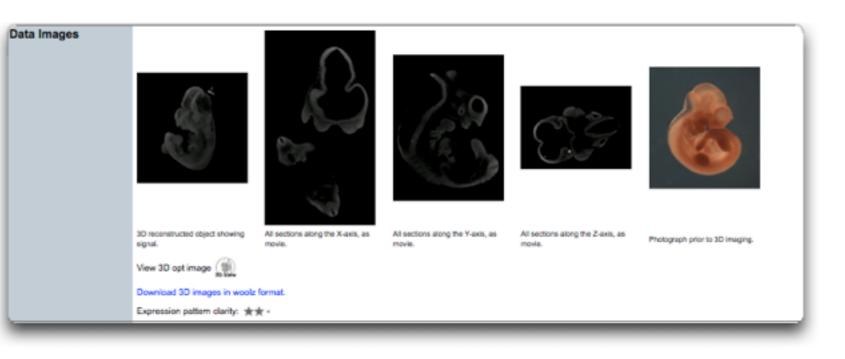




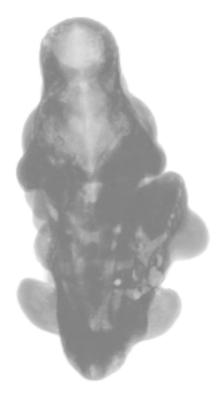


3D Mapping - Wnt signalling pathway

Wnt1	C.	TS17	10.5dpc	3D View	EMAGE:6132
Wnt2	Carlos Carlos	TS17	10.5dpc	3D View	EMAGE:6134
Wnt3		TS17	10.5dpc	3D View	EMAGE:6138
Wnt3A	C.S.	TS17	10.5dpc	3D View	EMAGE:6141
Wnt4	C.S.	TS17	10.5dpc	3D View	EMAGE:6142
Wnt5A		TS17	10.5dpc	3D View	EMAGE:6144
Wnt6	(1) (1)	TS17	10.5dpc	3D View	EMAGE:6148
Wnt7A		TS17	10.5dpc	3D View	EMAGE:6150



Wnt1







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





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

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





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 ^aMRC 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 mode development at the MRC Edinburgh is intended to scan a conventional microsco. The high pixel data rate (8 MHz peak) easily saturates most computer configurate threshold, pixels (i.e. intervals') into a set of interval parameters. These interval p microprocessors to give object parameters from which the cells can then be class The paper describes the hardware and software architecture, with comments on The linkage procedure used to reconstitute contiguous object descriptions is also the order of 1 ms.

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

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



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Patte Volun 1980

Woolz images

A fact interval processor

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

^aMRC 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

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





A fact interval processor G.A. ! Pattern Reco a MR(Volume 3, Issi Rece Data st Abst and Un Th Jim Piper^a a de Th ^aMRC Clinic thr Edinburgh E mi Received 14 Th Th Abstract the A variety of support si Keyw efficient ar construct image pro Patte Volun 1980 Keywords: Ir 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.

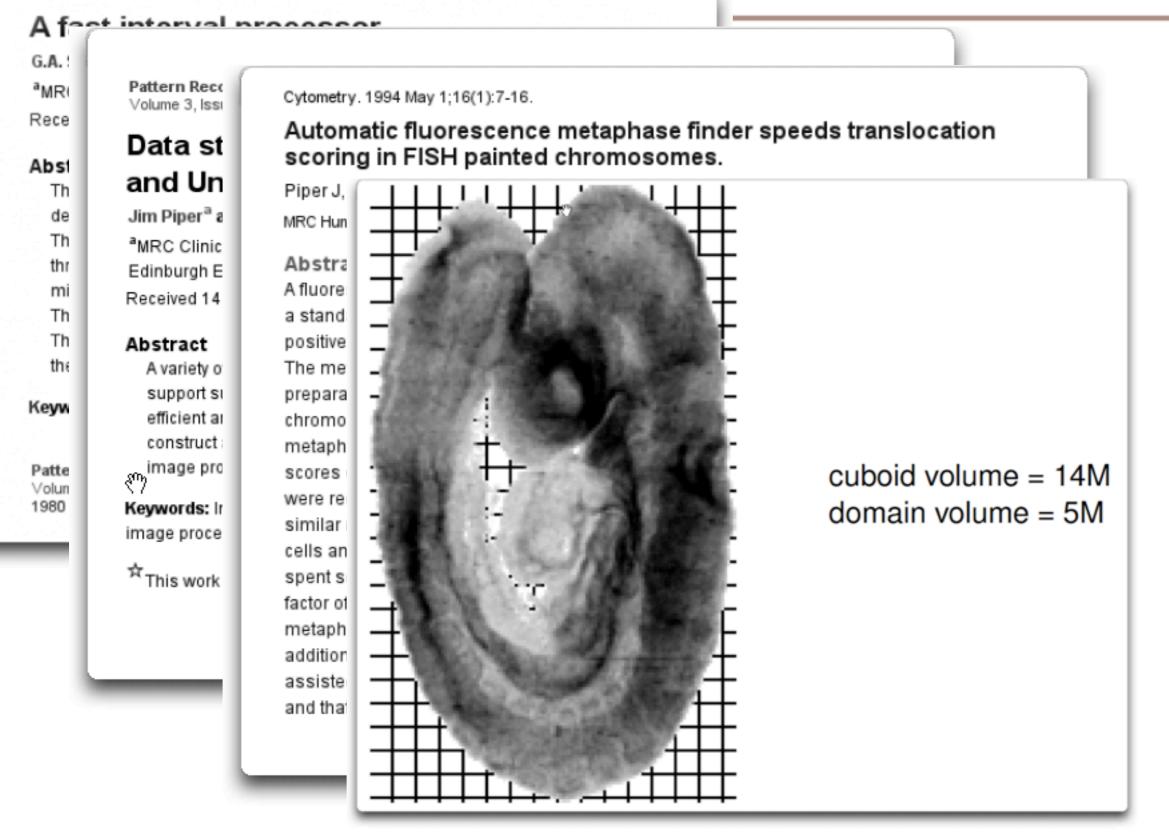
Abstract

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.



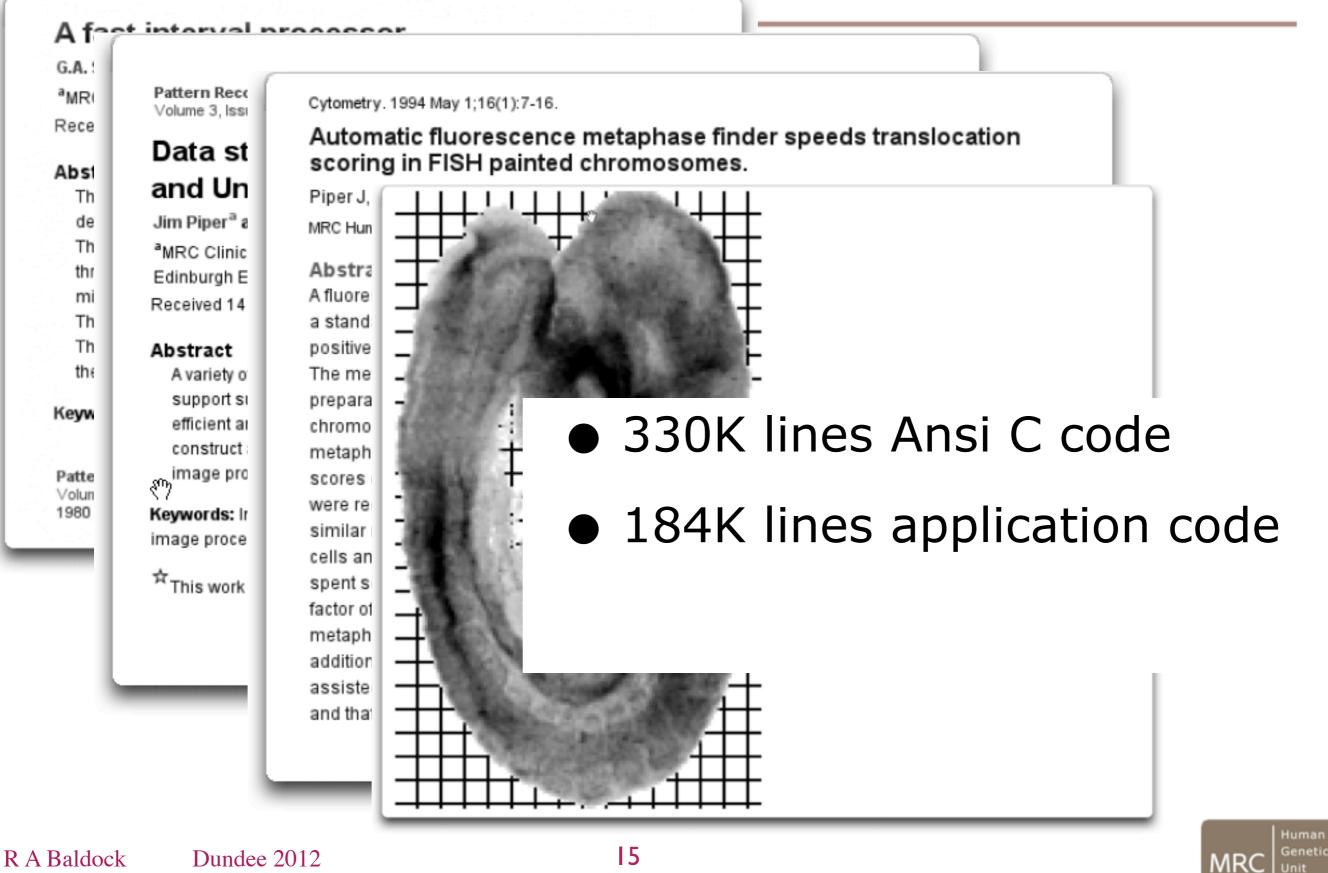
R A Baldock **Dundee 2012**













- Domain
 - Rectangle based
 Interval based

 - 3D planewise domains







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







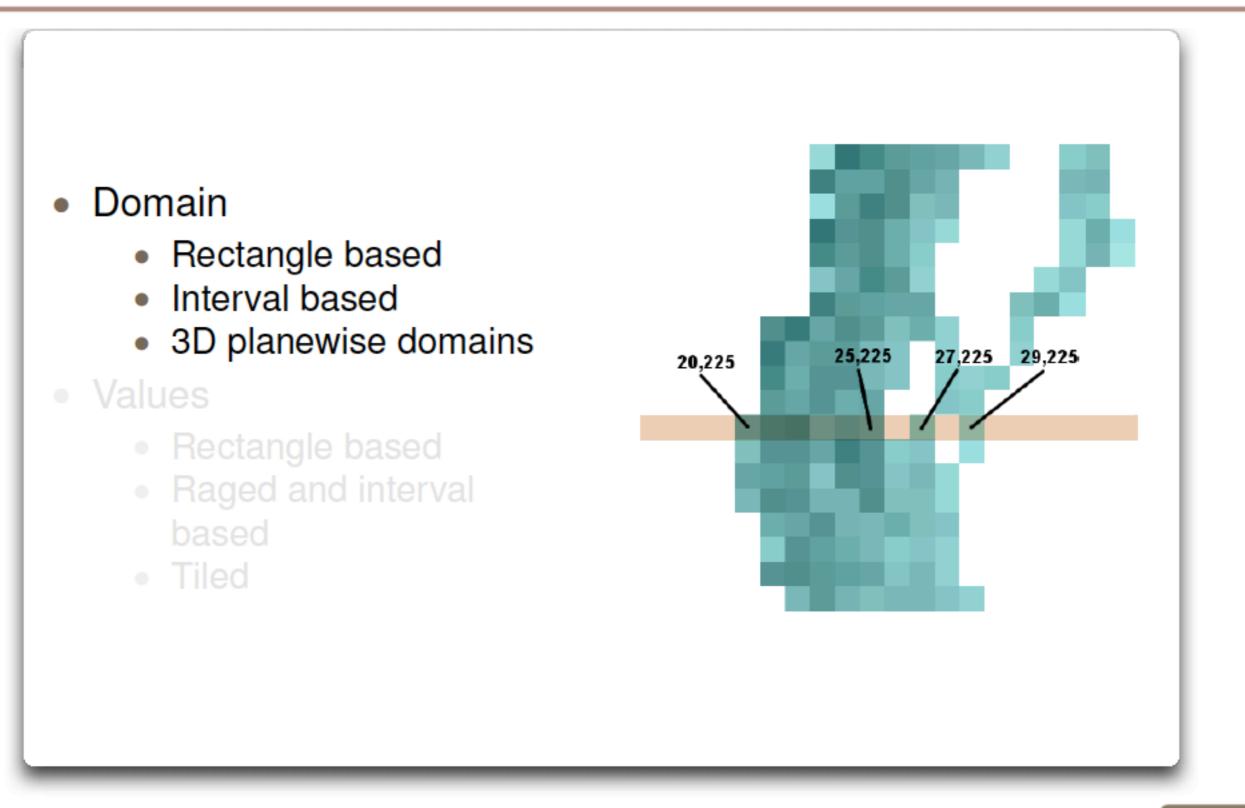
- Domain
 - Rectangle based
 - Interval based
 - 3D planewise domains
- Values
 - Rectangle based
 - Raged and interval based
 - Tiled





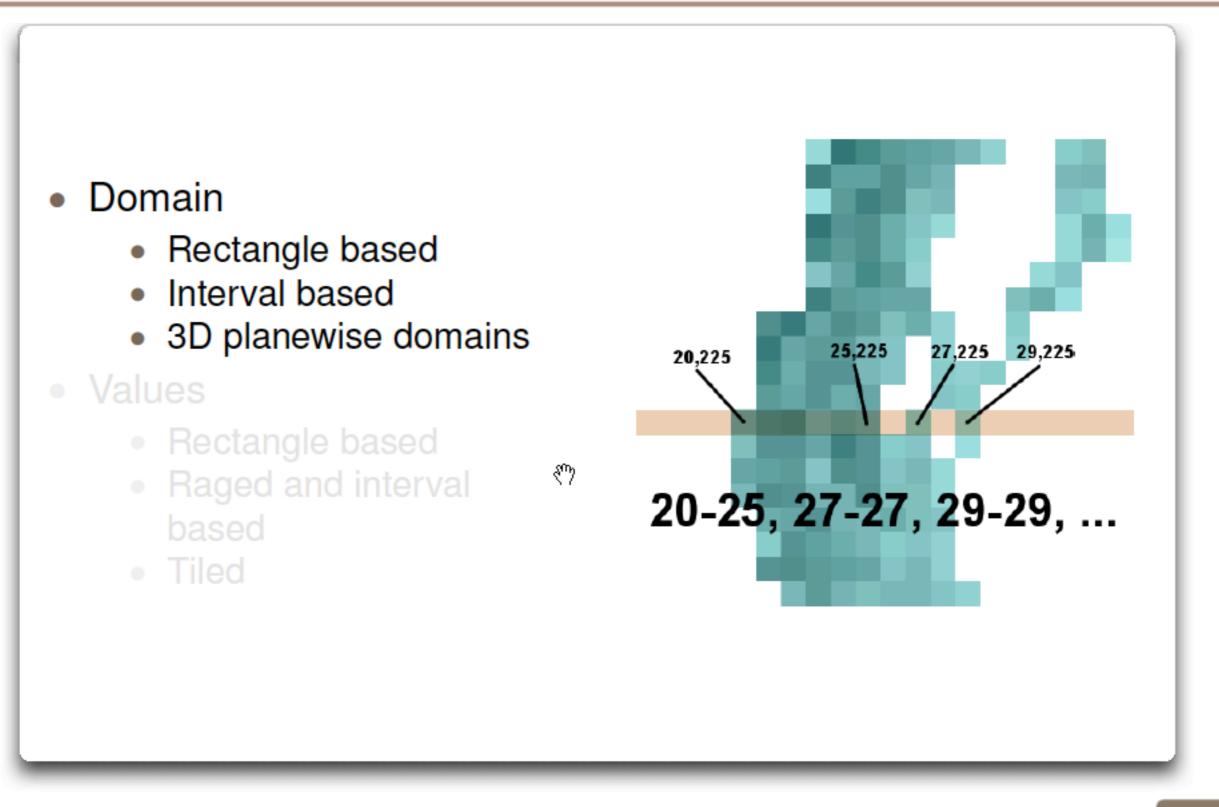
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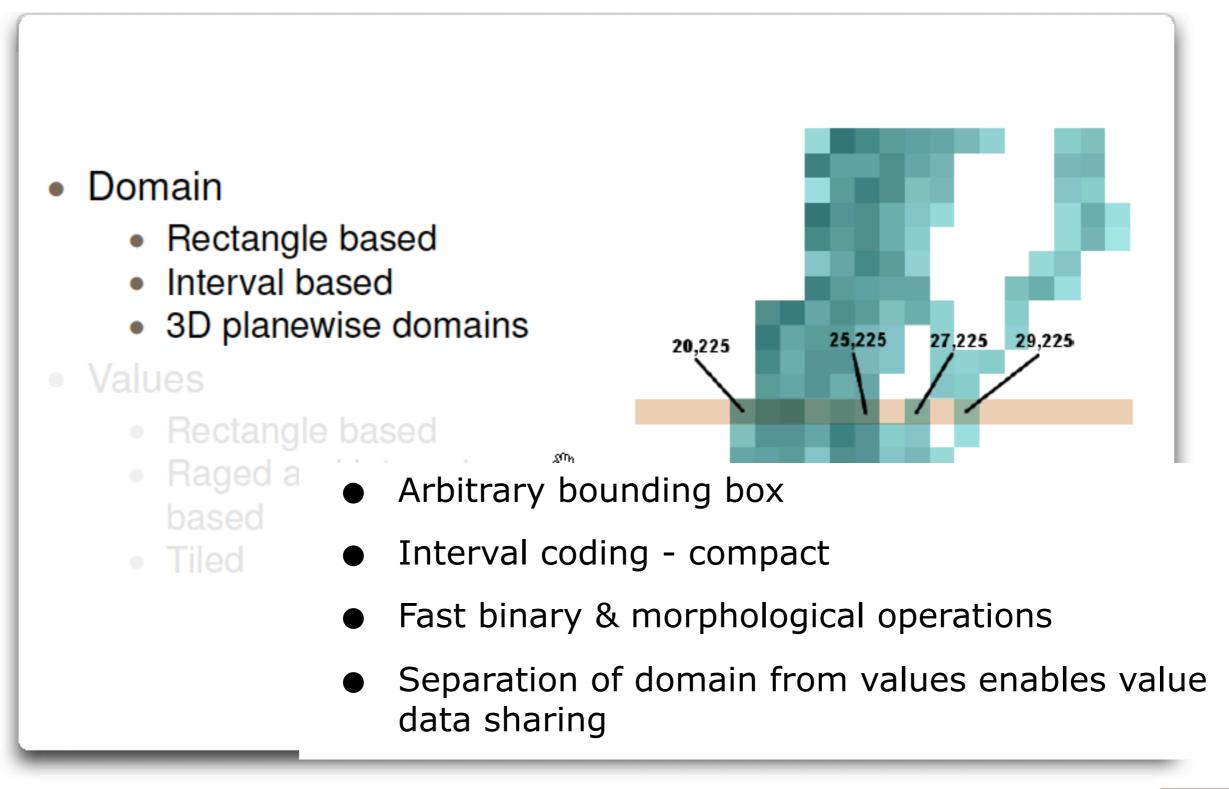






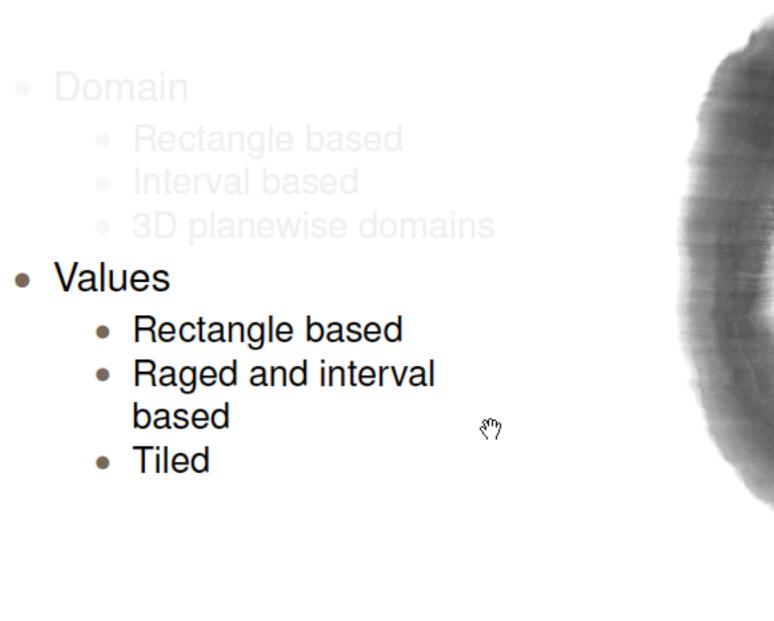










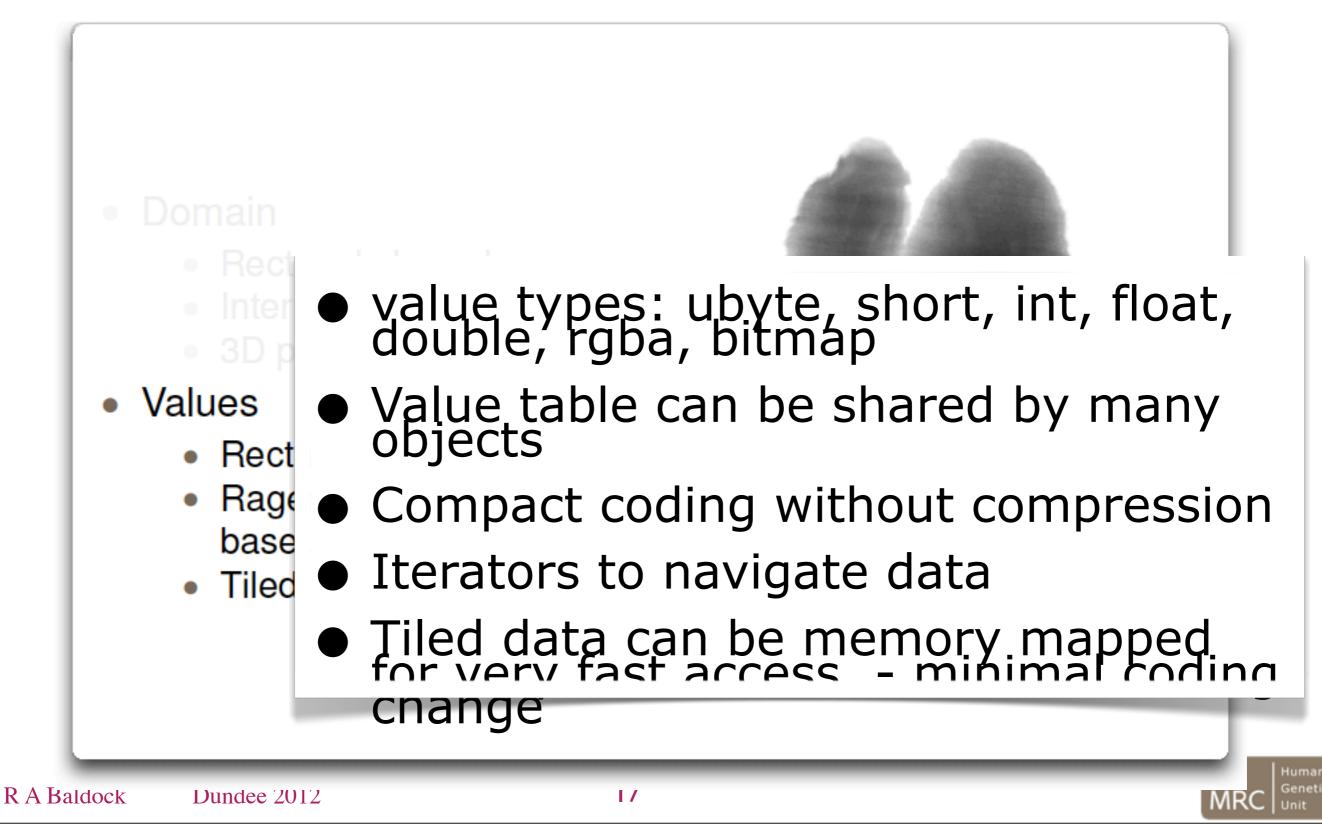




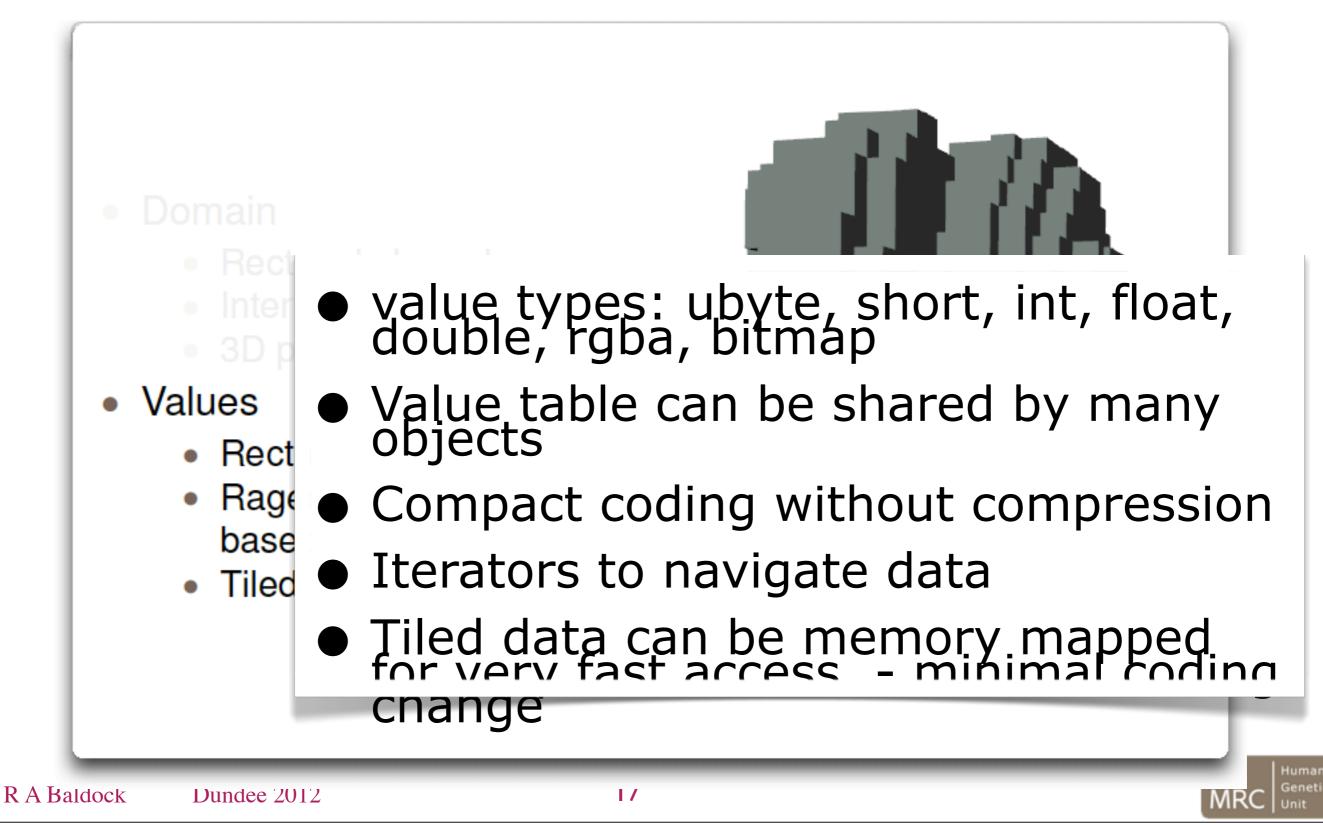
MRC Human Genetic Unit

R A Baldock Dundee 2012











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





- Polylines, boundary lists
- histograms
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$ \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} $	
---	--





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

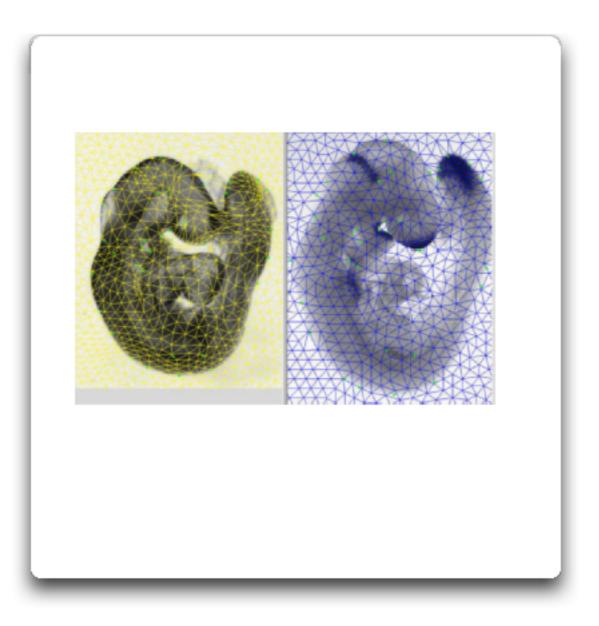
 $\Delta u = u - x$ $\Delta u = P_u(x, y) + \sum_{i=1}^{i=N} \lambda_i b(r_i)$ $b_{TPS}(r) = r^2 ln(r^2)$ $b_{MQ}(r) = \sqrt{r^2 + \delta^2}$ $b_{IMQ}(r) = \frac{1}{\sqrt{r^2 + \delta^2}}$





Woolz image objects

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

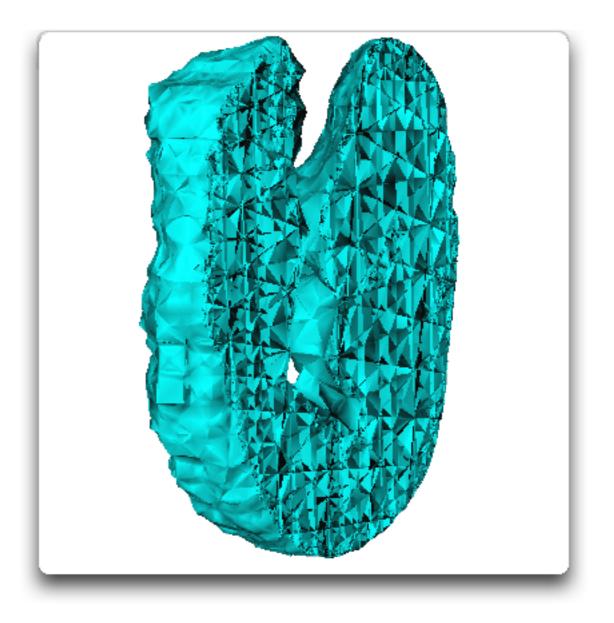






Woolz image objects

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







- 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.

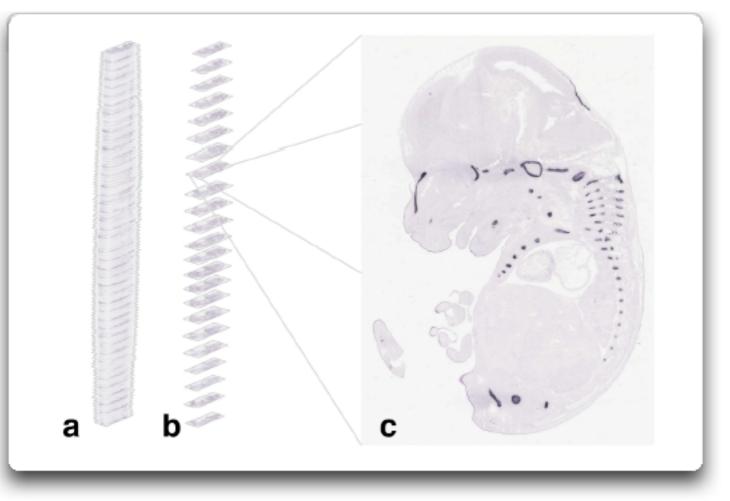




- Semi-automatic reconstruction
- Automated segmentation
- Manual mapping
- 2D pseudo wholemount
- full 3D in progress



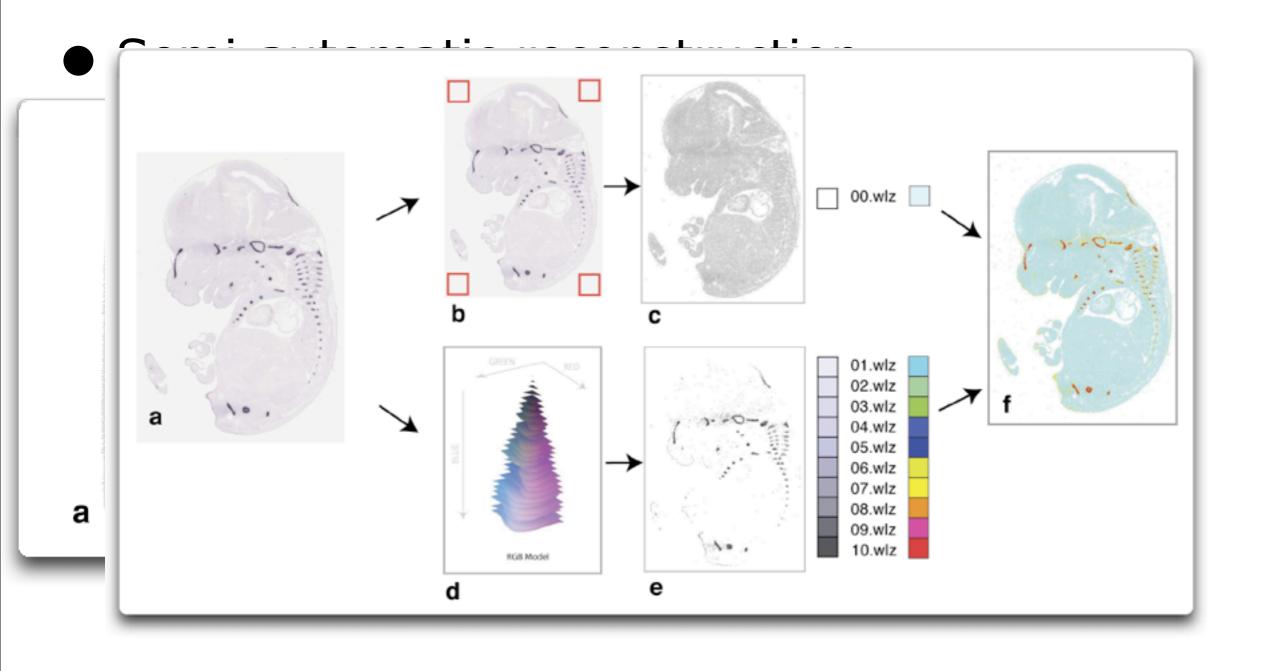
Semi-automatic reconstruction







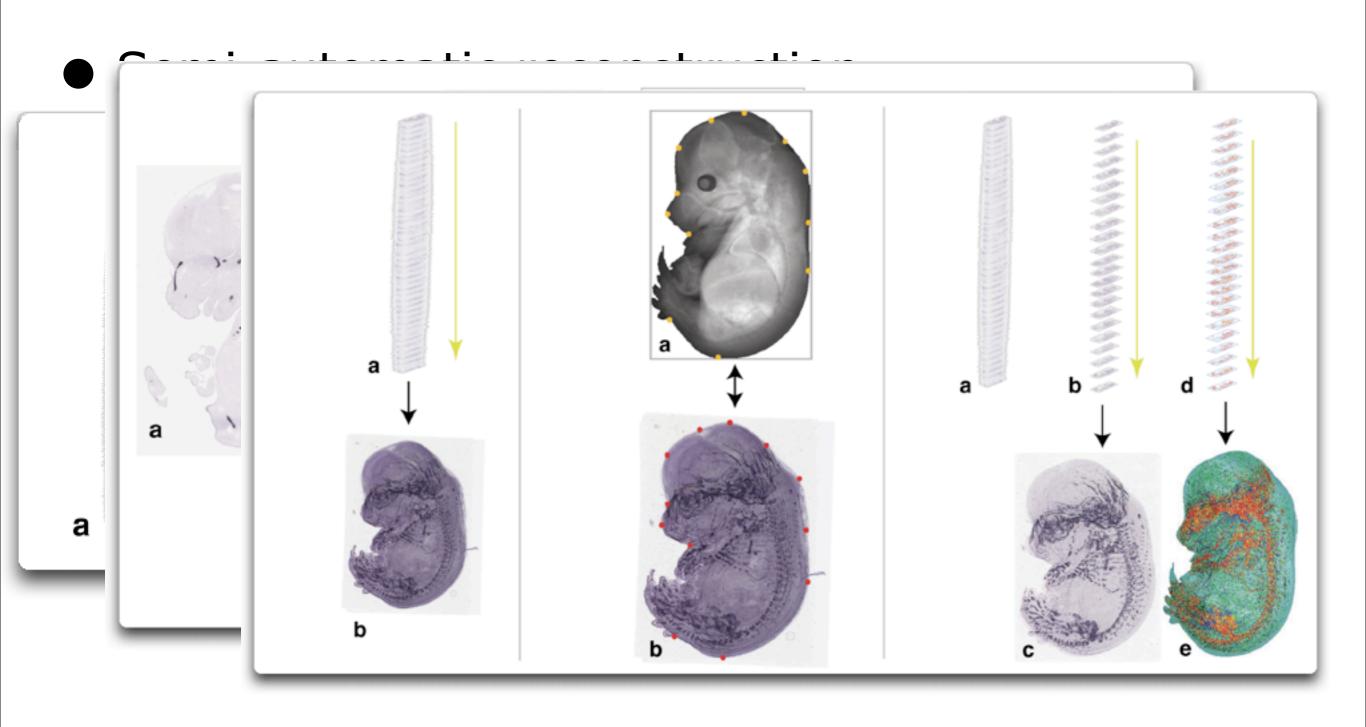
Pseudo Wholemount Mapping to Emap - done





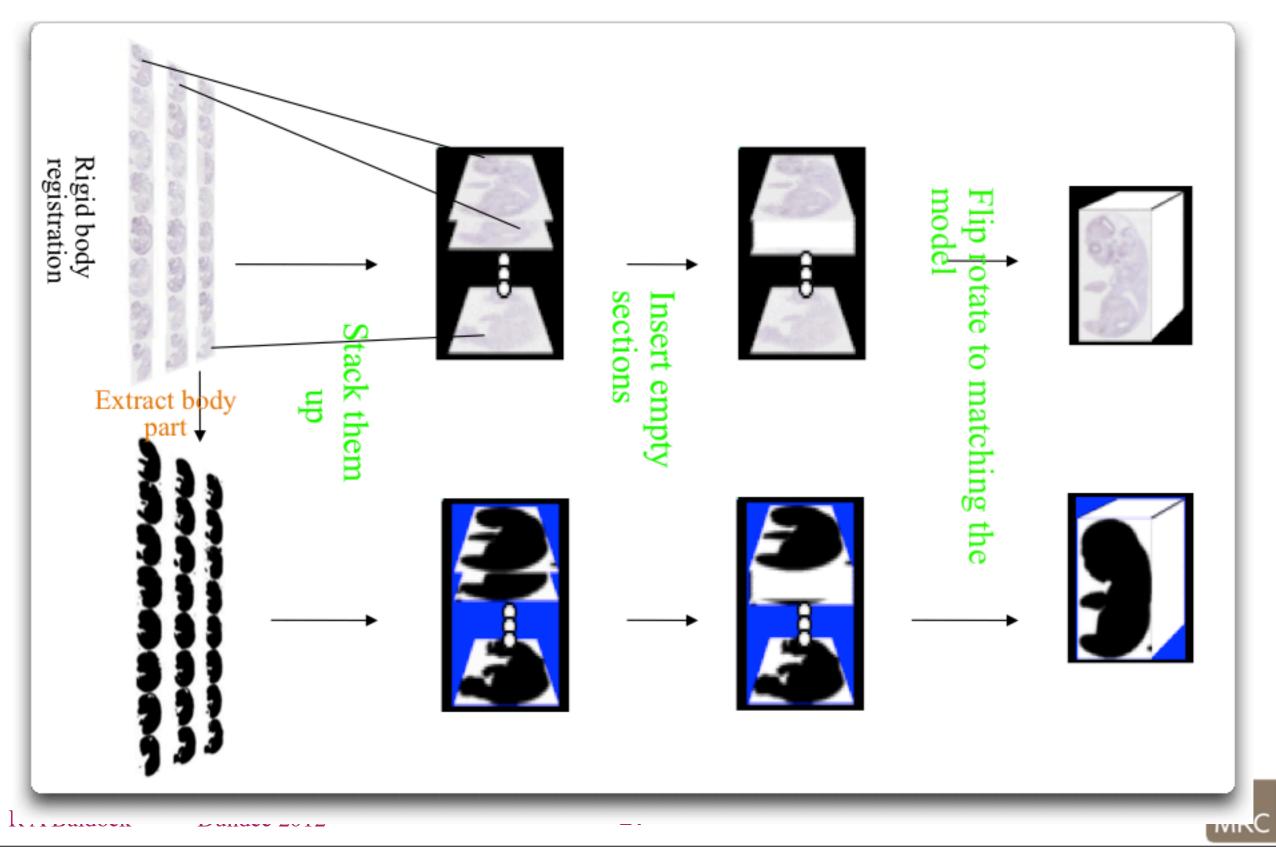


Pseudo Wholemount Mapping to Emap - done



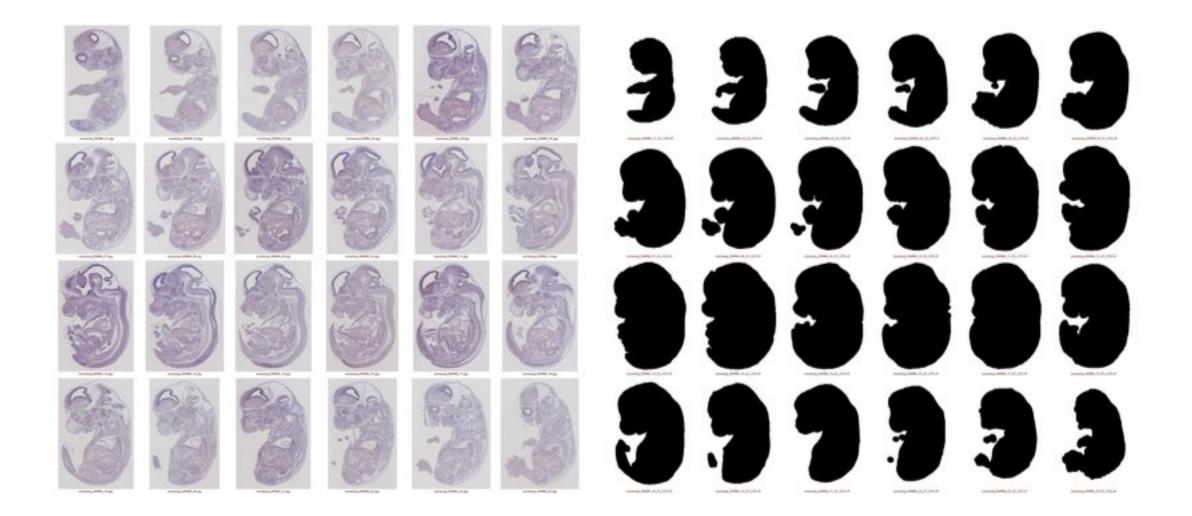






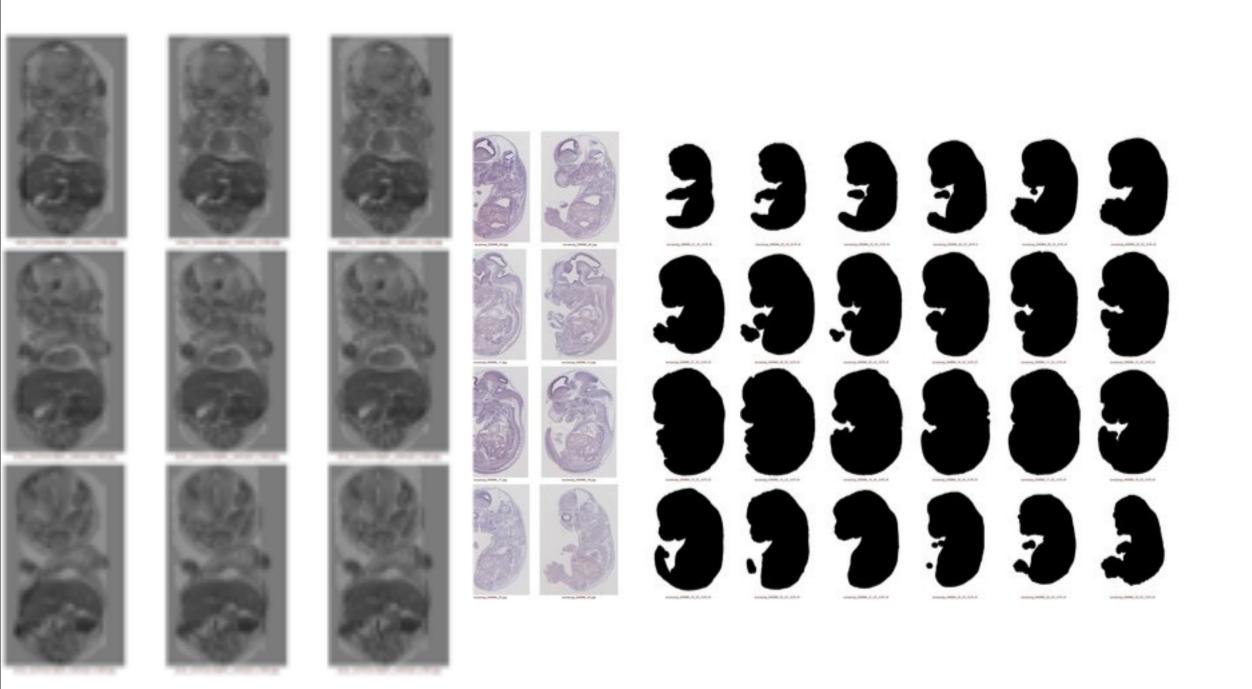
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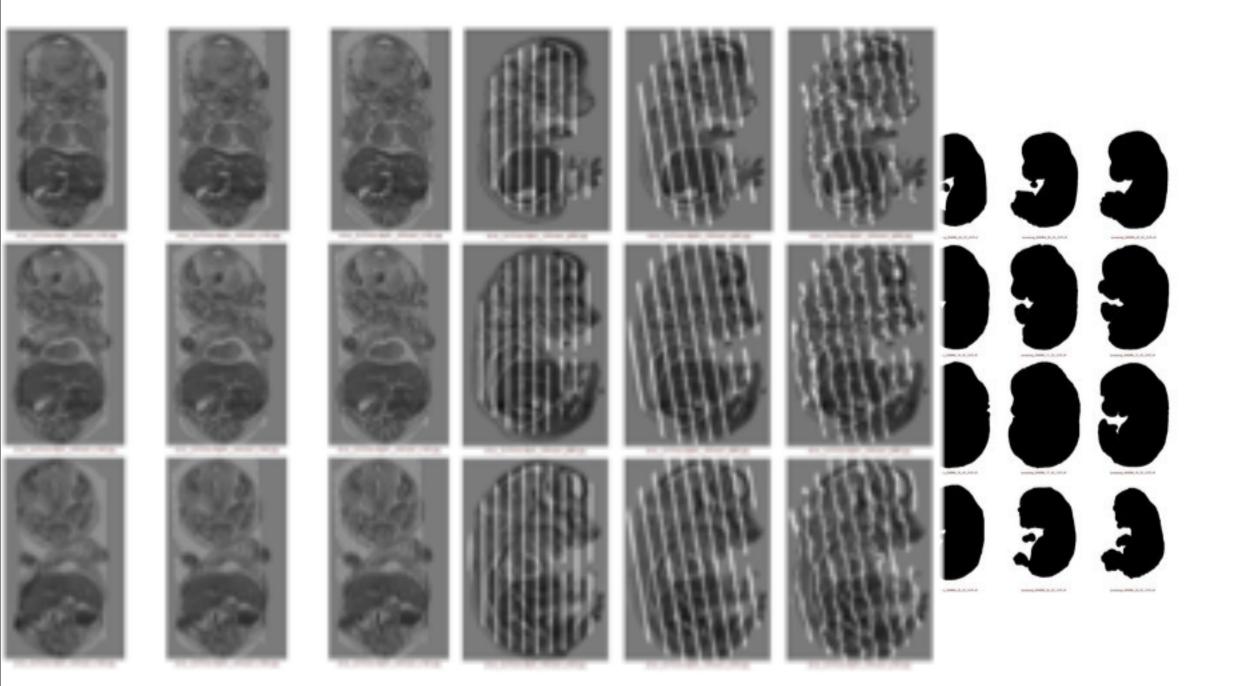






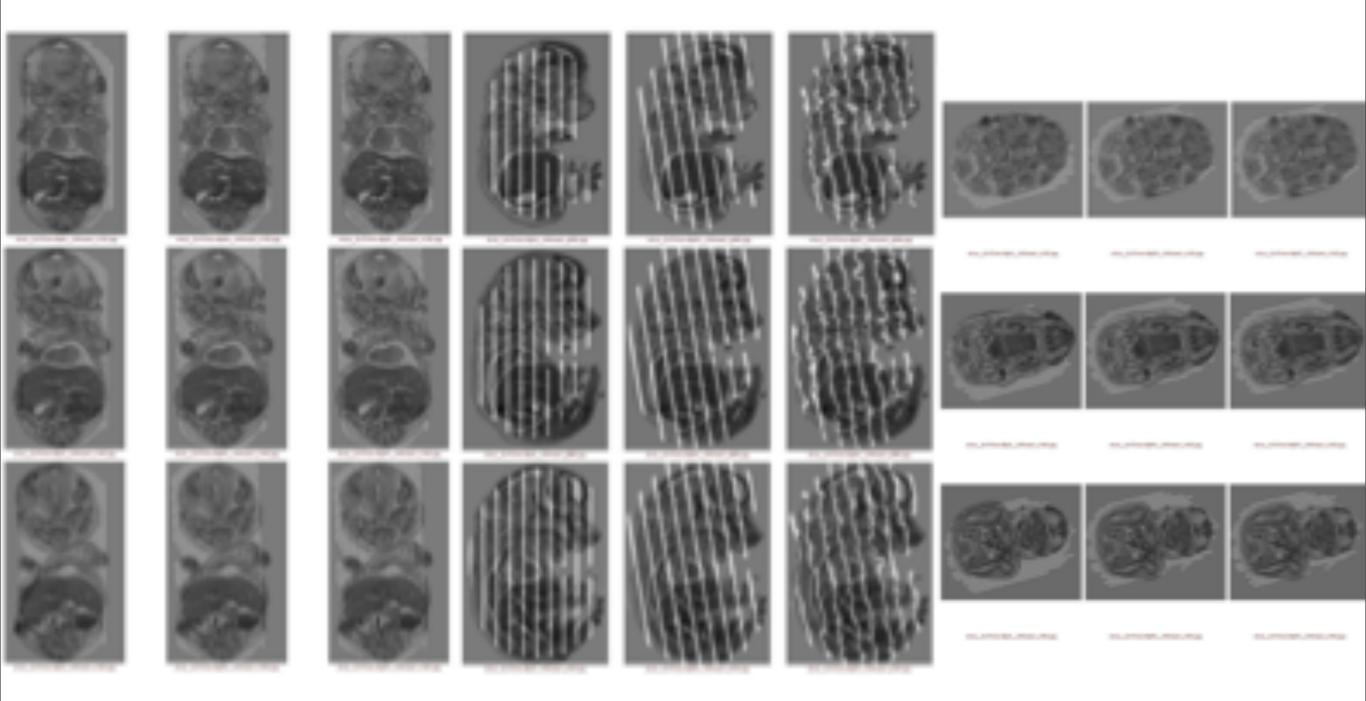
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Large Image Data

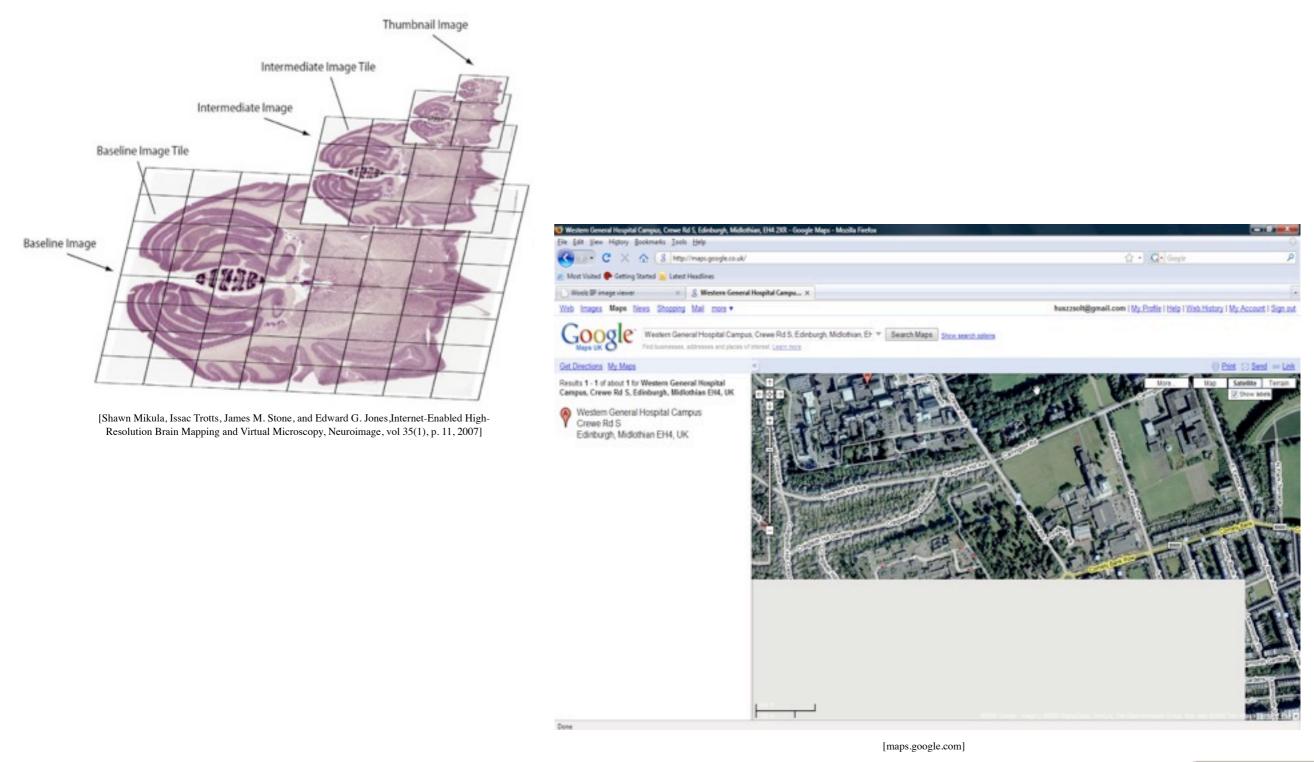
- Single reconstructions already 30+GB
- New EM embryo data ~0.5TB
- OPT data small (200MB) but many 5K
- Typical requirement to browse as sections
- Require arbitrary angle re-sectioning

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





Tiled Image Servers



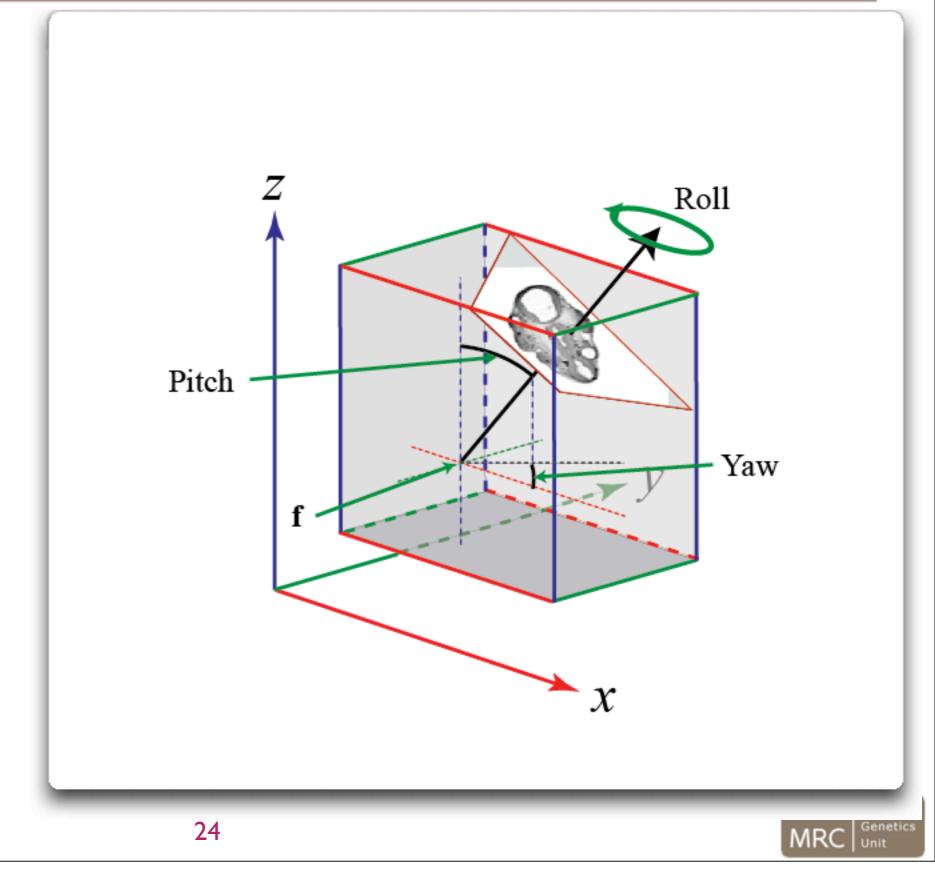
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Sectioning Parameters

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

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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 co-	PRL=T,X,Y
	ordinate	
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-	The pitch, yaw and roll angles of the sectioning plane	
angles		
Wlz-3d-bounding-	The first and last plane, line and column number of the object	
box		
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	

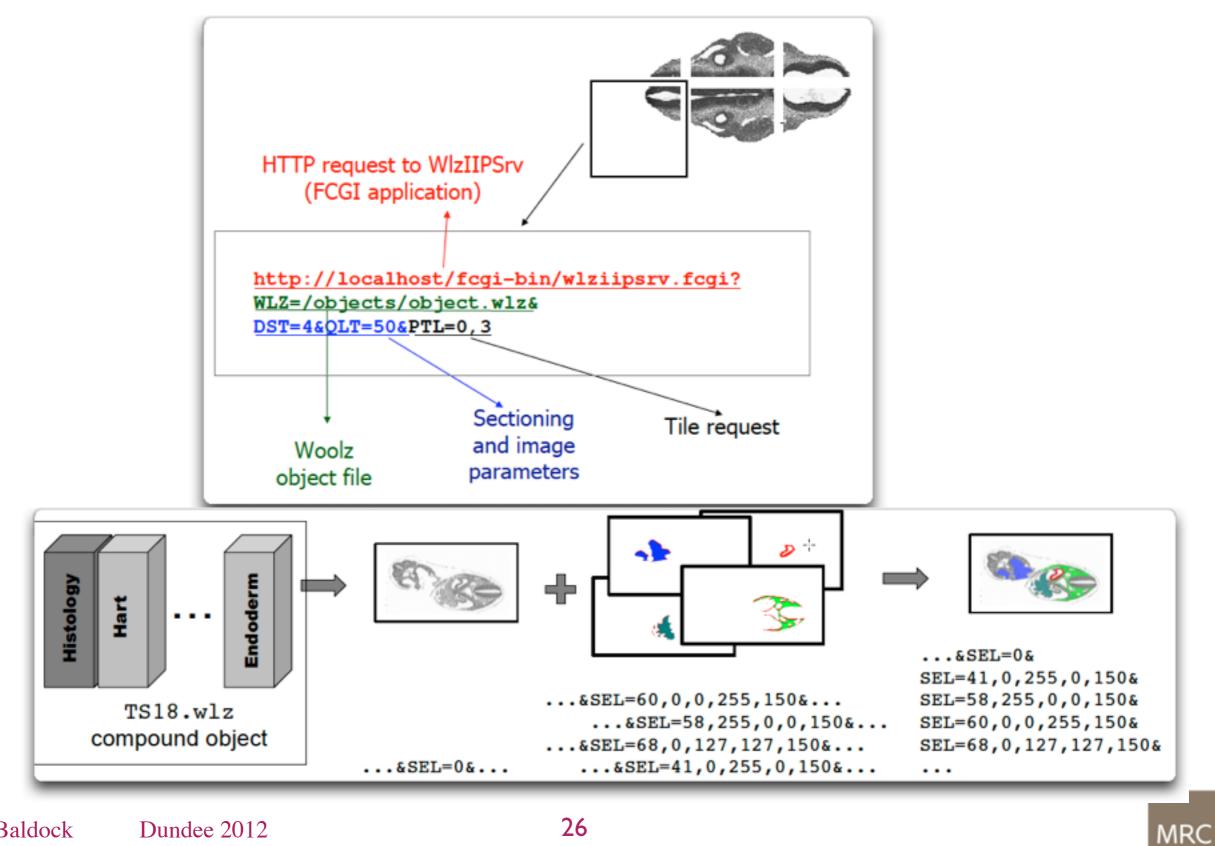
Table 2: Extended object overview

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IIP3D Web-App Architecture €map

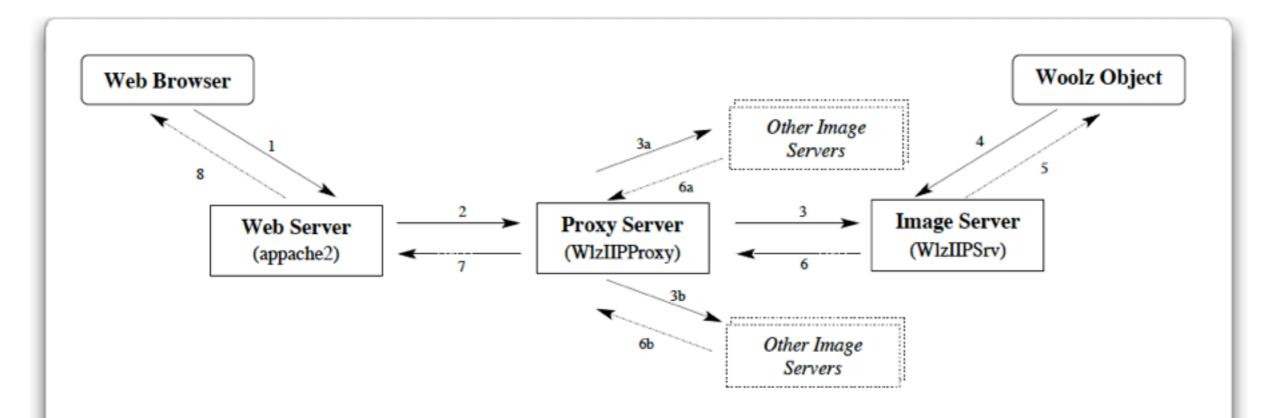


Figure 4: Architecture of IIP3D server using a proxy server. The web server passes the user requests to the proxy, which forwards them to individual IIP servers. These servers have direct access to the Woolz Object and return the requested data. The numbered lines show the order of the requests (continuous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

IIP3D Web-App Architecture €map

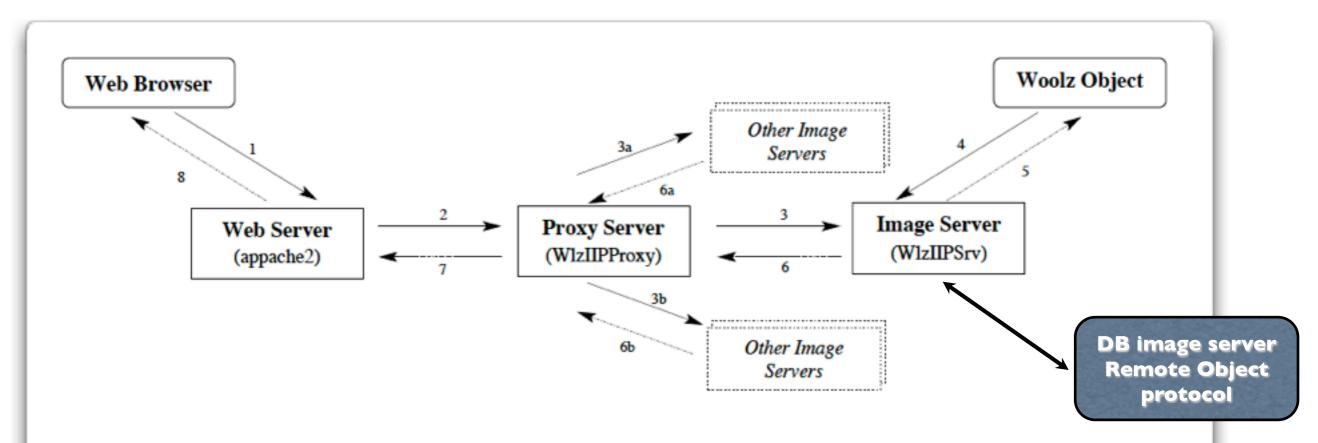
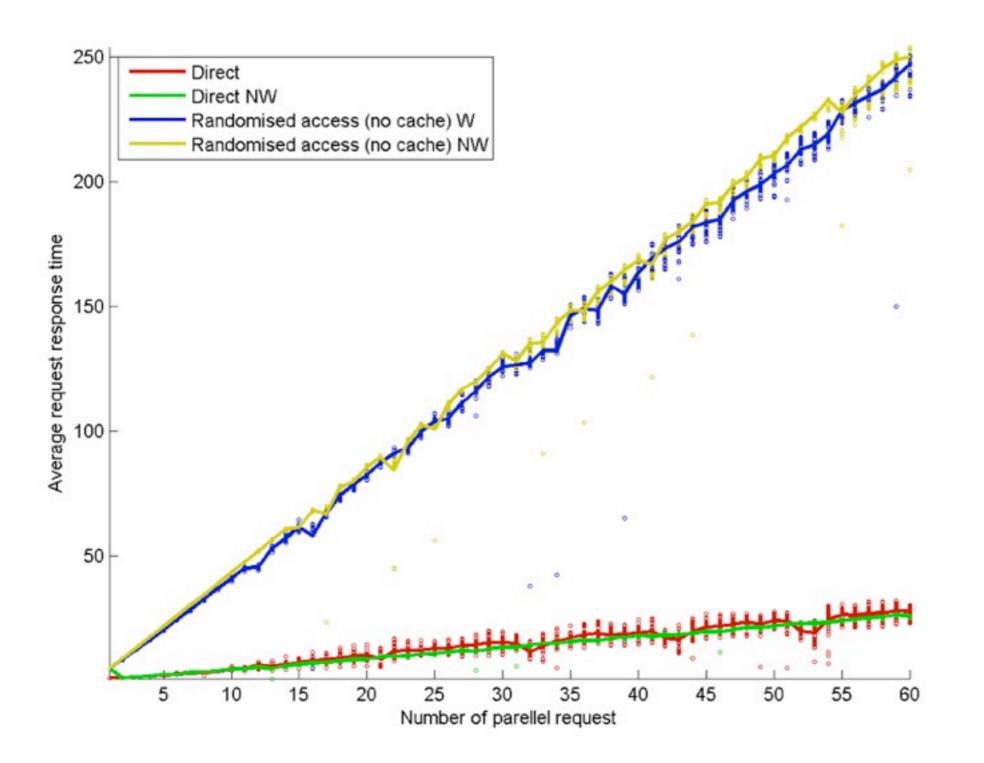


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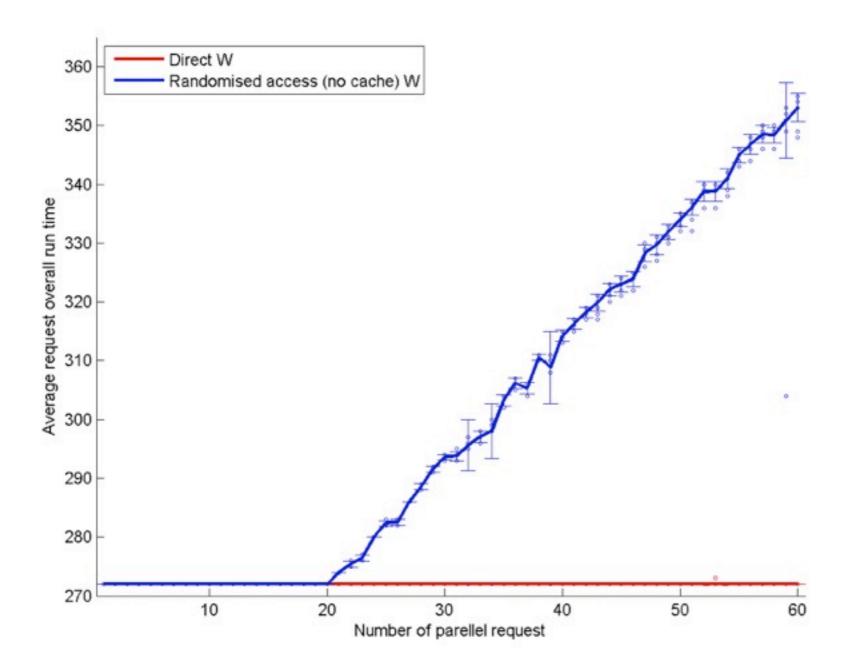


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Performance





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Human Genetics Unit



- 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







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





- 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

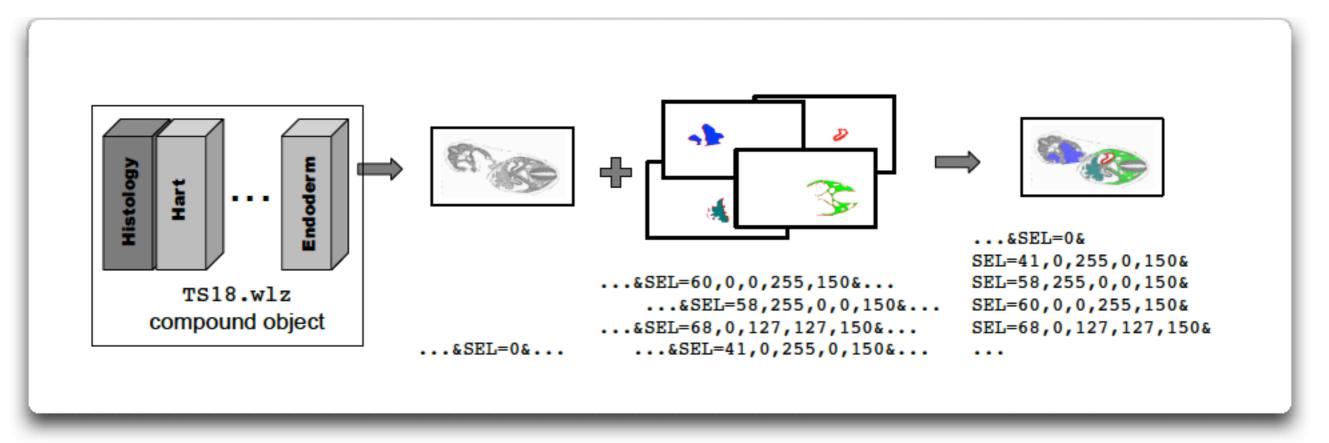






Image Processing IIP3D extensions

Operator	Description	
diff(<i>exp</i> , <i>exp</i>)	The difference between the two given domains.	
dilation(exp, radius)	The dilation of the domain by <i>radius</i> voxels.	
domain(<i>exp</i>)	The domain of an object.	
erosion(<i>exp</i> , <i>radius</i>)	The erosion of the domain by <i>radius</i> voxels.	
intersect (exp list)	The intersection of the domains in the given lists.	
threshold(exp,value,comparison)	Creates an object where the image values sat-	
	isfy the given <i>value</i> and <i>comparison</i> . 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|idx list) (,exp list)
exp list
         :=
idx list
              (idx | (idx-) | (idx-idx) | (-idx)) (,idx list)
         :=
         := idx
exp
              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) |
         := [0-9]+
idx
         := [1-9][0-9]*
uint
            [-+]?[0-9]*.?[0-9]+([eE][-+]?[0-9]+)?
val
         :=
              (lt)|(le)|(eq)|(ge)|(gt)
         :=
cmp
```

Table 3: Syntax for morphological expressions.



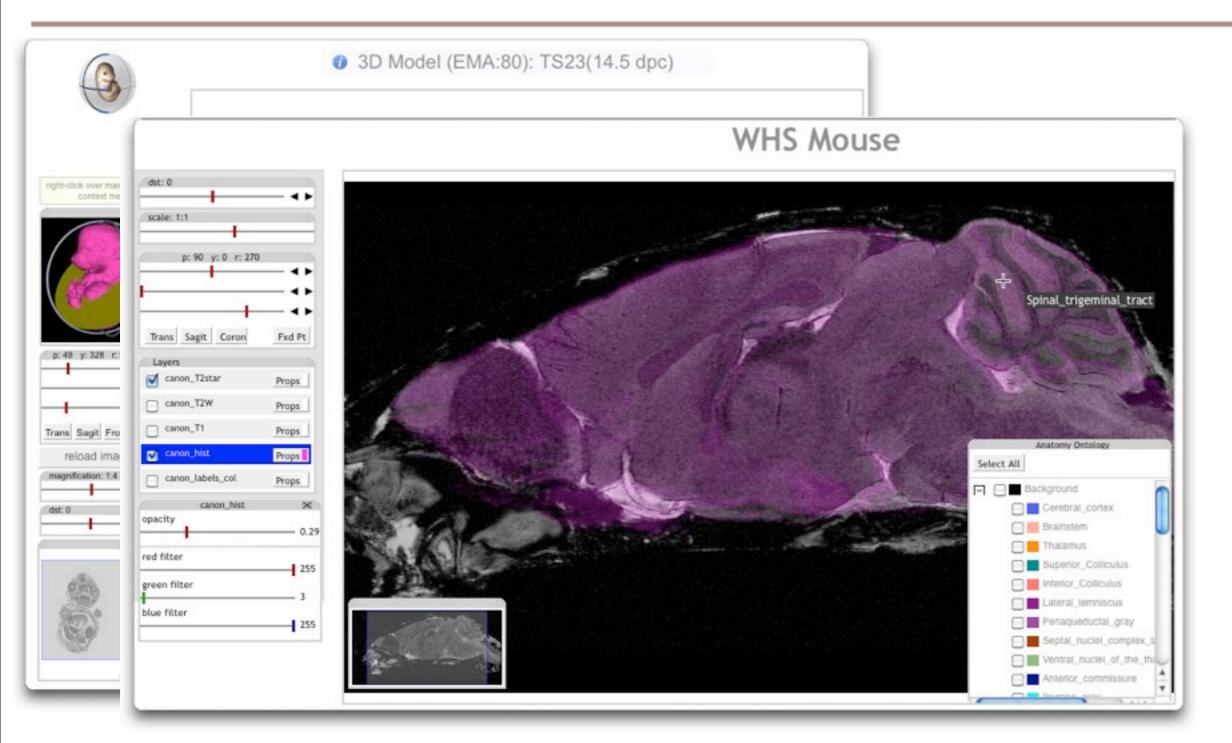
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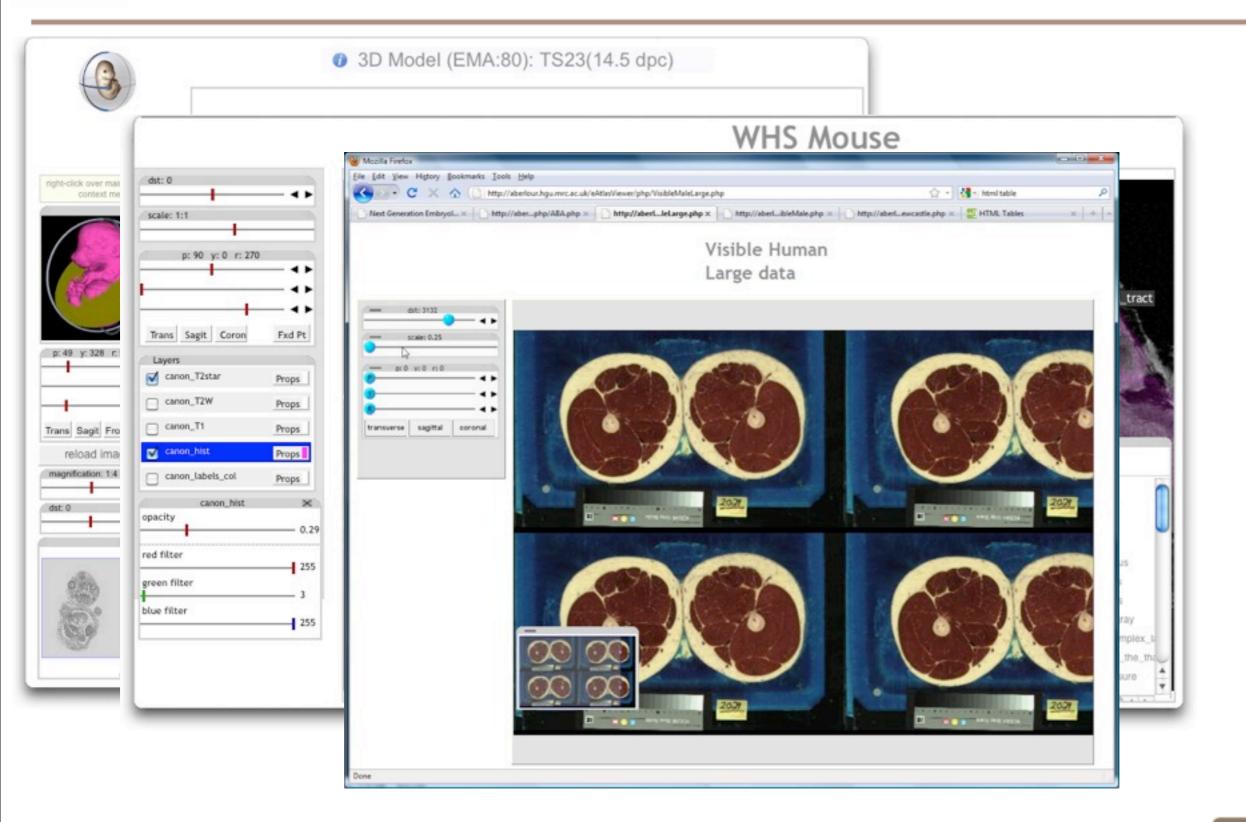
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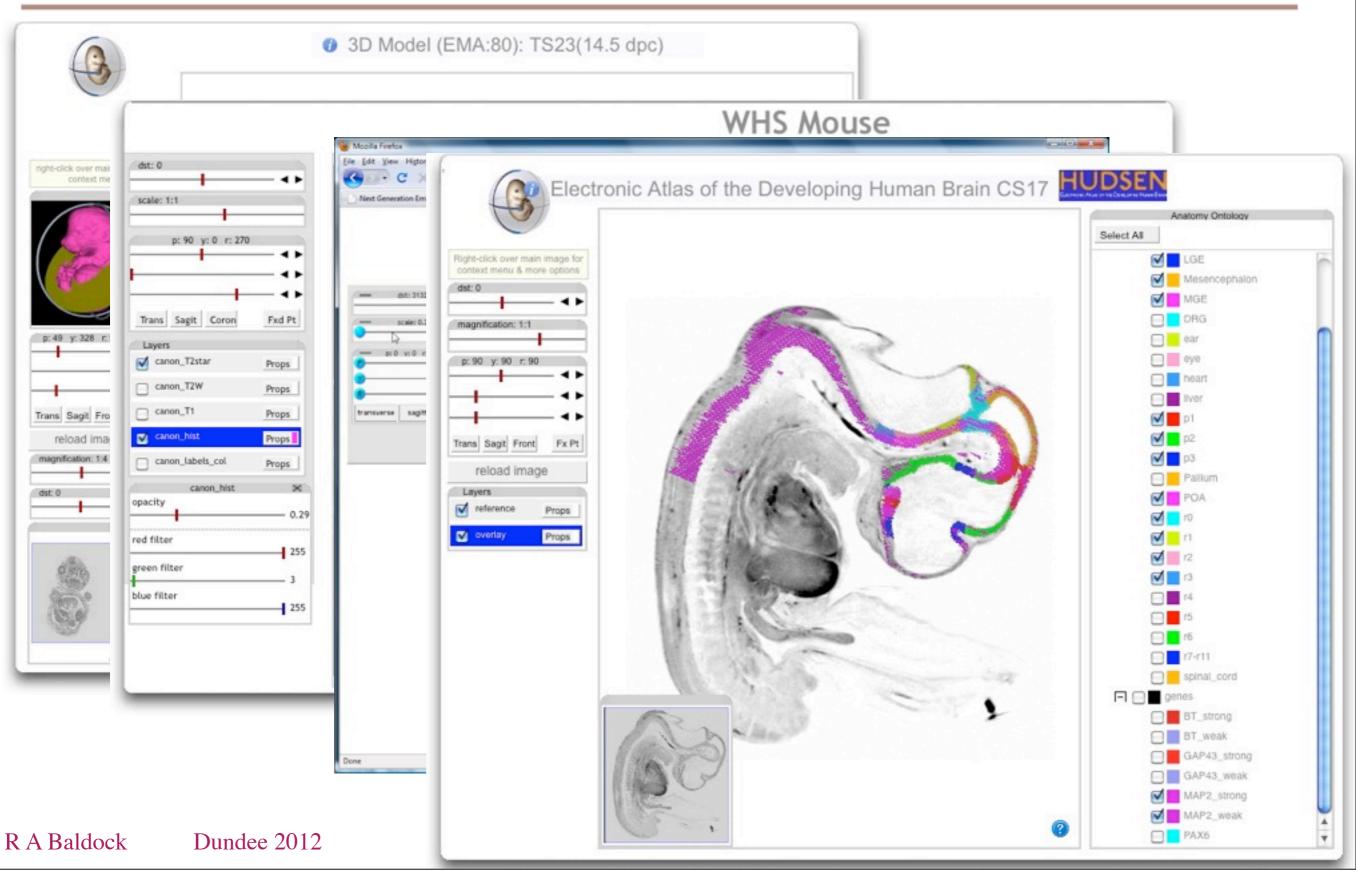














- IIP3D viewer extension to 3D visualisation
 - Use X3Dom Javascript binding to X3D
- navigation feedback
- Anatomy visualisation
 - see demo

• Extend to 4D





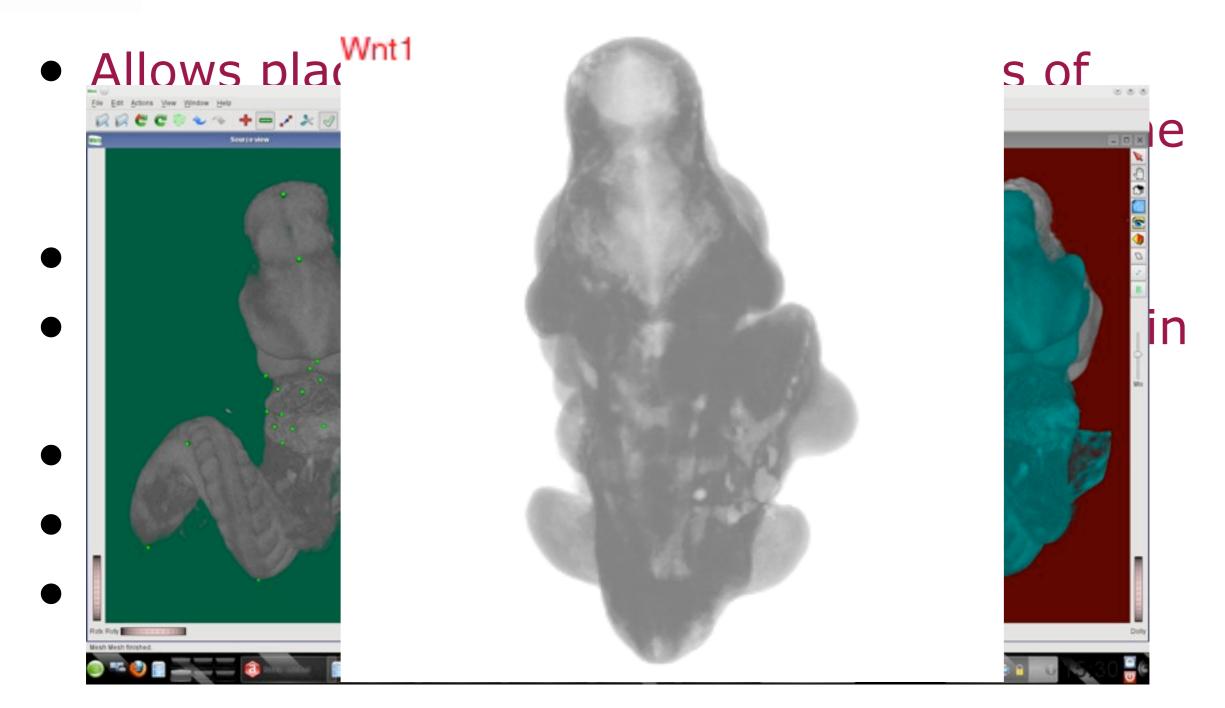
3D mapping - WlzWarp



- 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!)





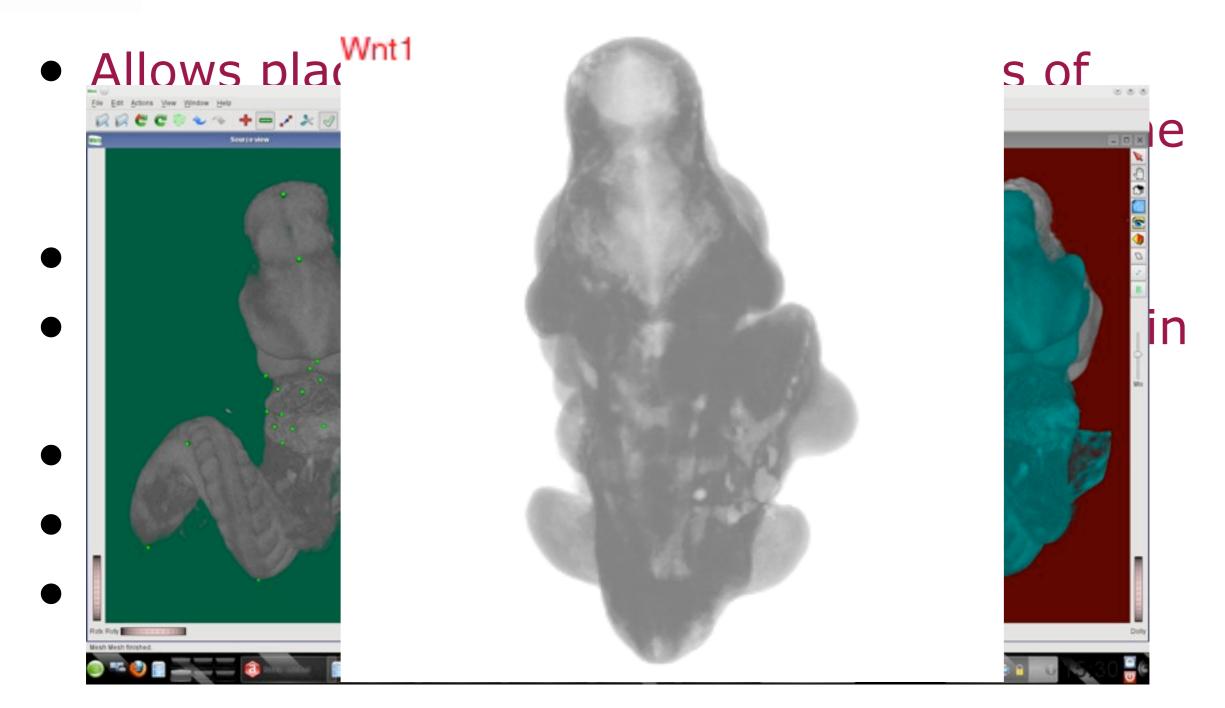


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21/4/11







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21/4/11



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



R A Baldock Dundee 2012



Lineage & the Brain

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



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eMouseAtlas



MRC Human Genetics Unit, Edinburgh

EMAGE:

Chris Armit Shanmugasundaram Venkataraman Lorna Richardson Peter Stevenson

EMAP:

Albert Burger Bill Hill Nick Burton Yiya Yang Julie Moss Liz Graham Allyson Ross NIH GUDMAP: Simon Harding Bernard Haggerty Koosum Roochum

> BBSRC: Mike Wicks

FP7 RICORDO: Xu Gu

Wellcome OME: Jianguo Rao

Duncan Davidson Richard Baldock

Colin Semple Pedro Coutinho Ian Overton



Heriot Watt University

Albert Burger



University of Edinburgh

Douglas Armstrong Nestor Milyeav



Institute of Human Genetics, Newcastle University

Susan Lindsay Janet Kerwin

Other

Jonathan Bard Matt Kaufman



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