

The Mouse Atlas Database: An Atlas-Based IMage Resource

Richard Baldock

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



• Bill Hill

• Jianguo Rao



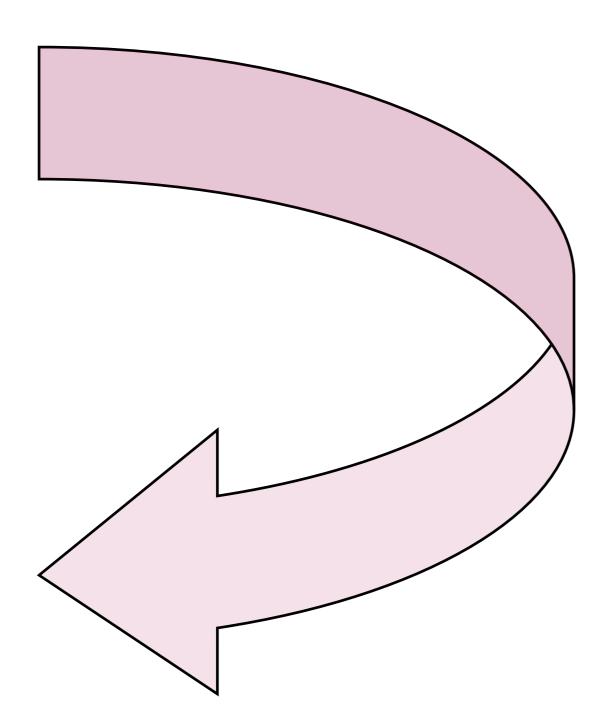




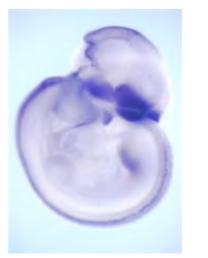


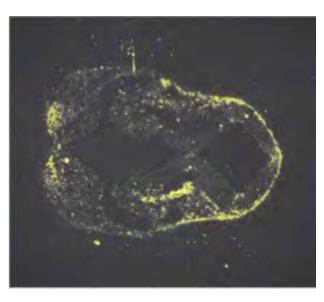
eMouseAtlas - Development and Gene-Expression

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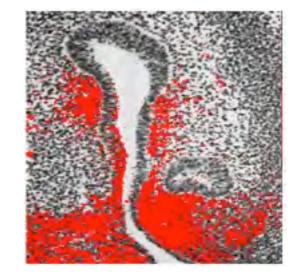


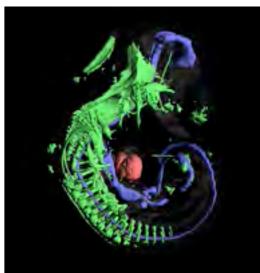
GENE EXPRESSION





Carol Wicking, University of Queensland



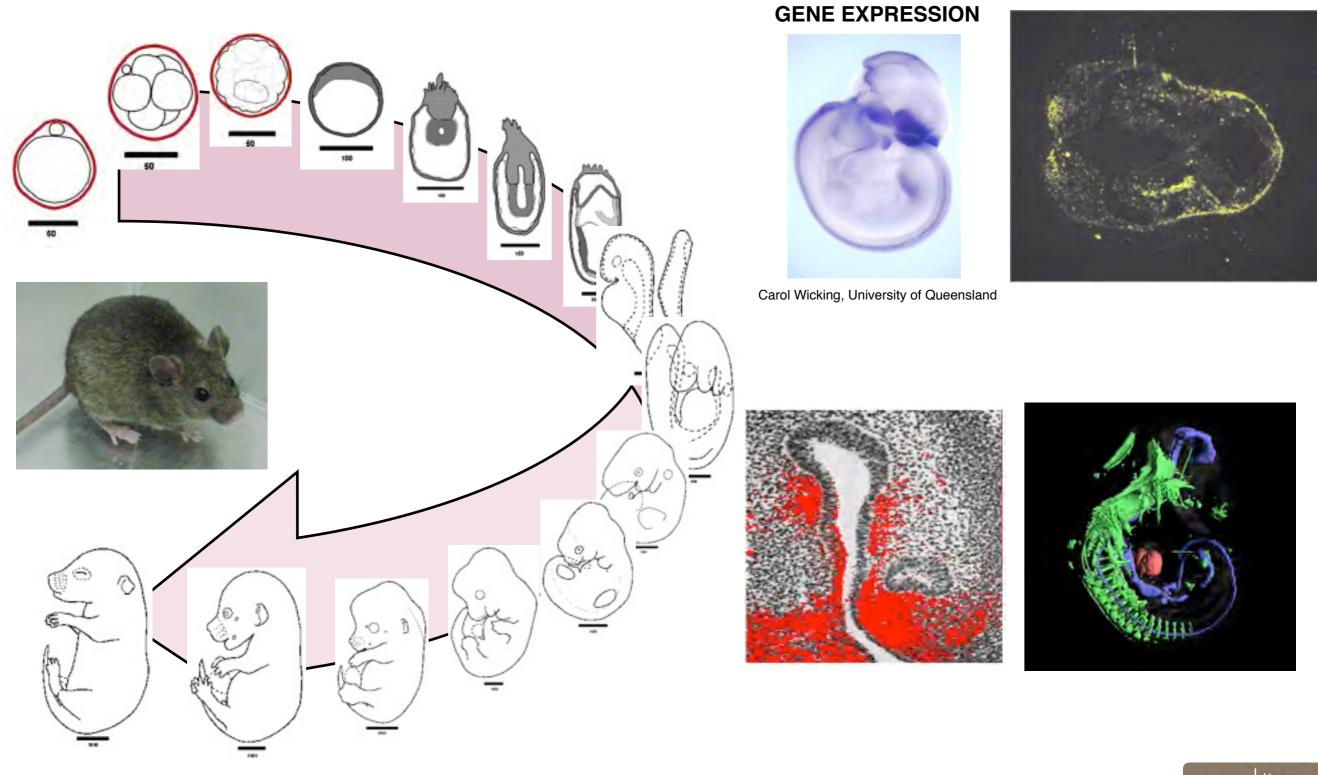




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eMouseAtlas - Development and Gene-Expression



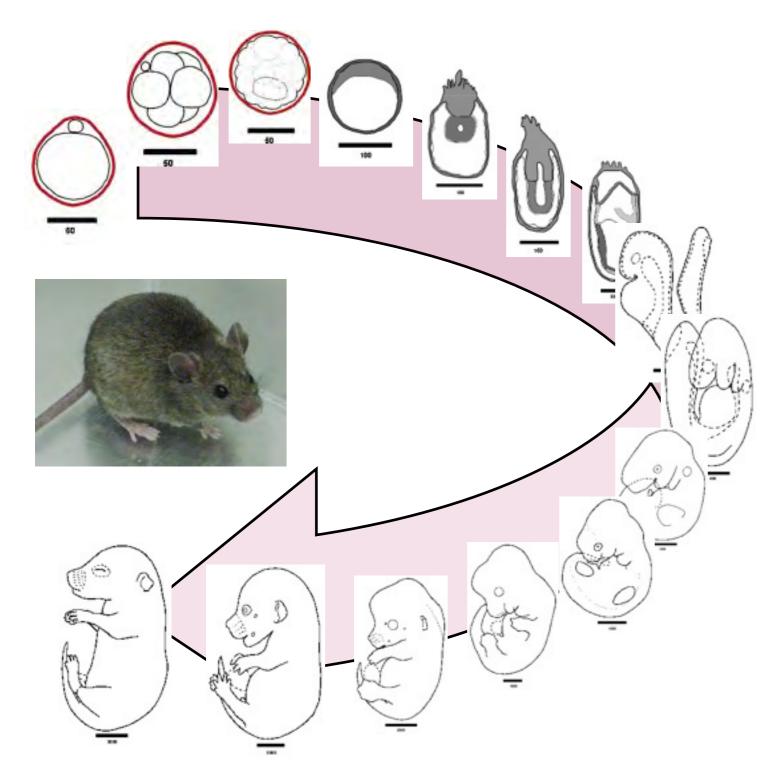


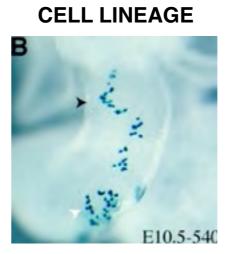




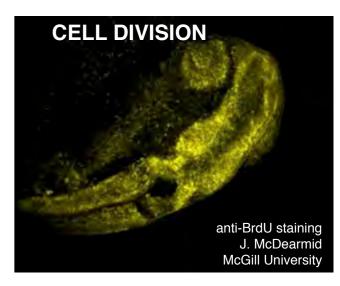
eMouseAtlas - Development and Gene-Expression

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Sigolène Meilhac Institut Pasteur



APOPTOSIS



Acridine Orange J. Burns University of Bristol

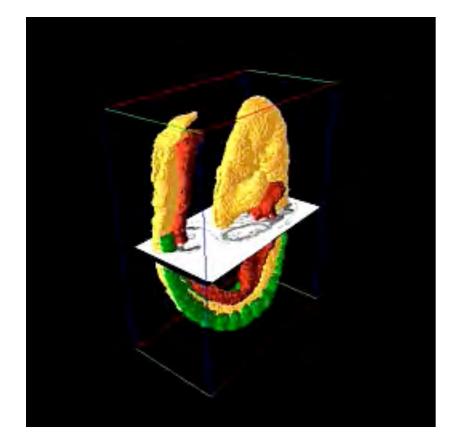
TRANSGENICS

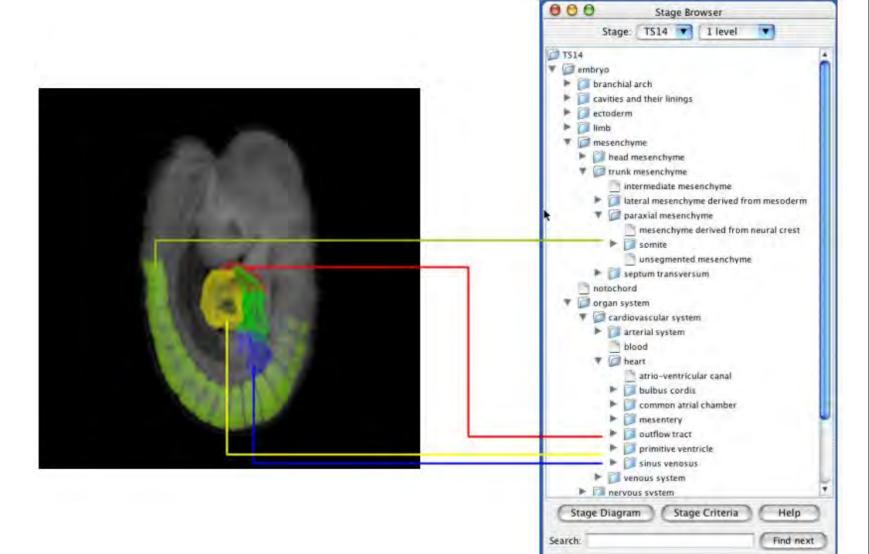






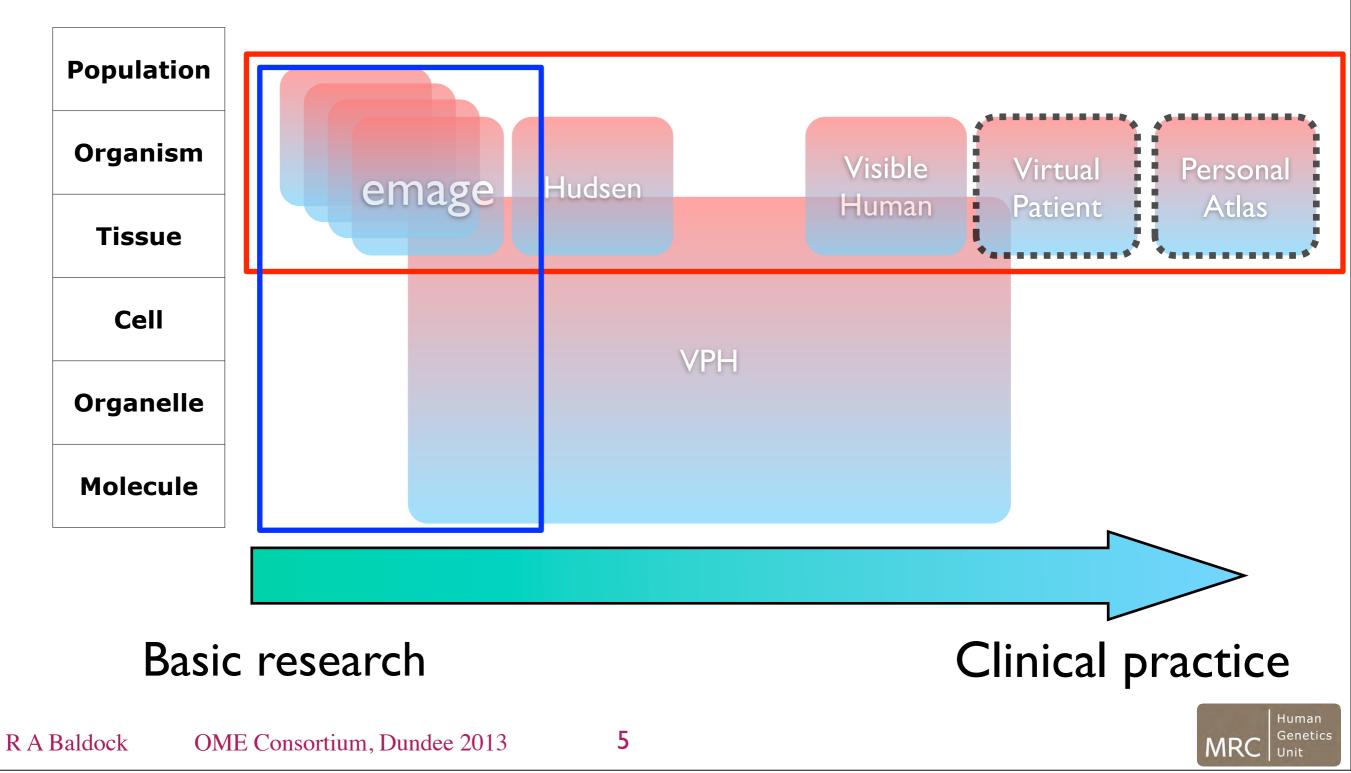
eMouseAtlas Framework



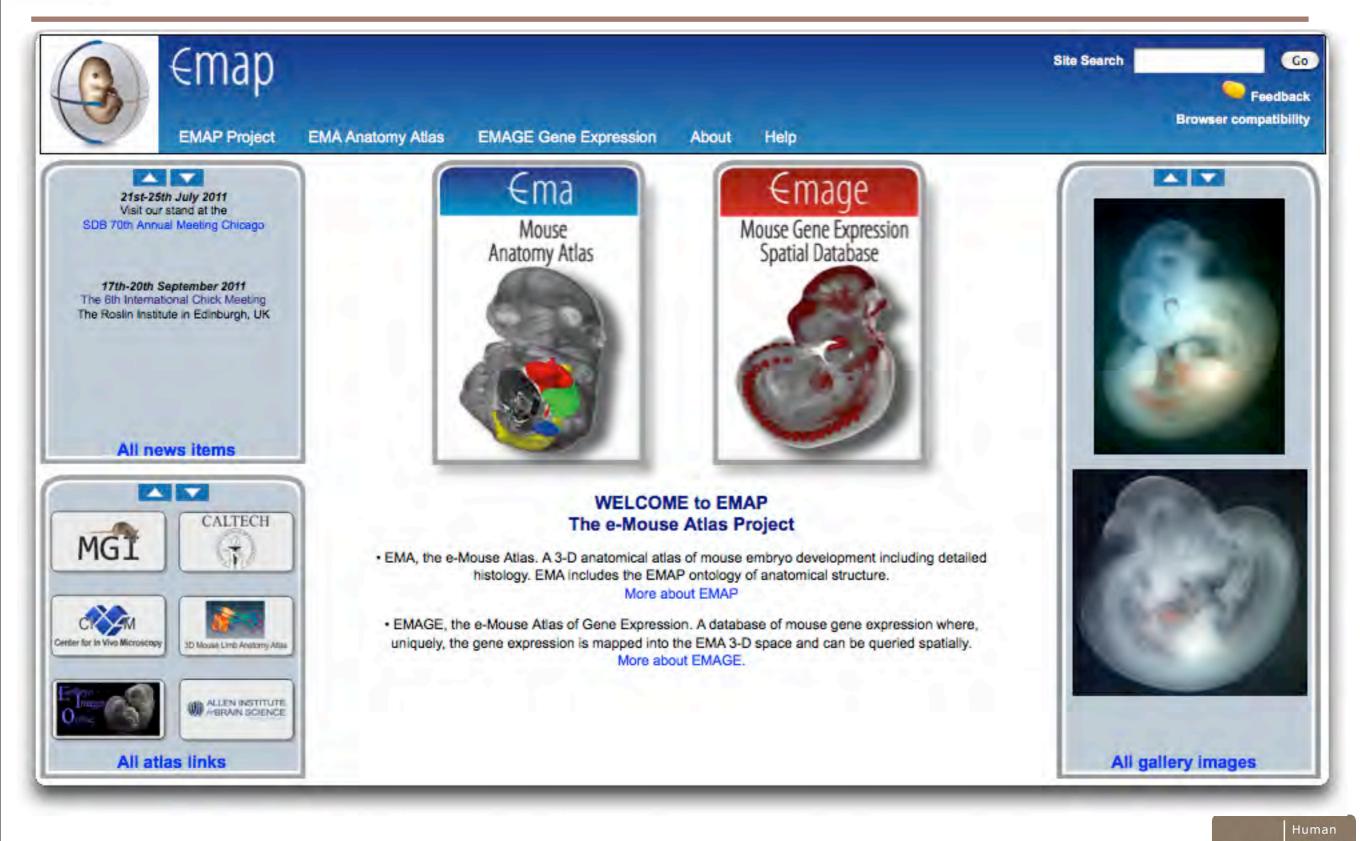










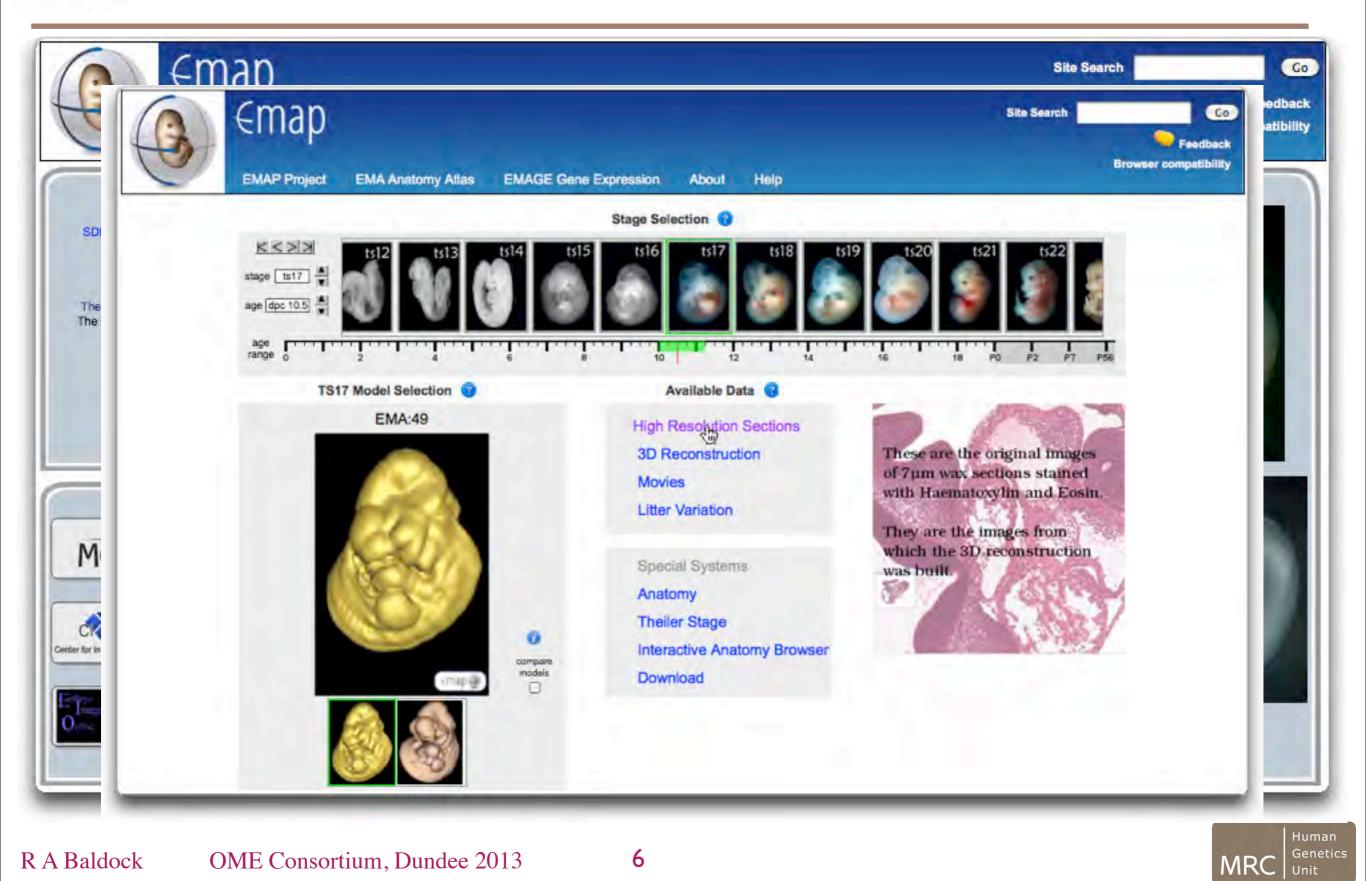


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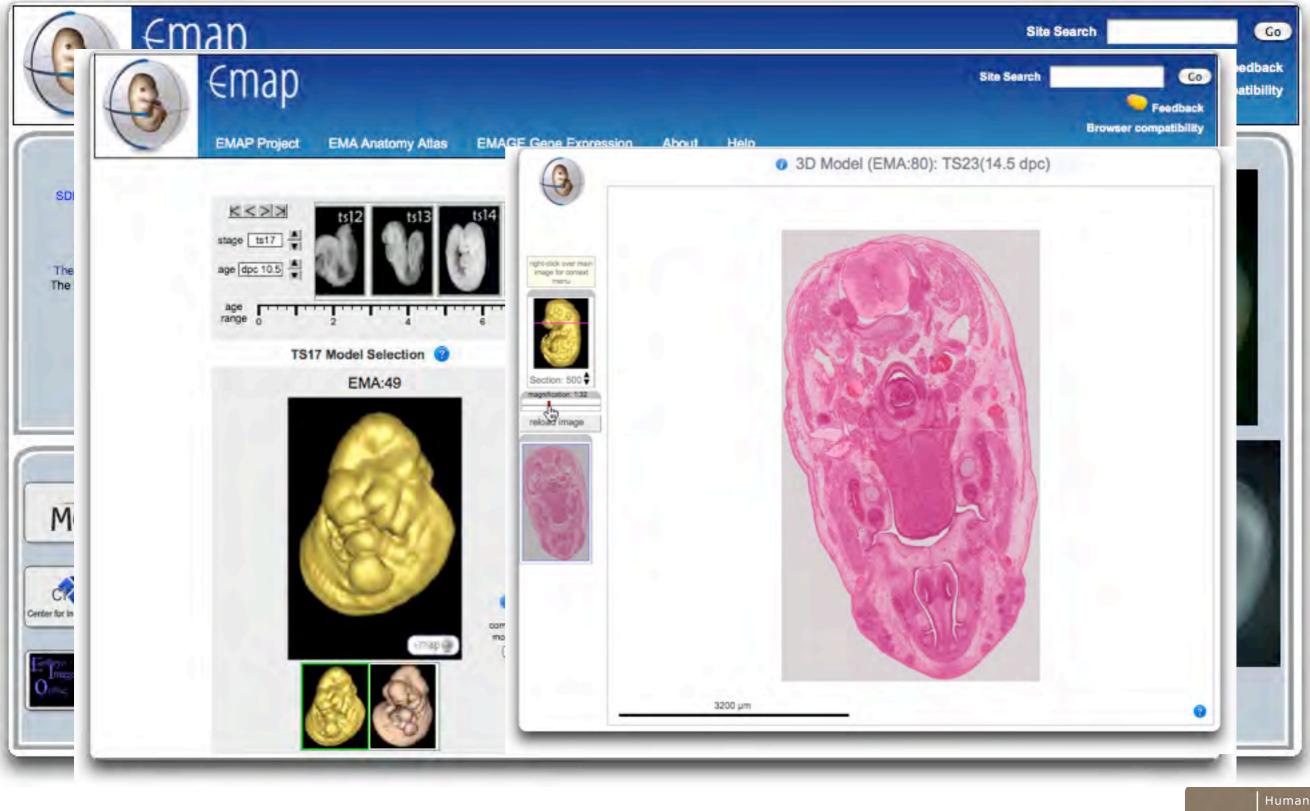
MRC









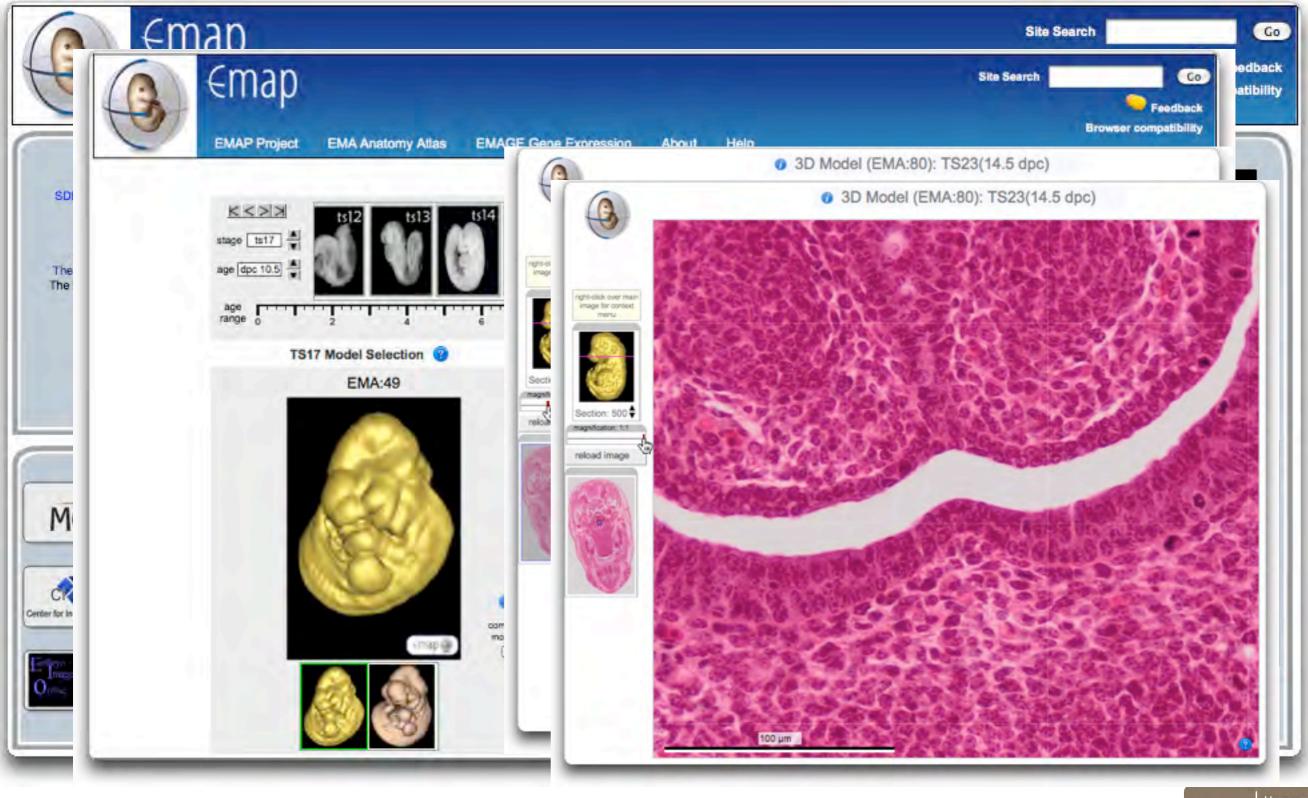


OME Consortium, Dundee 2013 Thursday, 28 February 2013

R A Baldock

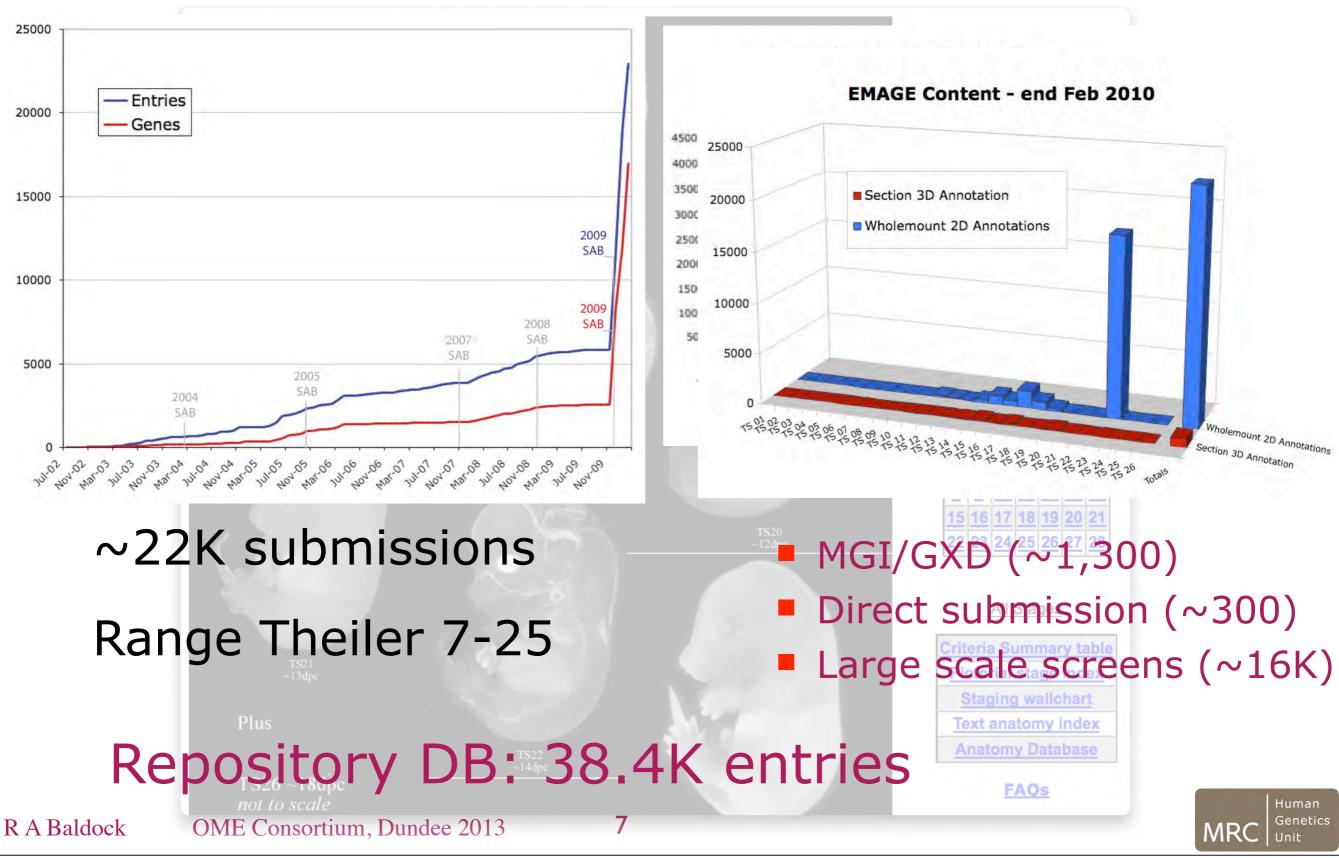
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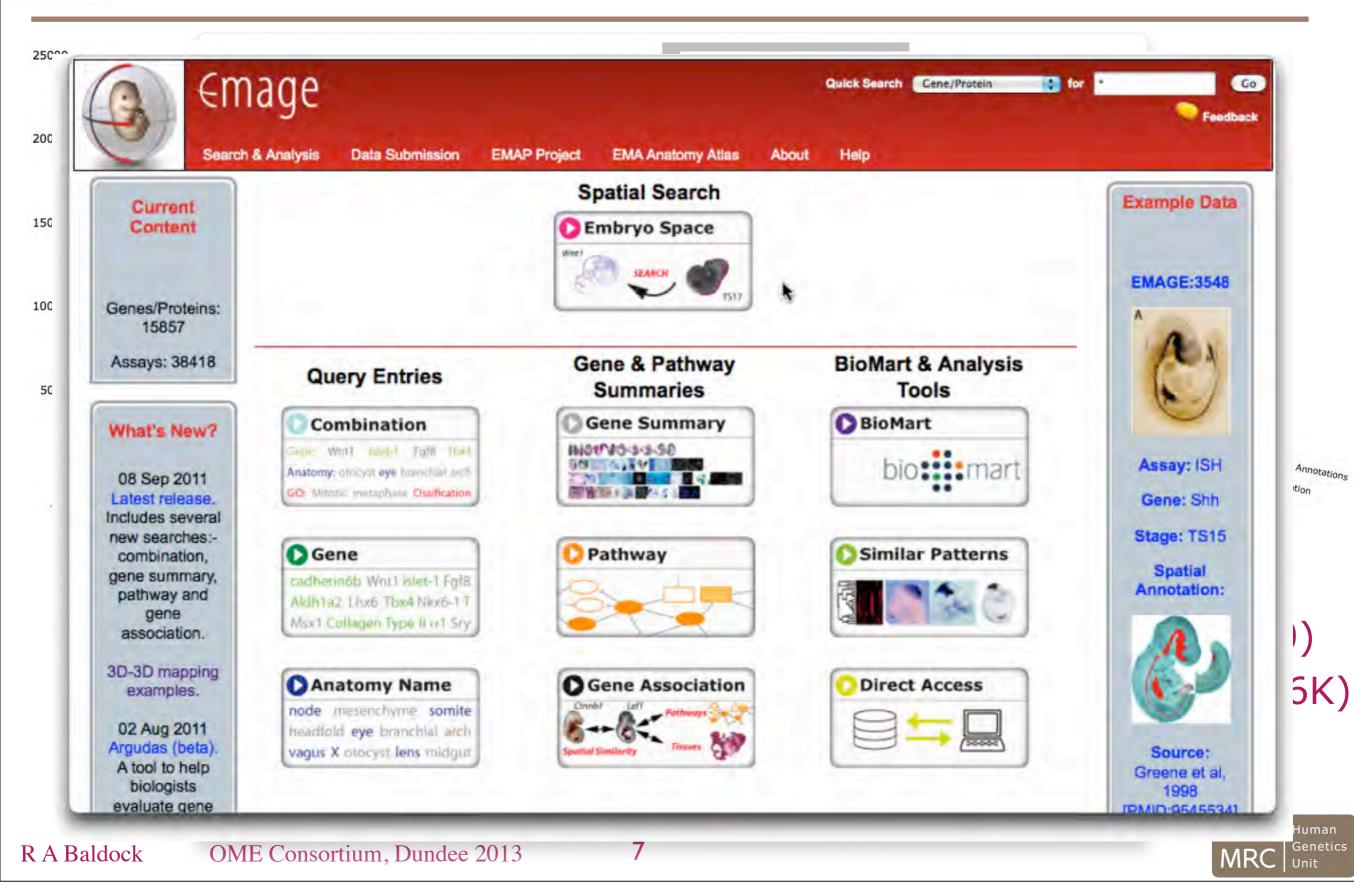


EMAGE - current status



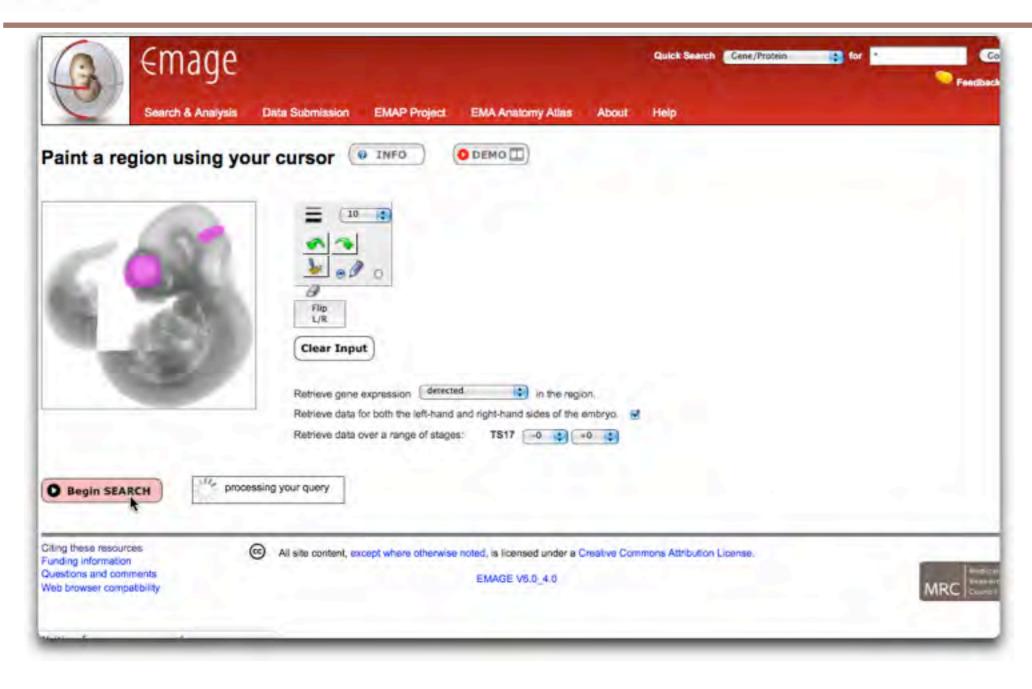
Emap

EMAGE - current status





EMAGE Embryo Space





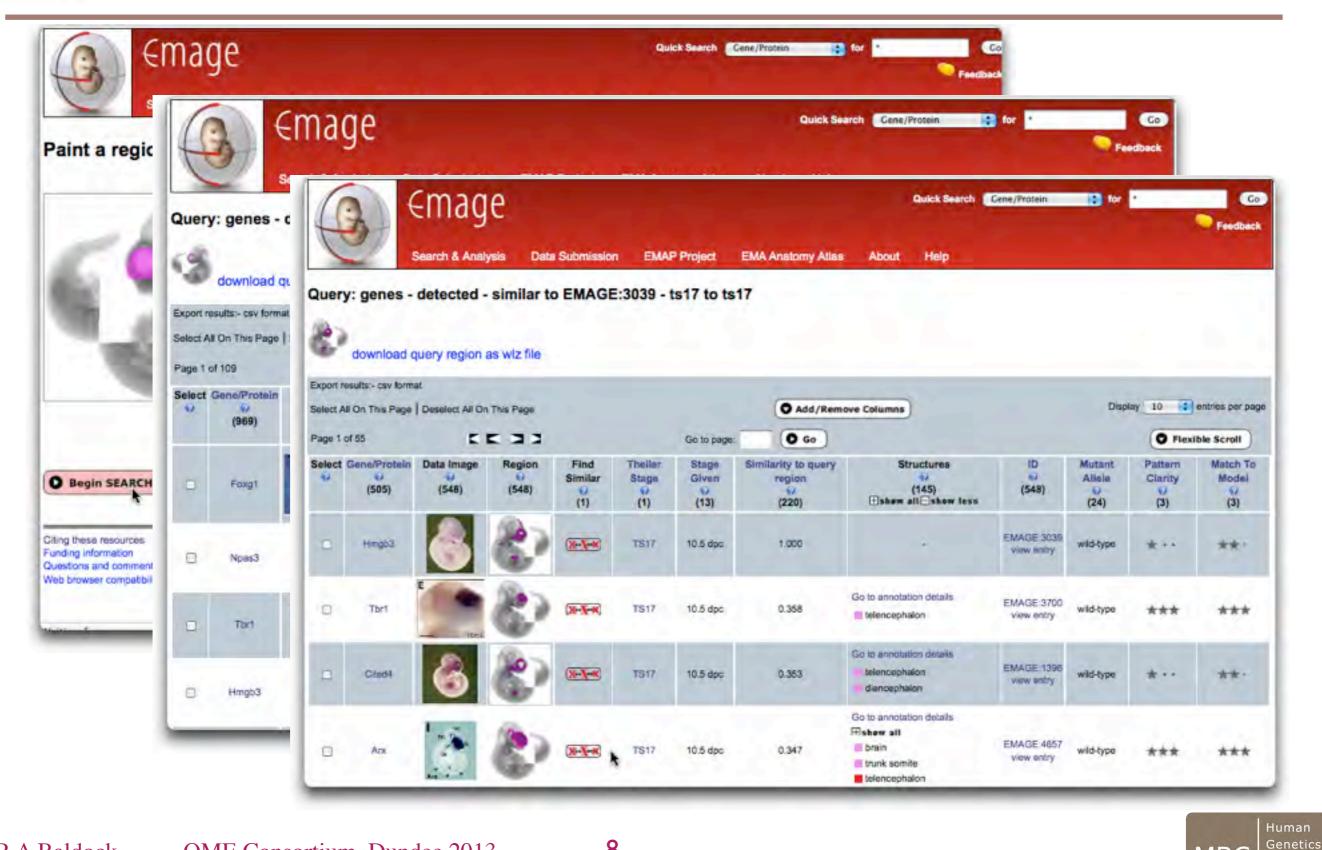
EMAGE Embryo Space

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EMAGE Embryo Space



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- 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

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Human

Unit

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Genetics

- interactive
- arbitrary complexity
- Automated fine tuning (ITK/ANTS)
- Editor review





3D Data Mapping - WlzWarp

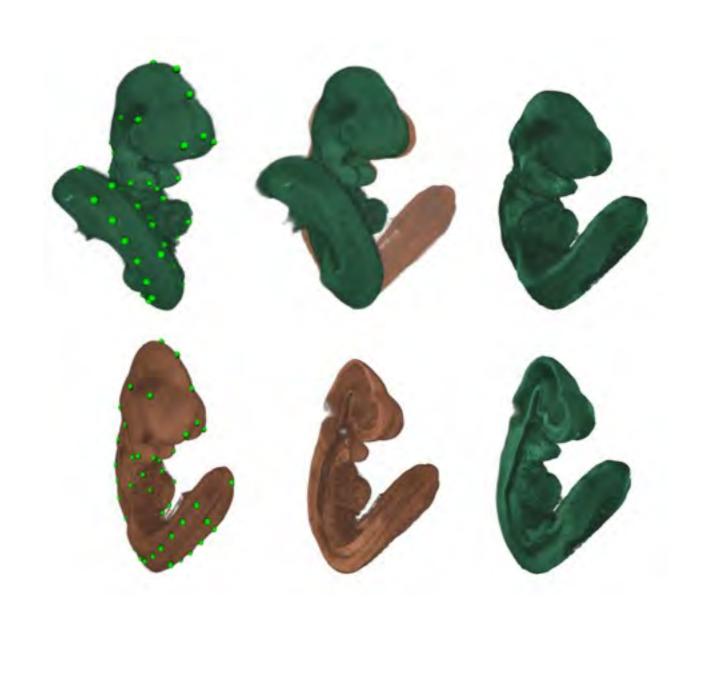


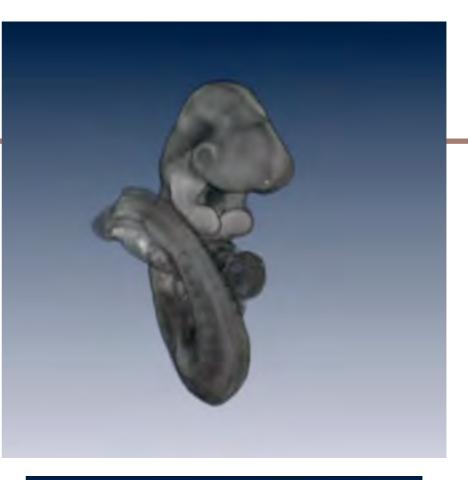






3D Data Mapping - WlzWarp



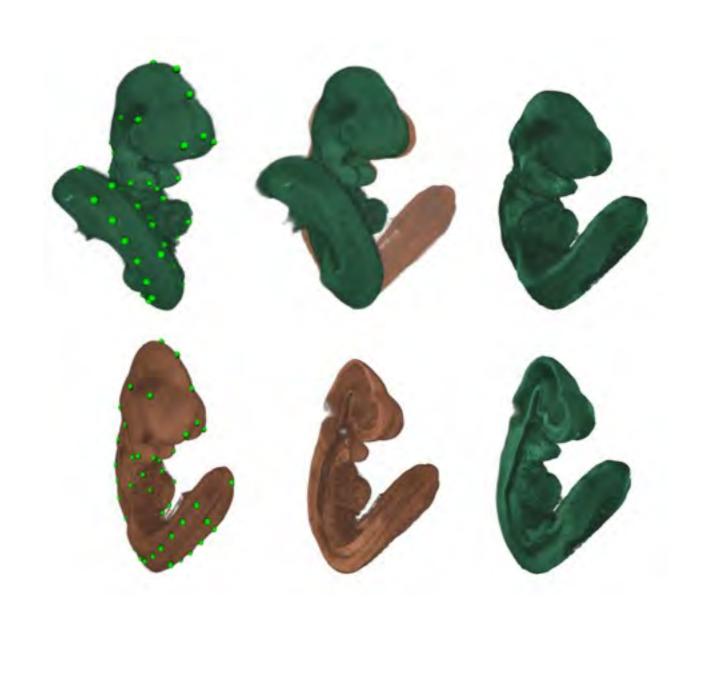


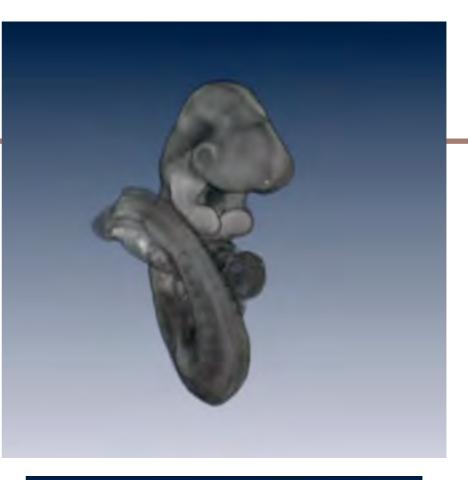






3D Data Mapping - WlzWarp











3D Mapping - Wnt signalling pathway

13

Wnt1	C.S	TS17	10.5dpc	3D View	EMAGE:6132
Wnt2	C.S.	TS17	10.5dpc	3D View	EMAGE:6134
Wnt3	6.0	TS17	10.5dpc	3D View	EMAGE:6138
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Wnt4	6.3	TS17	10.5dpc	3D View	EMAGE 6142
Wnt5A	6	TS17	10.5dpc	3D View	EMAGE.6144
Wnt6	6	TS17	10.5dpc	3D View	EMAGE:6148
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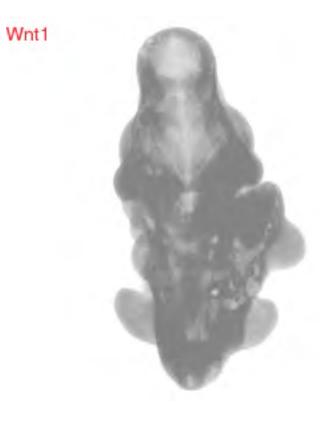


3D Mapping - Wnt signalling pathway

13

Wnt1	Ci.	TS17	10.5dpc	3D View	EMAGE:6132
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Wnt6	60	TS17	10.5dpc	3D View	EMAGE:6148
Wnt7A	C.	TS17	10.5dpc	3D View	EMAGE:6150







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3D Visualisation

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

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- Multi-layer
- Interactive overlays
- WebGL



Human

Unit

MRC

Genetics



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

- Embed woolz images
- Sparse reconstruction & mapping
- large image data
- Annotation overlay and visualisation
- 3D mapping e.g. OPT images
- Project image archiving EMAP, GUDMAP etc.

15

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 development at the MRC Edinburgh is intended to scan a conventional micro The high pixel data rate (8 MHz peak) easily saturates most computer config threshold, pixels (i.e. intervals') into a set of interval parameters. These intermicroprocessors to give object parameters from which the cells can then be The paper describes the hardware and software architecture, with commentu-The linkage procedure used to reconstitute contiguous object descriptions in the order of 1 ms.

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

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







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

Data structures for image processing in a C language and Unix environment $\stackrel{\star}{\sim}$

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.

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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.





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Abstract

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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.

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Af G.A. ! Pattern Reco ^aMR(Cytometry. 1994 May 1;16(1):7-16. Volume 3, Issi Rece Automatic fluorescence metaphase finder speeds translocation Data st scoring in FISH painted chromosomes. Abst and Un Piper J, Th Jim Piper^a a de MRC Hun Th ^aMRC Clinic Abstra thr Edinburgh E A fluore mi Received 14 a stand Th Th positive Abstract the A variety of The me support si prepara Keyw efficient ar chromo construct : metaph image pro cuboid volume = 14M Patte scores Volun were re Keywords: Ir domain volume = 5M 1980 similar image proce cells an ☆ This work spent s factor of metaph addition assiste and that





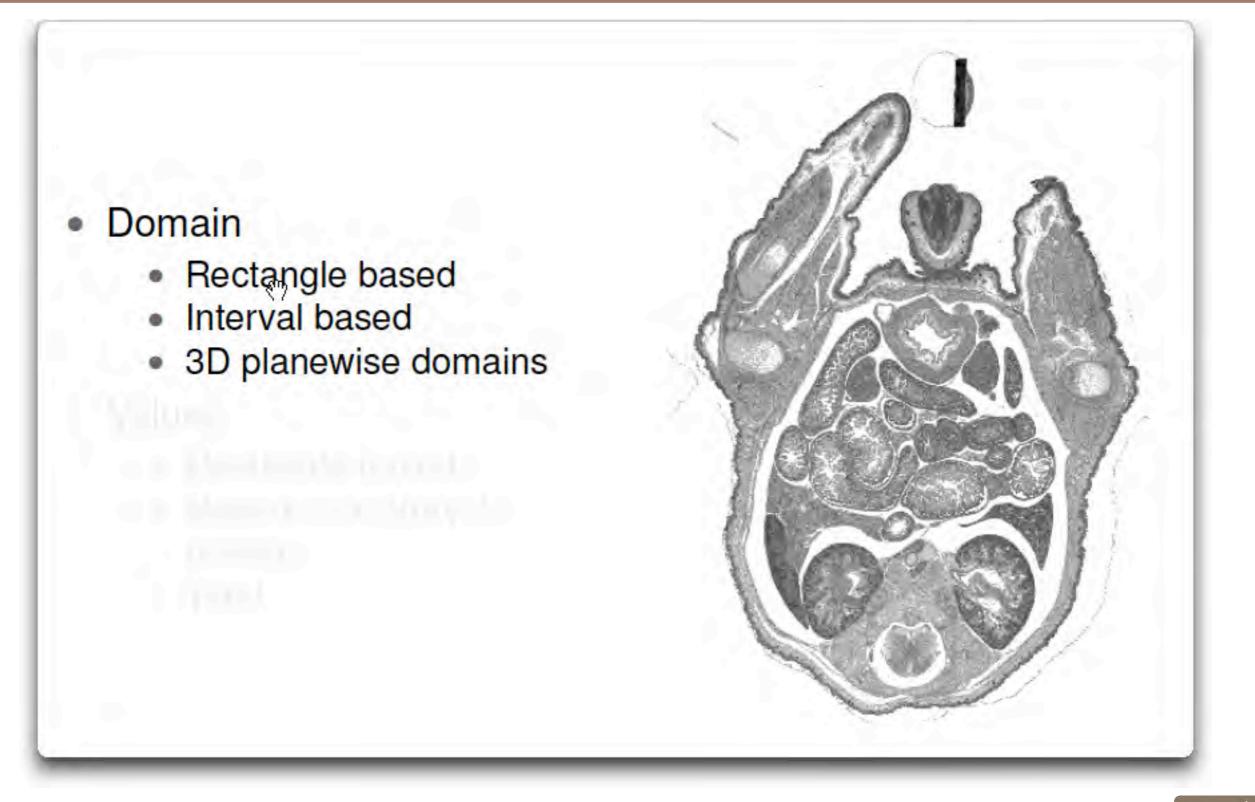


Af G.A. ! ^aMR(Pattern Reco Cytometry, 1994 May 1;16(1):7-16. Volume 3, Issi Rece Automatic fluorescence metaphase finder speeds translocation Data st scoring in FISH painted chromosomes. Abst and Un Piper J, Th Jim Piper^a a de MRC Hun Th ^aMRC Clinic Abstra thr Edinburgh E A fluore mi Received 14 a stand Th Th positive Abstract the The me A variety of prepara support si Keyw 330K lines Ansi C code efficient ar chromo construct : metaph image pro Patte scores Volun were re Keywords: Ir 184K lines application code 1980 similar image proce cells an ☆ This work spent s factor of metaph addition assiste and that Human 16 Genetics OME Consortium, Dundee 2013 **R** A Baldock

MRC



Woolz Images

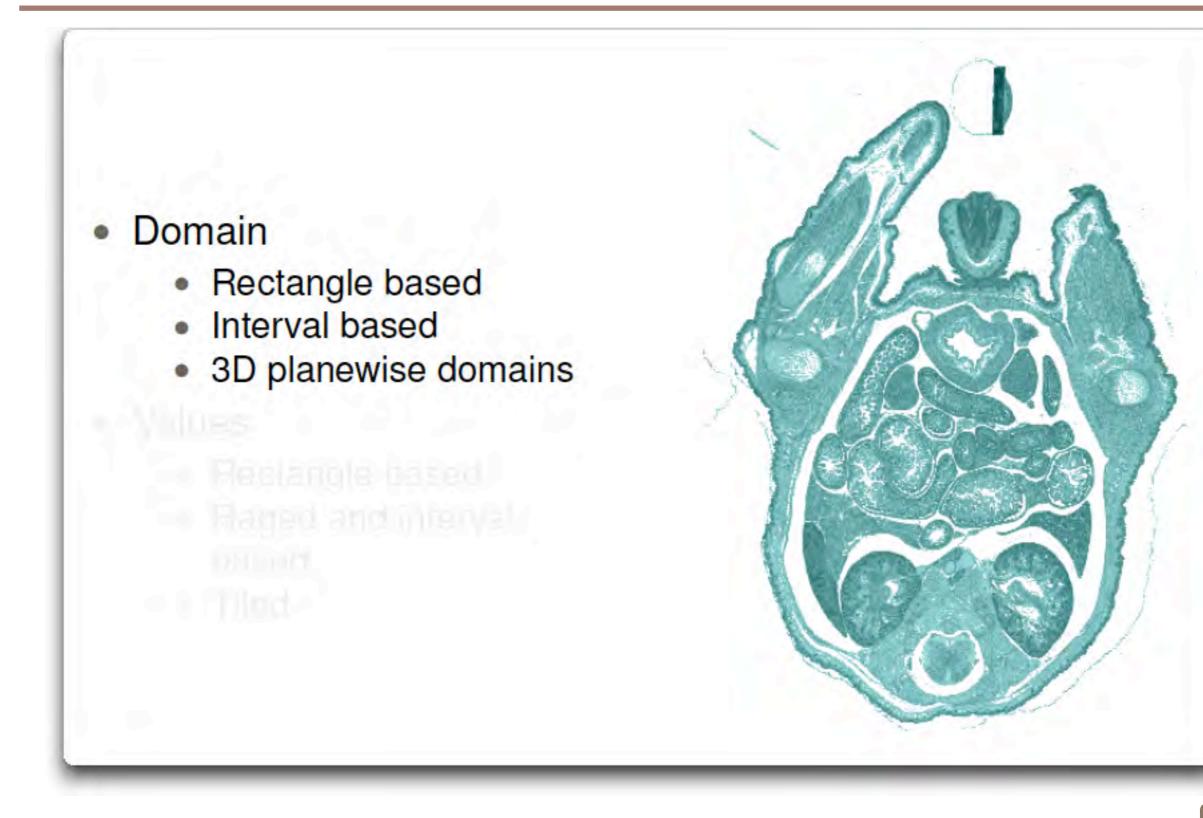








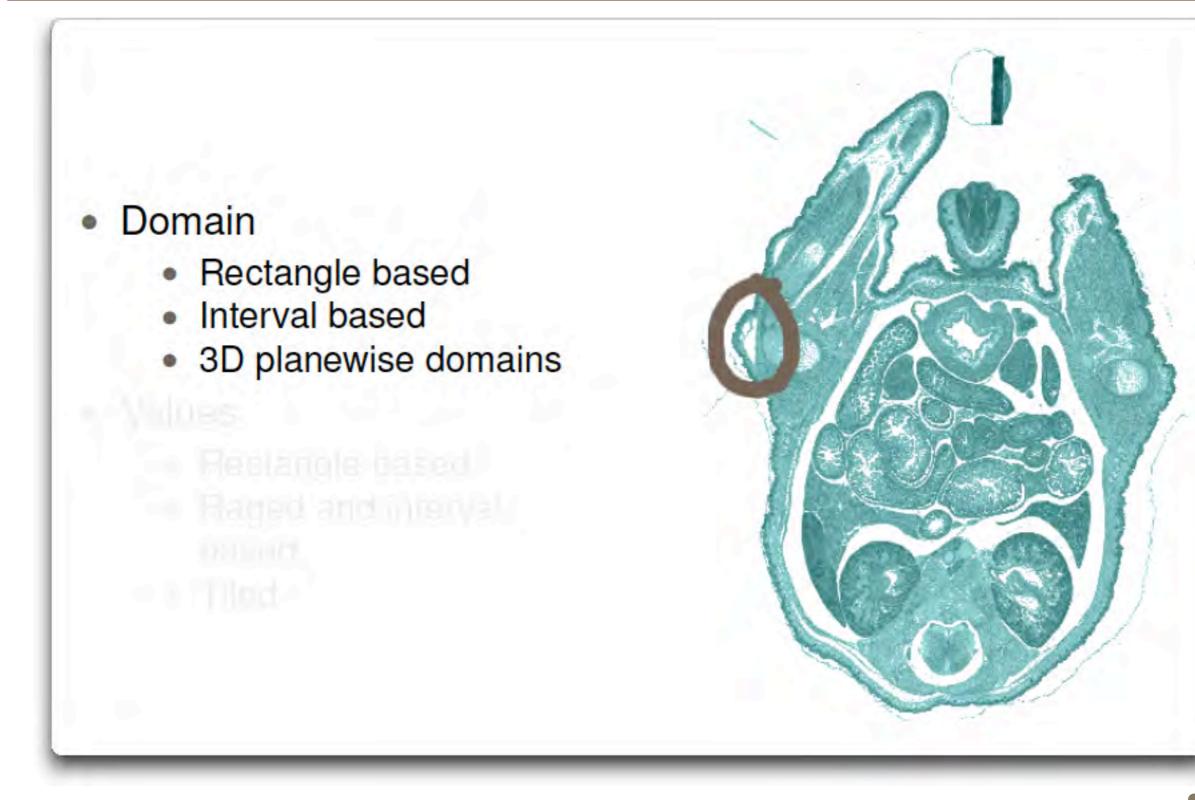
Woolz Images





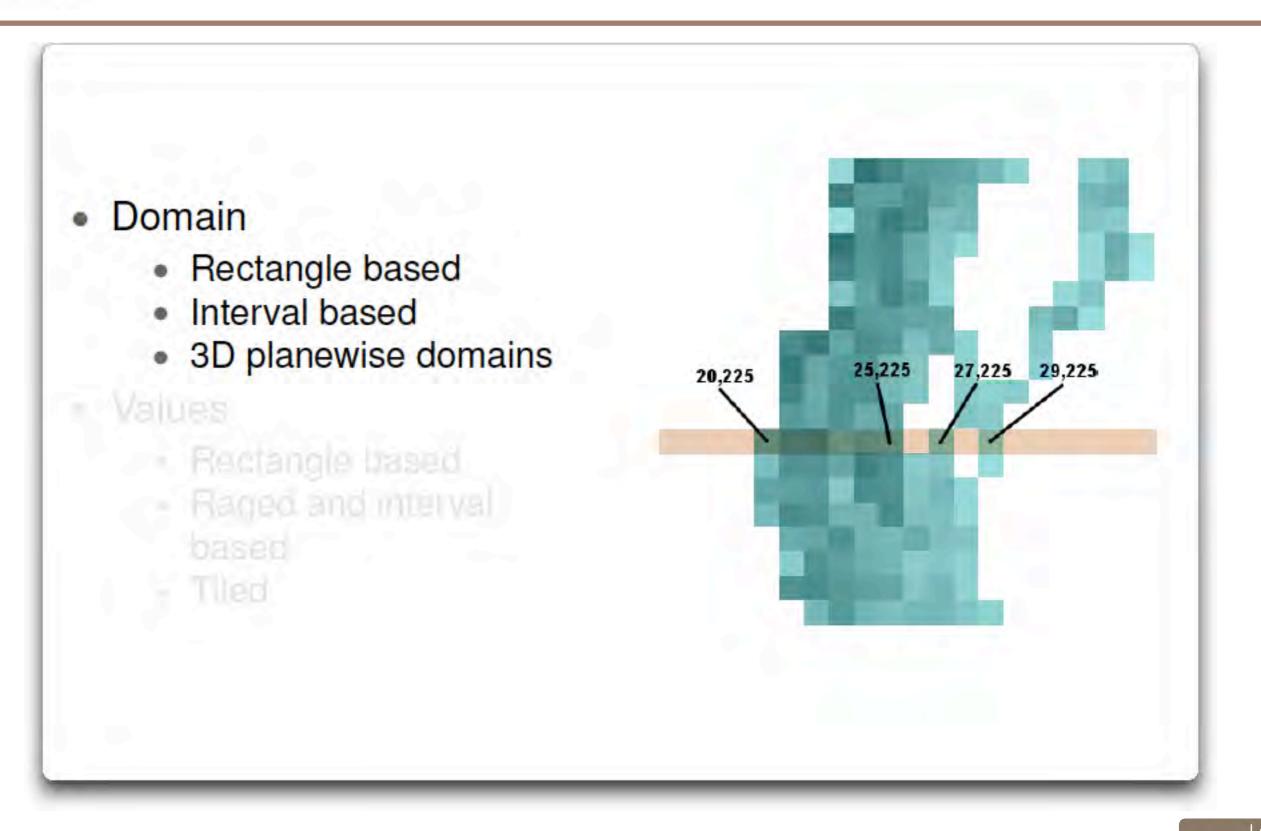


Woolz Images







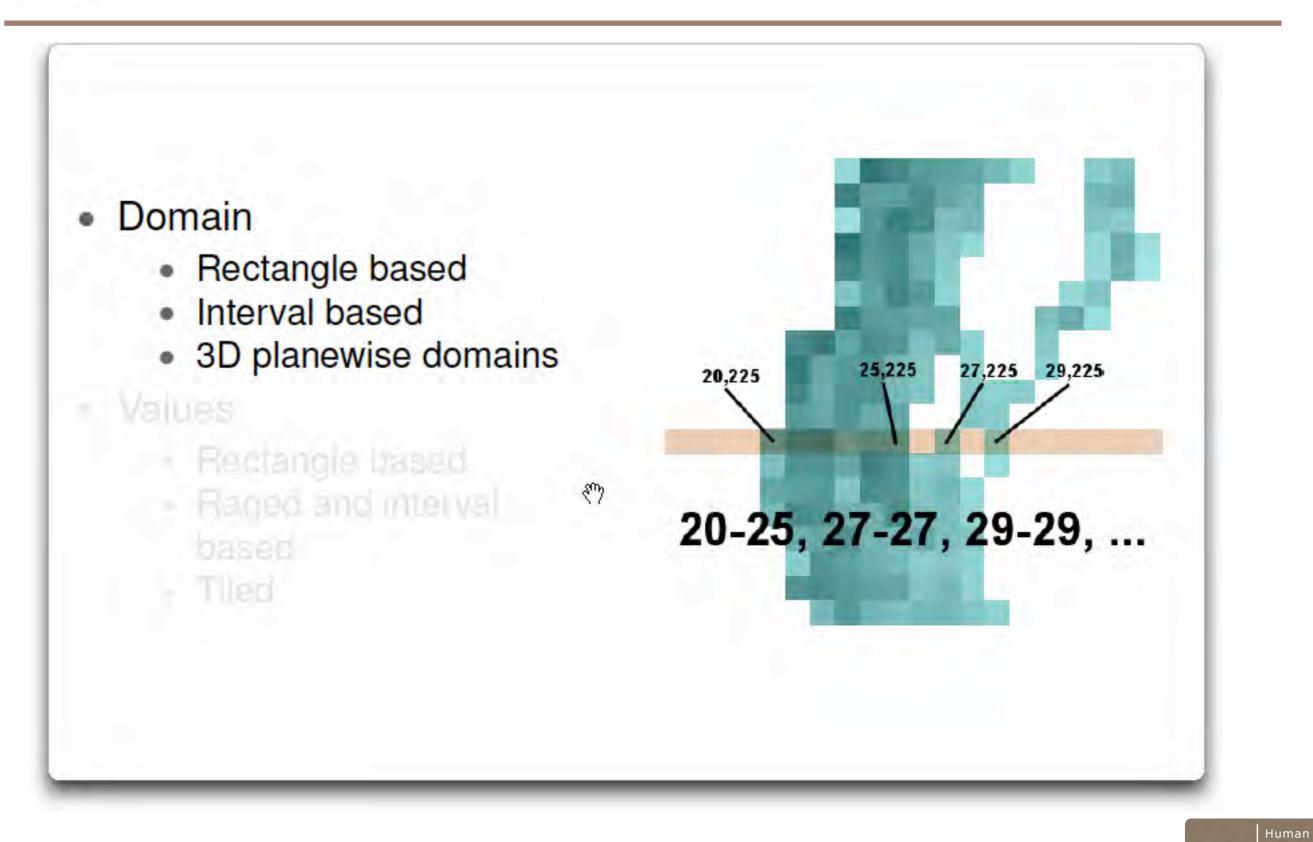


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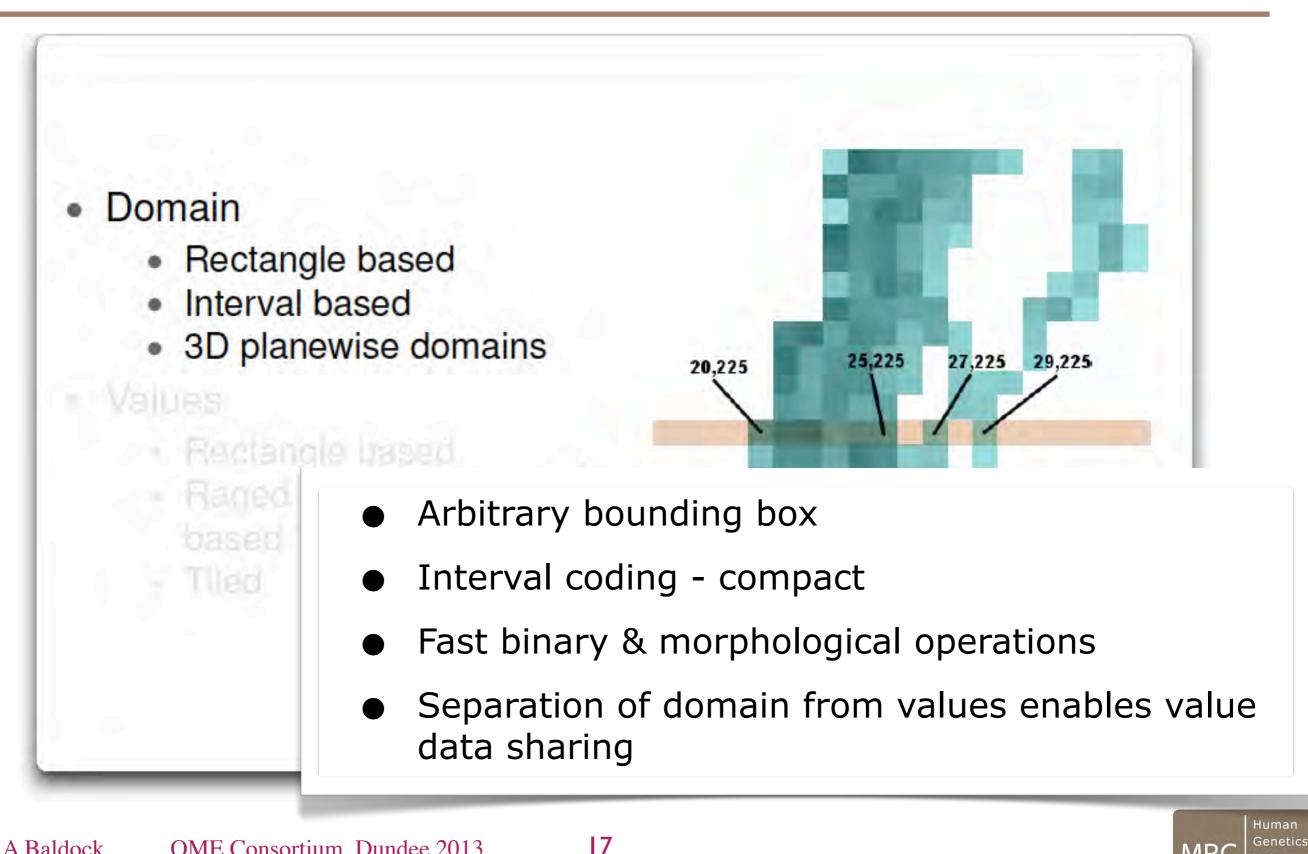
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Genetics

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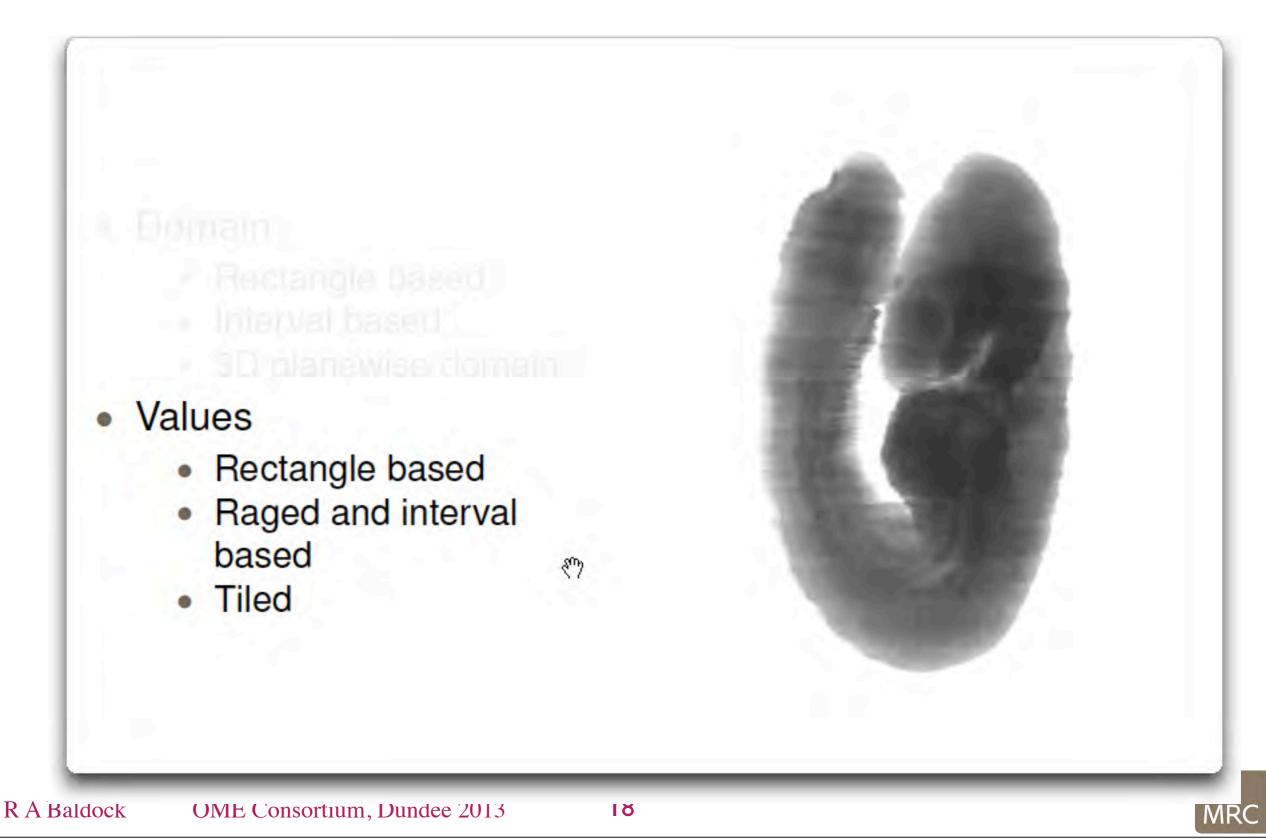




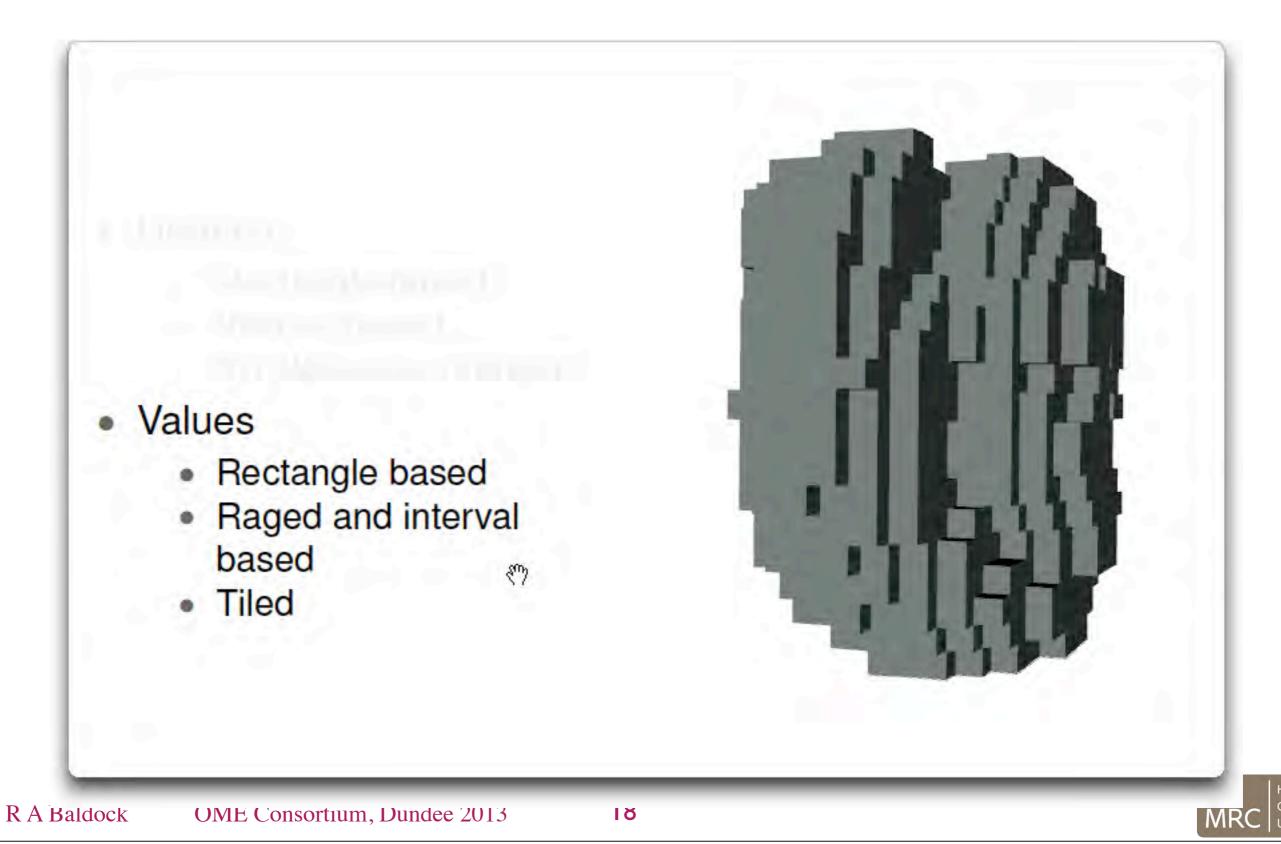


MRC

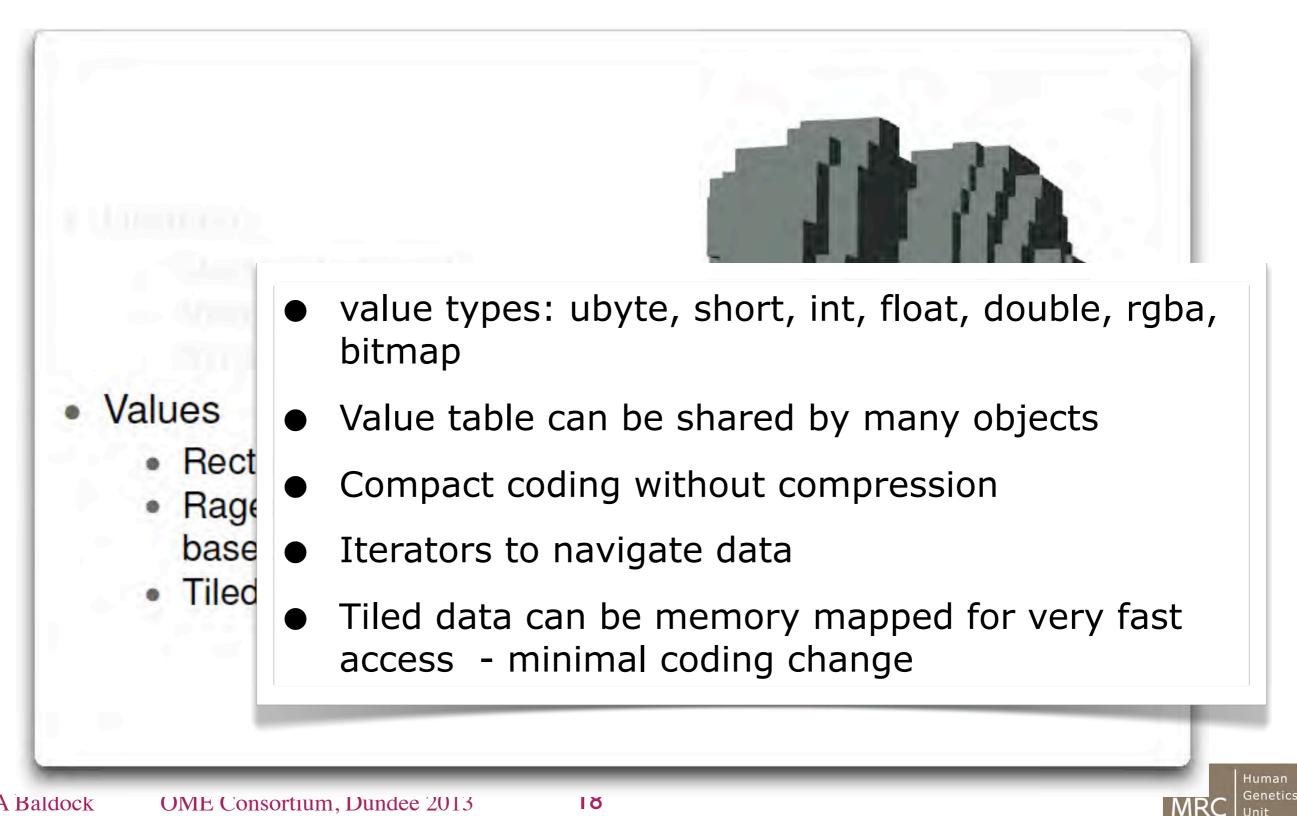












R A Baldock



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





- Polylines, boundary lists
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+ + +	$\begin{bmatrix} 2 & t_{03} \\ 2 & t_{13} \end{bmatrix}$
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} t_{23} \\ t_{33} \end{array}$
0 0	t_{33})
	-00 /





- Polylines, boundary lists
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 - conforming mesh

$$\Delta u = u - x$$

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

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

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

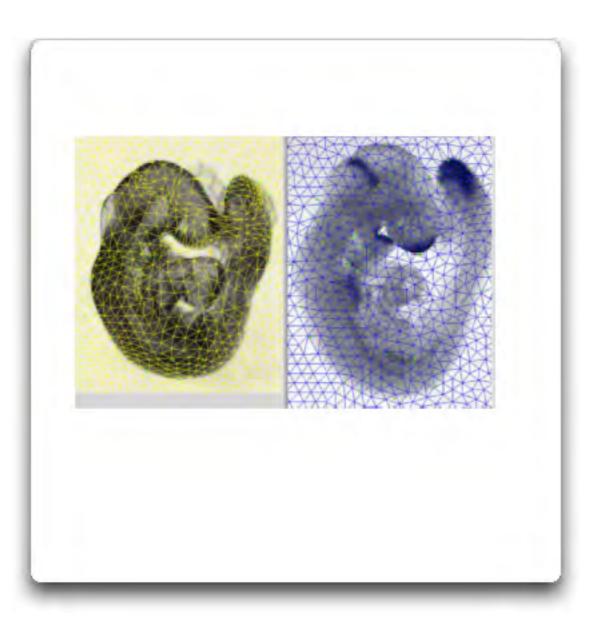
$$b_{IMQ}(r) = \frac{1}{\sqrt{r^2 + \delta^2}}$$





Woolz image objects

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

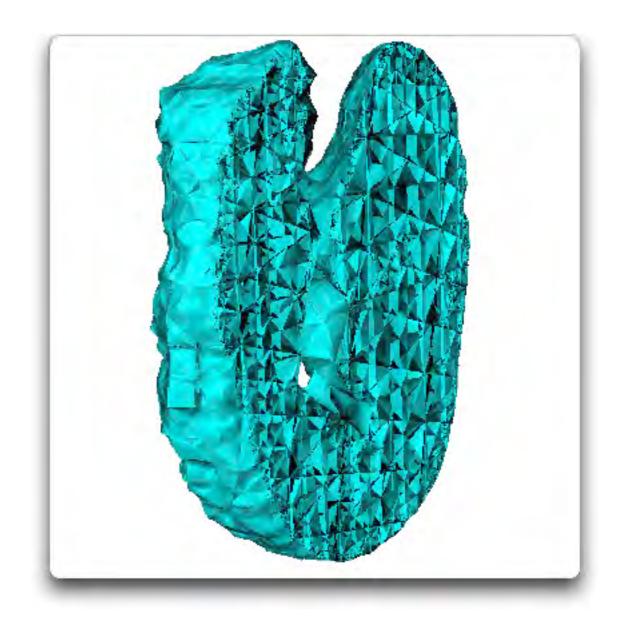






Woolz image objects

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







Woolz image objects

- Review of OME image structures
- Woolz to GitHub
- JavaWlz re-instated
- Incorporation into ImageJ (Fiji)
- Issue of expressivity arbitrary spatial domain location and offsets

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Human

Unit

MR

Genetics

• to be continued....







- 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.





Human

Unit

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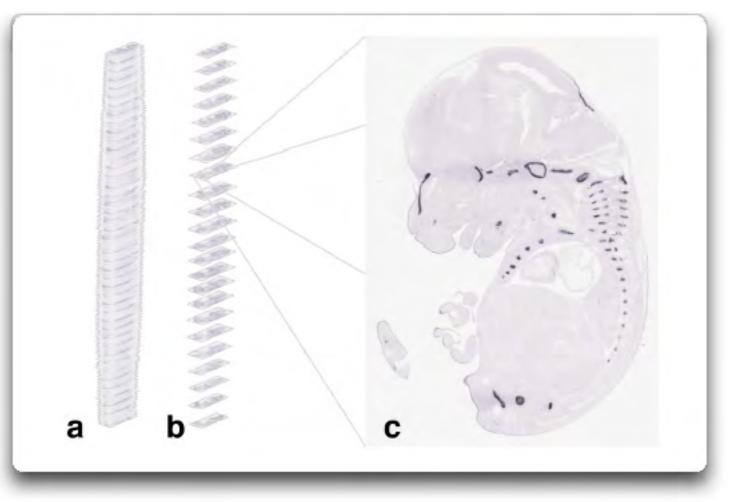
Genetics

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





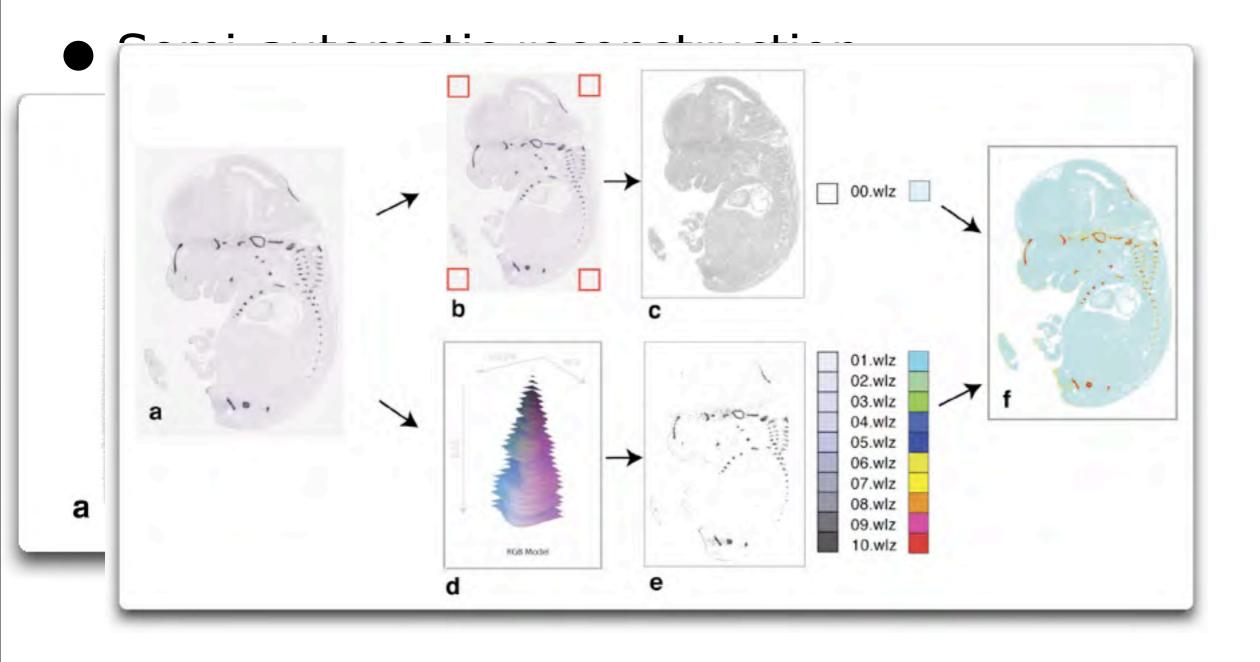
Semi-automatic reconstruction







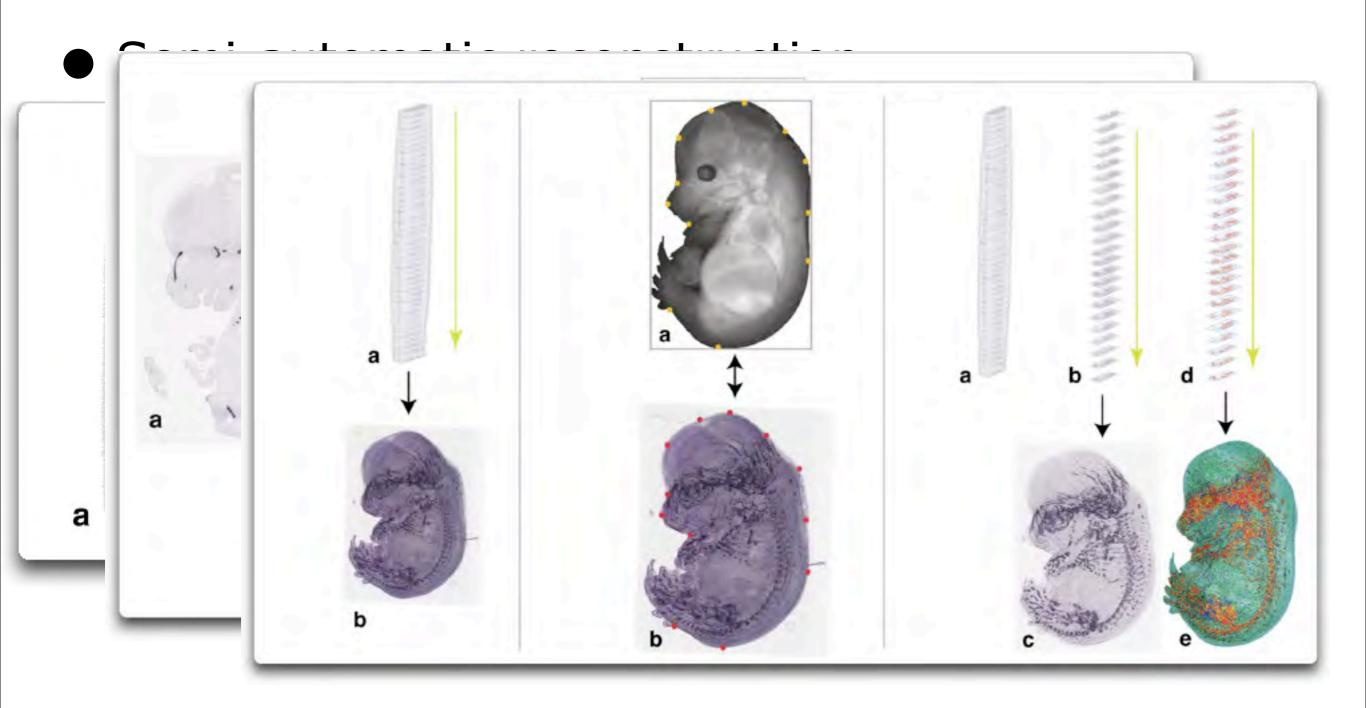
Pseudo Wholemount Mapping to Emap - done







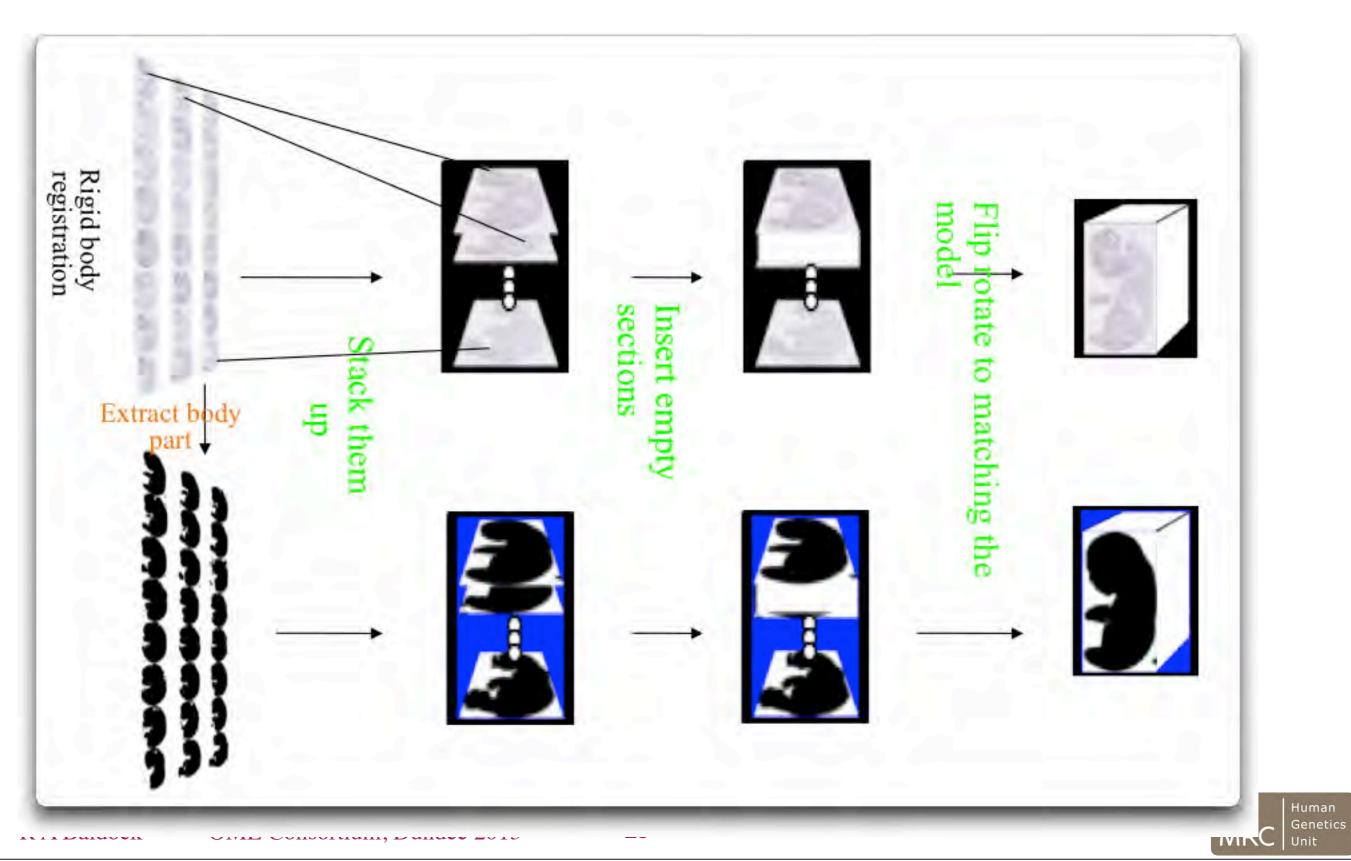
Pseudo Wholemount Mapping to Emap - done











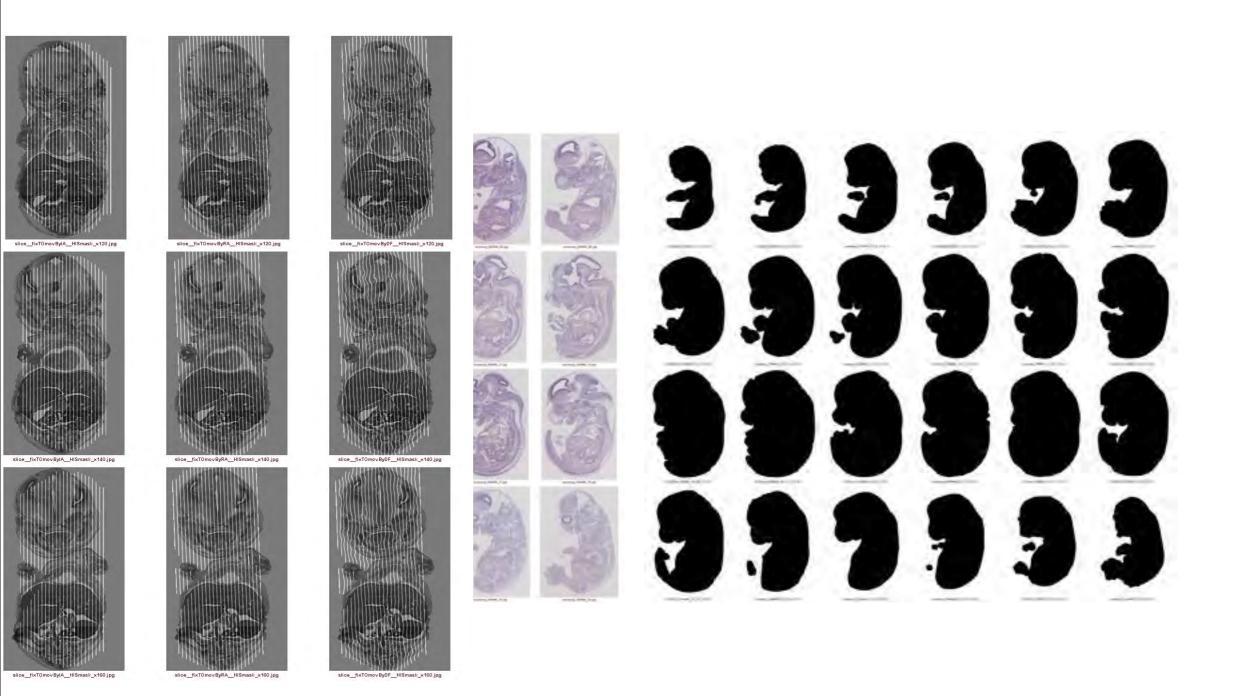




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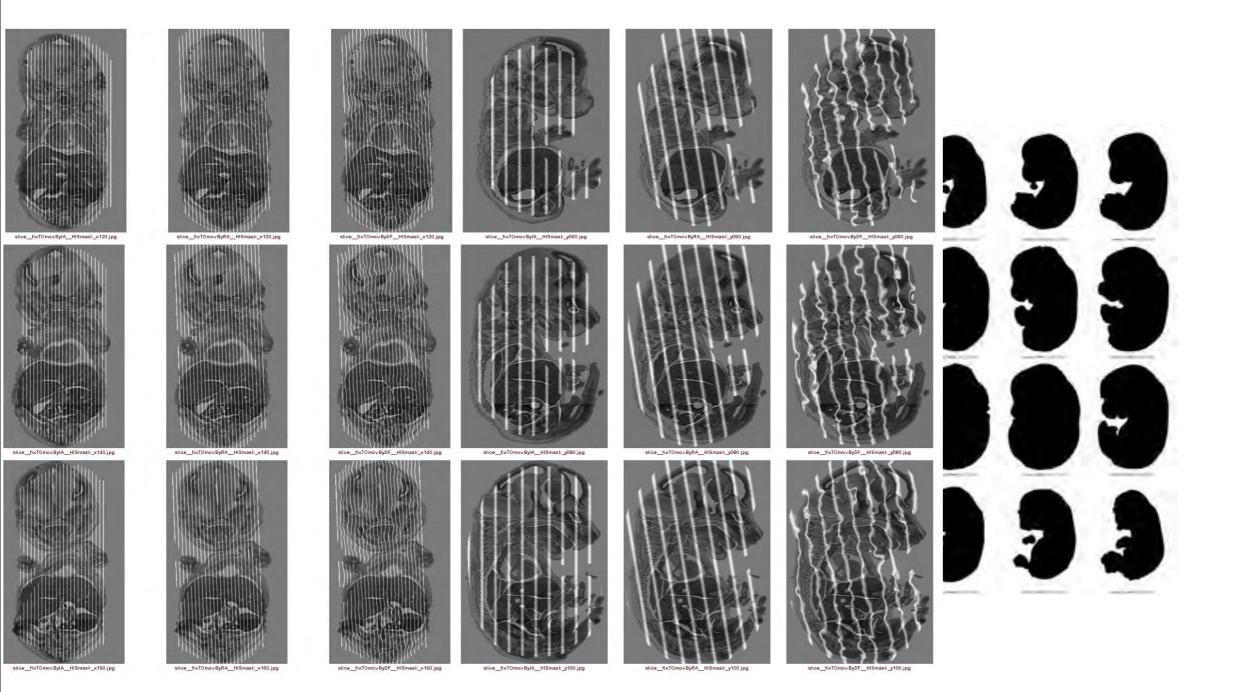


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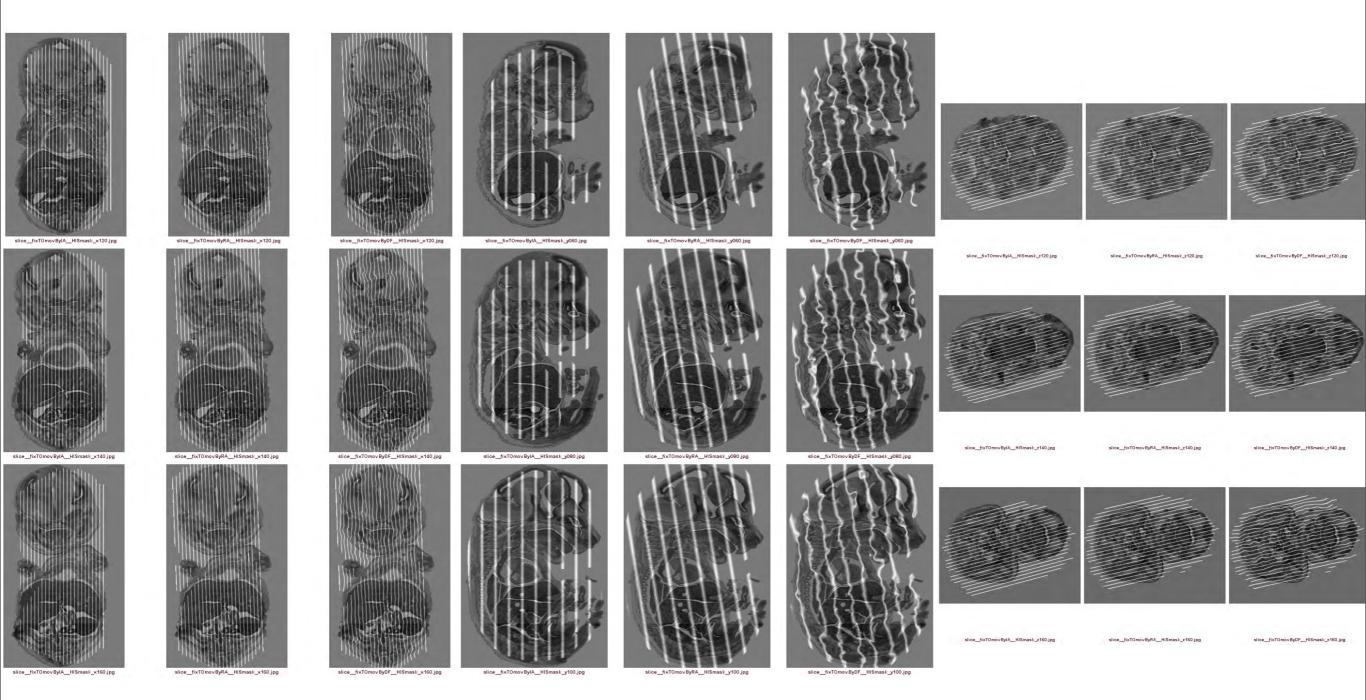




23







23



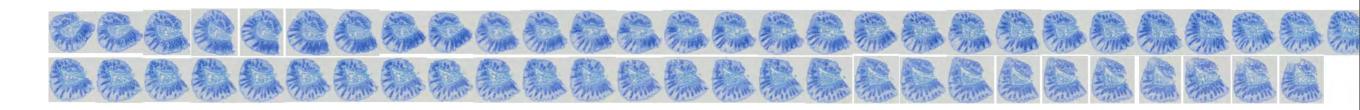


- Typical task:
 - > 2D high-res (.3 micron) histology
 - serial sections (1-2 micron)
 - > 3D image for tissue module geometry and stats
 - reconstruction using non-linear registration
 - "user-friendly" i.e. no developer intervention





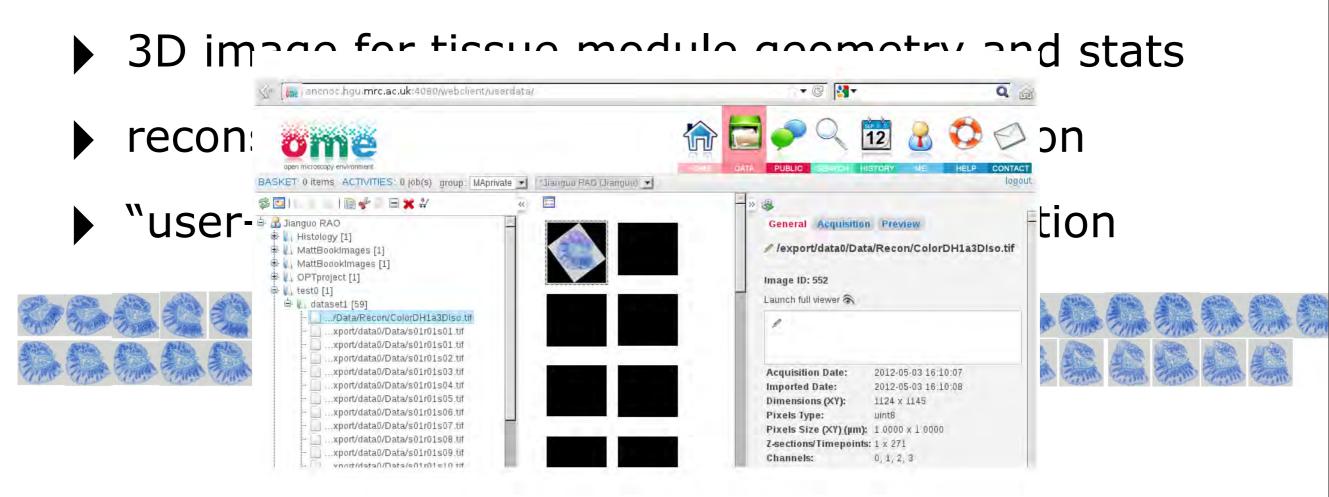
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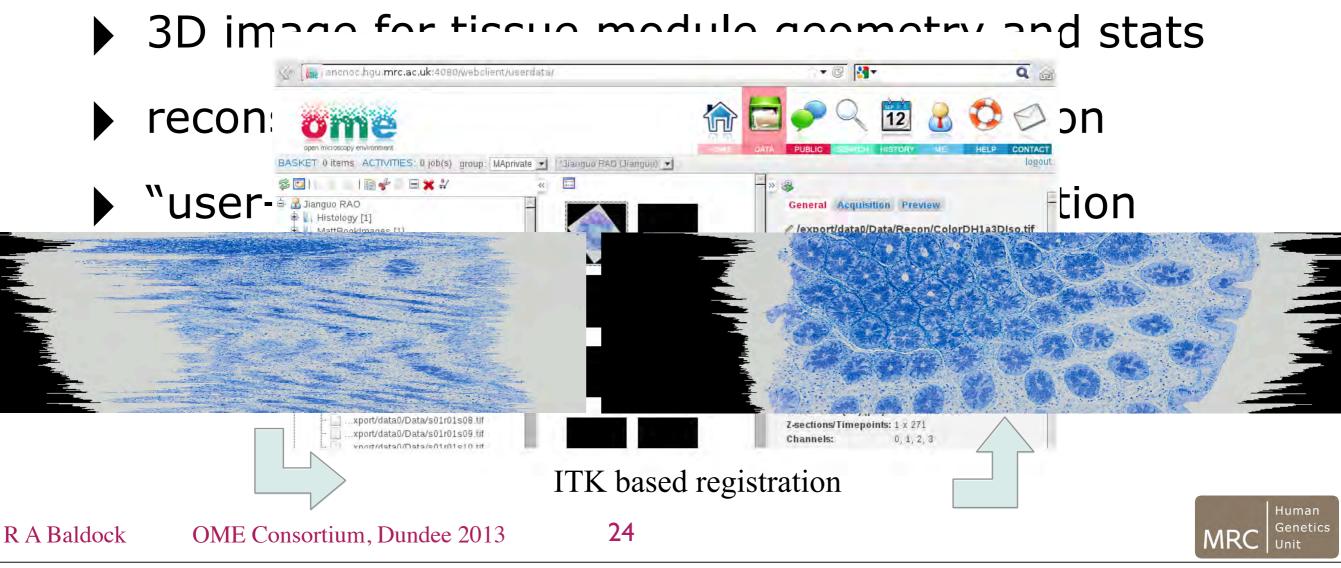


- Typical task:
 - > 2D high-res (.3 micron) histology
 - serial sections (1-2 micron)



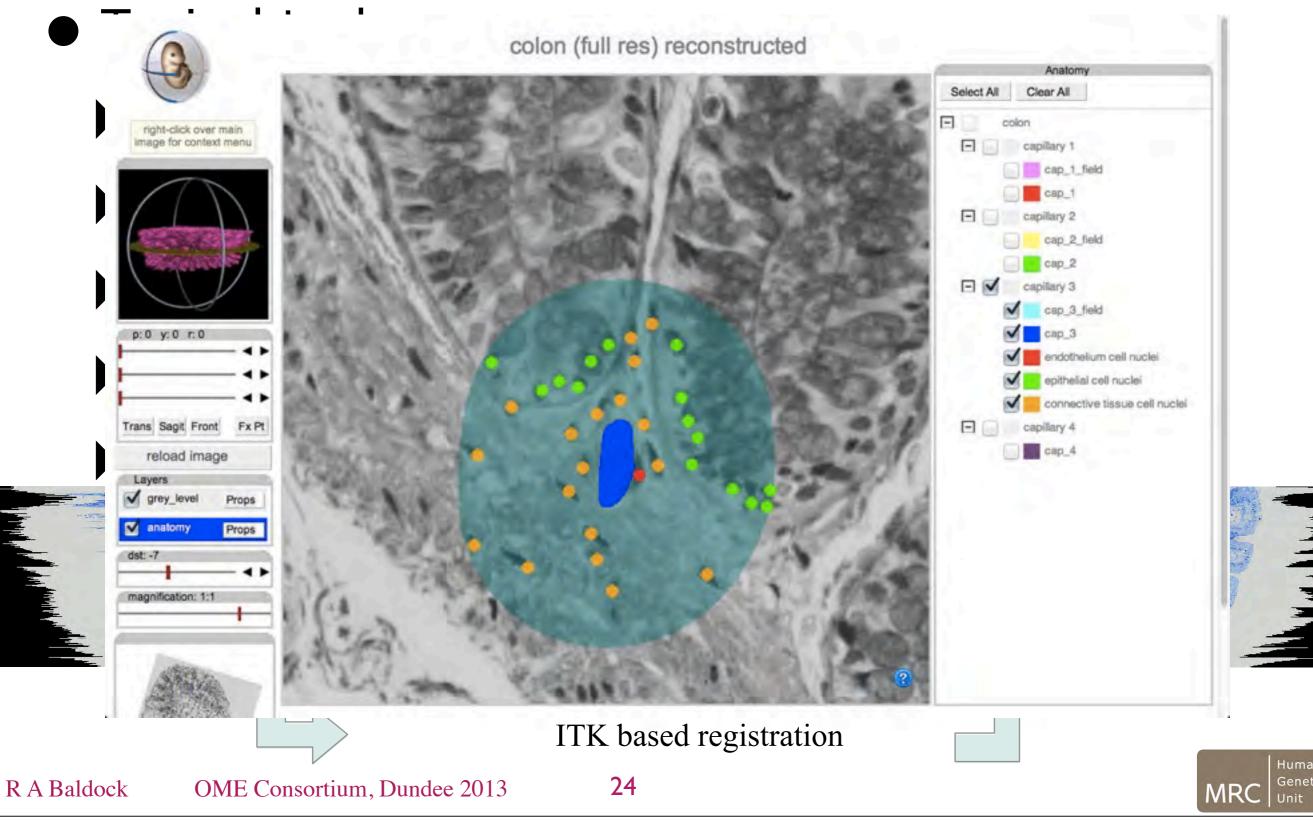


- Typical task:
 - 2D high-res (.3 micron) histology
 - serial sections (1-2 micron)





Serial Section Reconstruction





Large Image Data

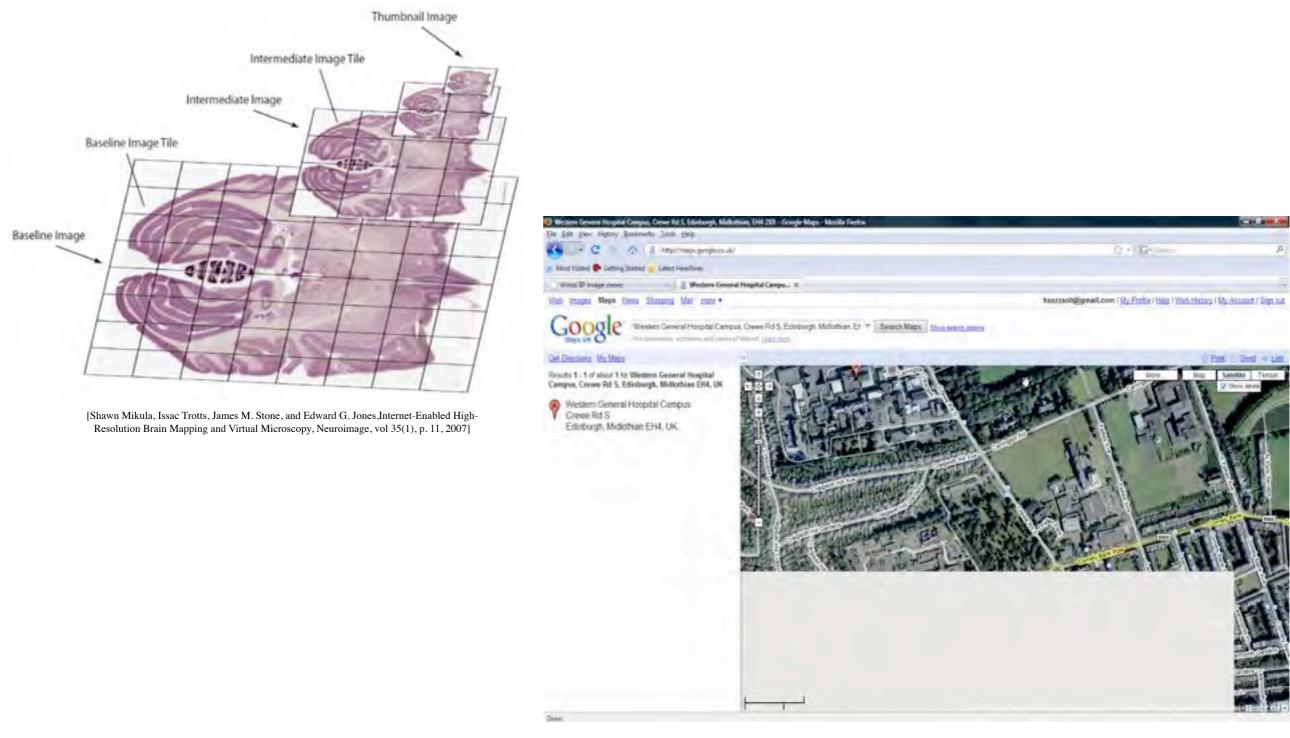
- Single light microscopy reconstructions already 30+GB, microCT sets ~200GB
- New EM embryo data ~0.5TB
- OPT data small (200MB) but many 5K
- Typical requirement to browse as sections
- Require arbitrary angle re-sectioning

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





Tiled Image Servers



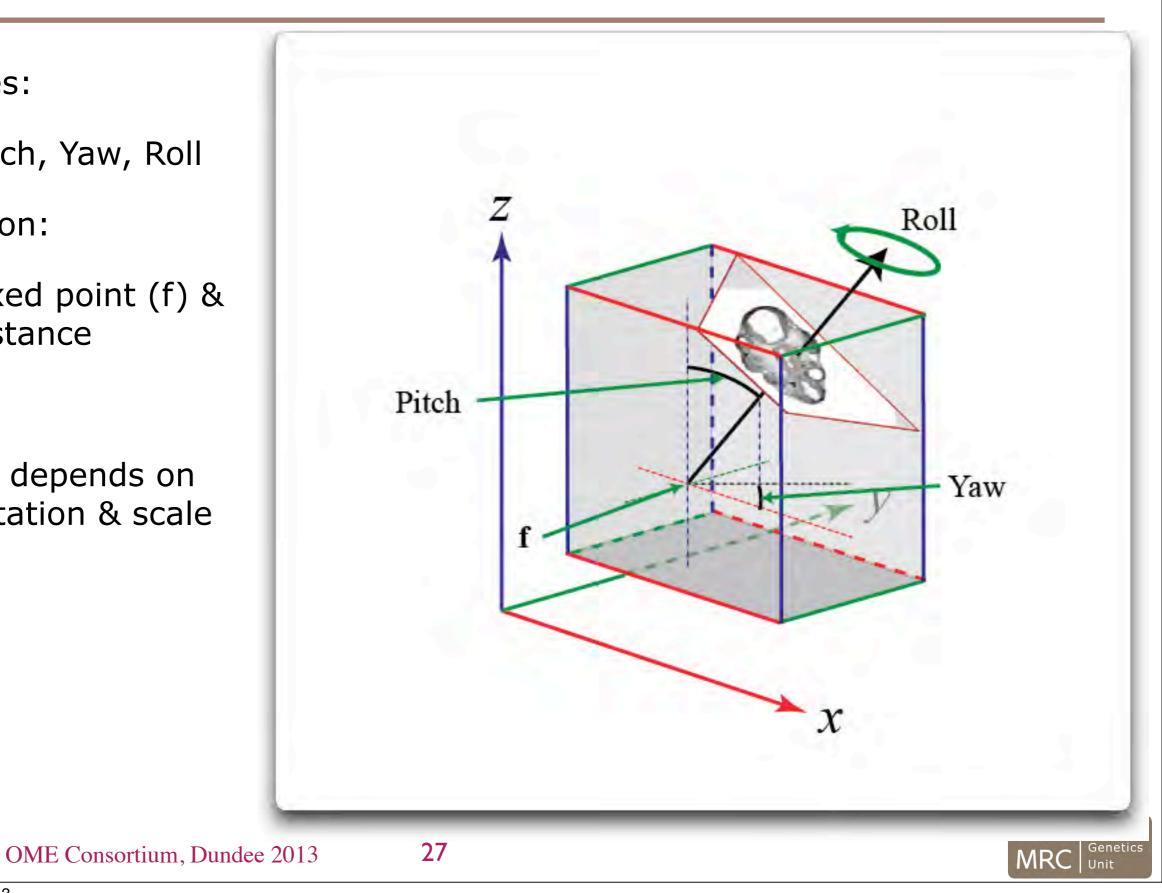
[maps.google.com]





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- 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- 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

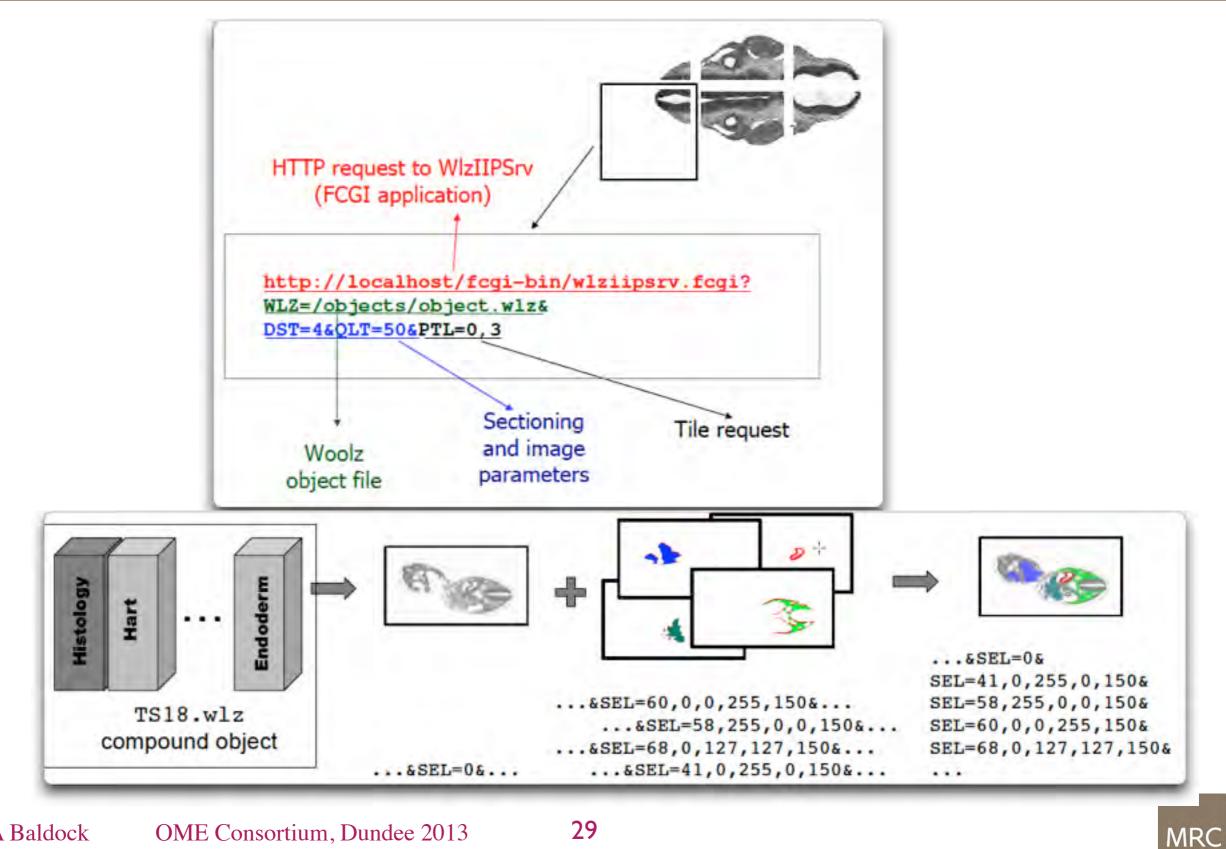
Table 2: Extended object overview

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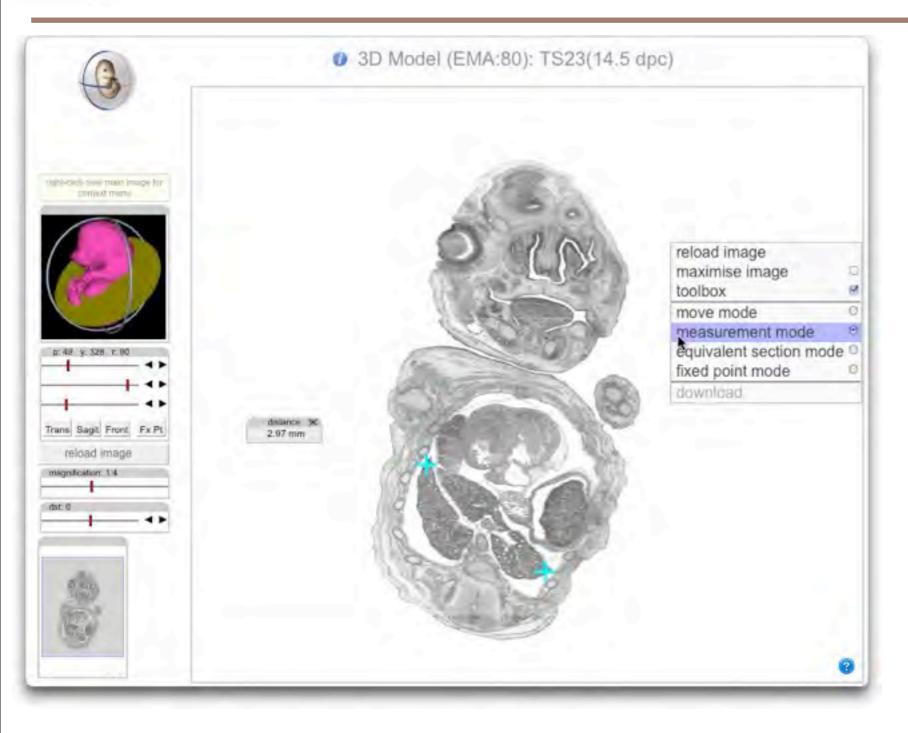
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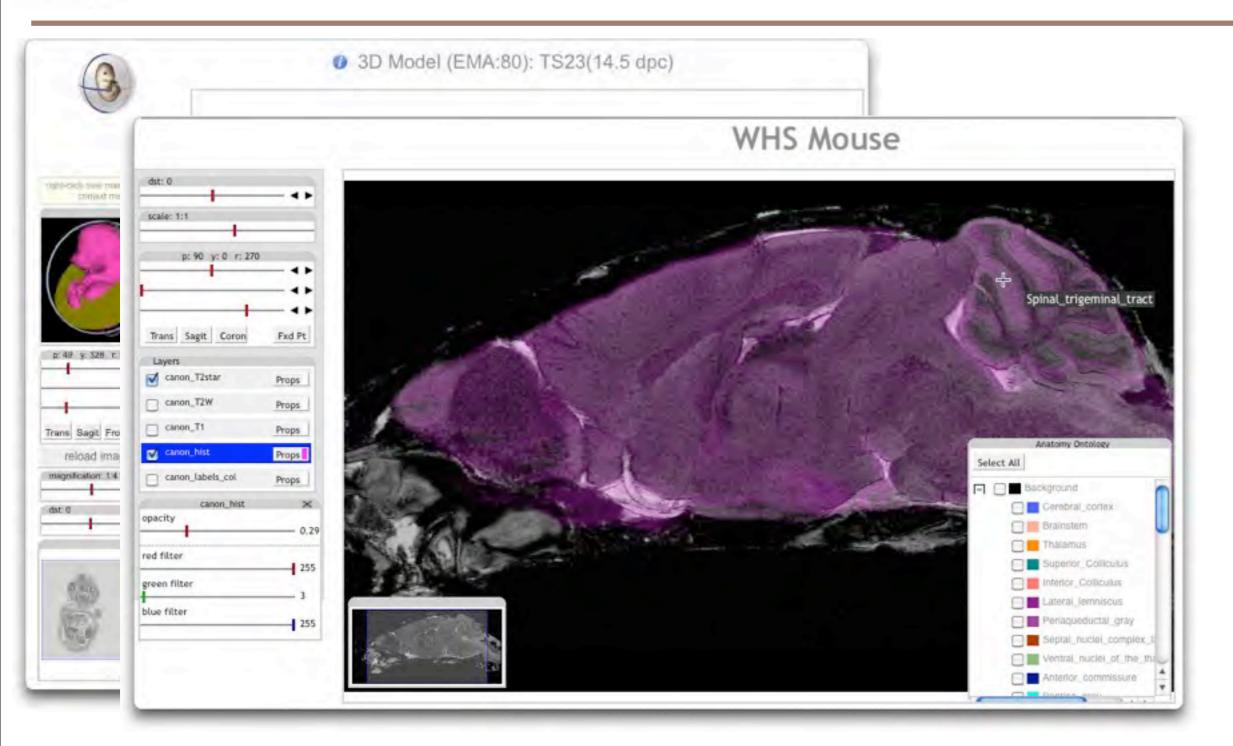




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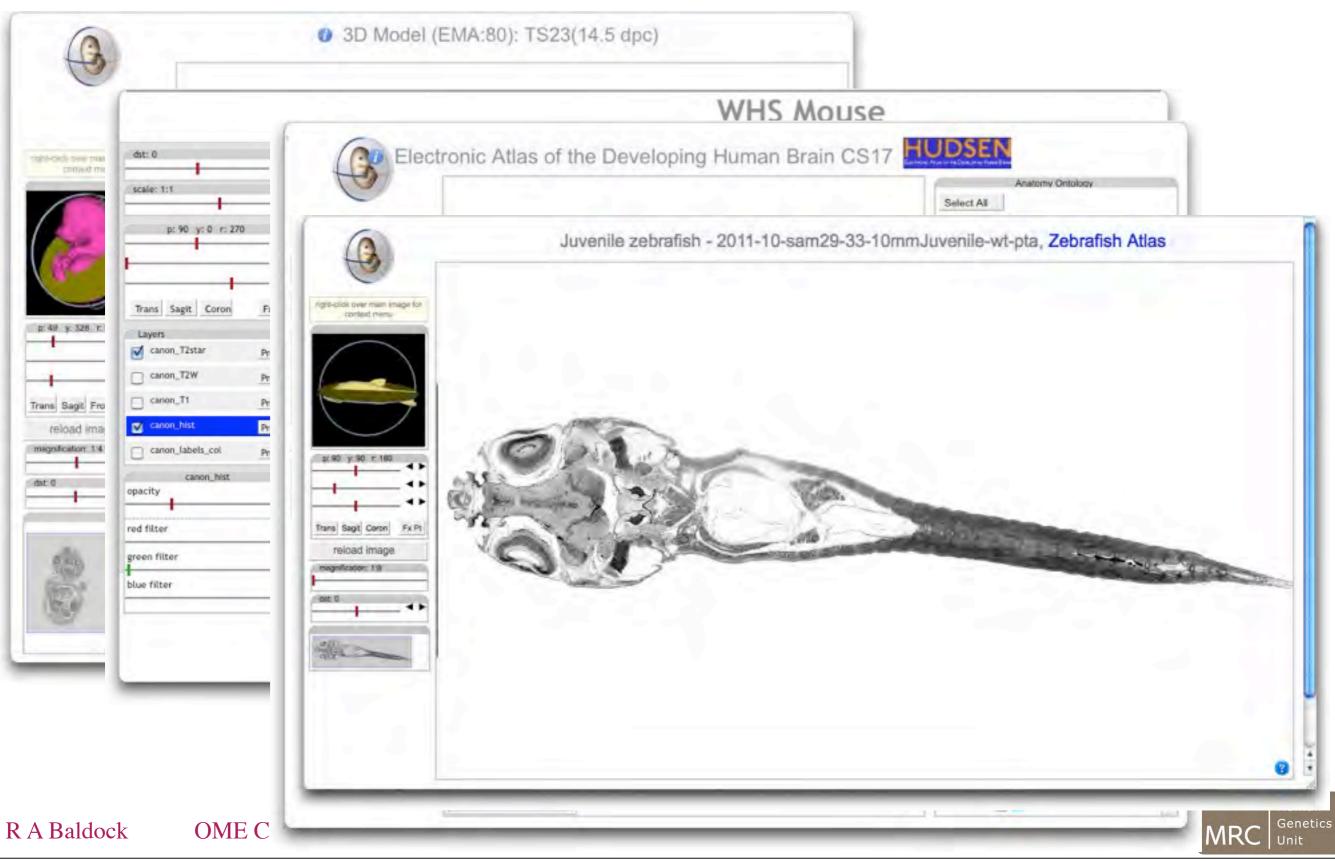






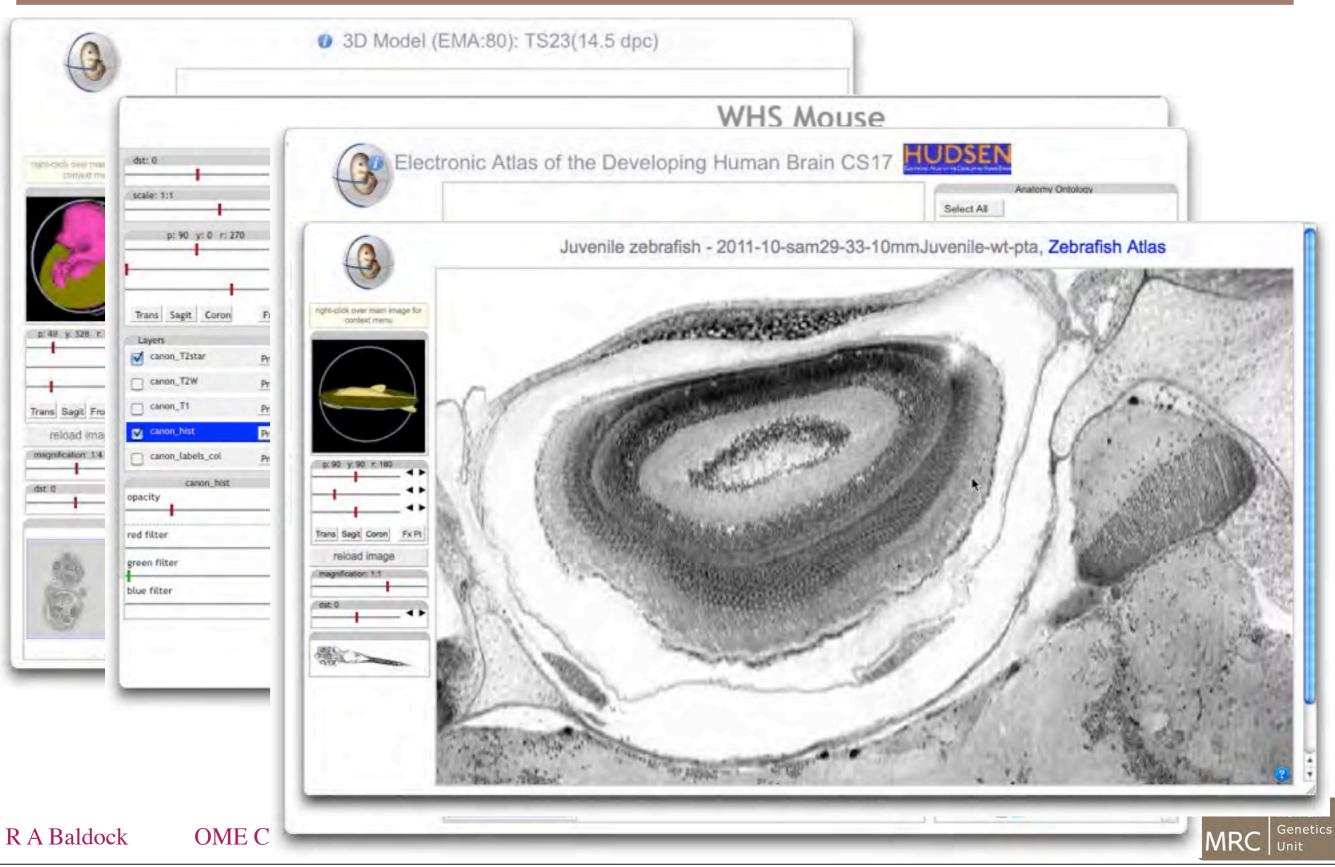








IIP3D Examples



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Operator	Description
diff(exp,exp)	The difference between the two given domains.
dilation (exp, radius)	The dilation of the domain by <i>radius</i> 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 sat-
	isfy 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 1	:=	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.

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MAP Purpose	The difference between the two given domains voxels. Defines a colour or grey value mapping. Grey values outside the mapped region are clamped to the minimum and maximum output colour componentor grey values. There may be 1,2,3 or 4 mapping specifications given; with a single mapping specification meaning a grey value mapping, two specifications a grey with alpha mapping, three an RGB mapping and
MAP Purpose	Defines a colour or grey value mapping. Grey values outside the mapped region are clamped to the minimum and maximum output colour componentor grey values. There may be 1,2,3 of 4 mapping specifications given; with a single mapping specification meaning a grey value mapping, two specifications a grey with
Syntax Input Param- eters	four an RGB α mapping. MAP=mspec[,mspec[,mspec[,mspec]]] where mspec=t, 11, 1u, 01, ou, p0, p1 t \in IDENTITY / LINEAR / GAMMA / SIGMOID The mapping function FLOAT 11 Input lower grey value FLOAT 11 Input upper grey value FLOAT 01 Output lower colour component or grey value FLOAT 01 Output upper colour component or grey value FLOAT 01 Output upper colour component or grey value FLOAT p0 Gamma (γ)or first sigmoid parameter (μ) FLOAT p1 Second sigmoid parameter (σ)
Response Example	none \Rightarrow MAP=LINEAR,0,4095,0,255 Input grey values in the range 0-4095 are mapped to output values with the range 0- 255 IDENTITY
	Response

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SEL=0&MAP=LINEAR,0,255,255,0&QLT=50&CVT=jpeg

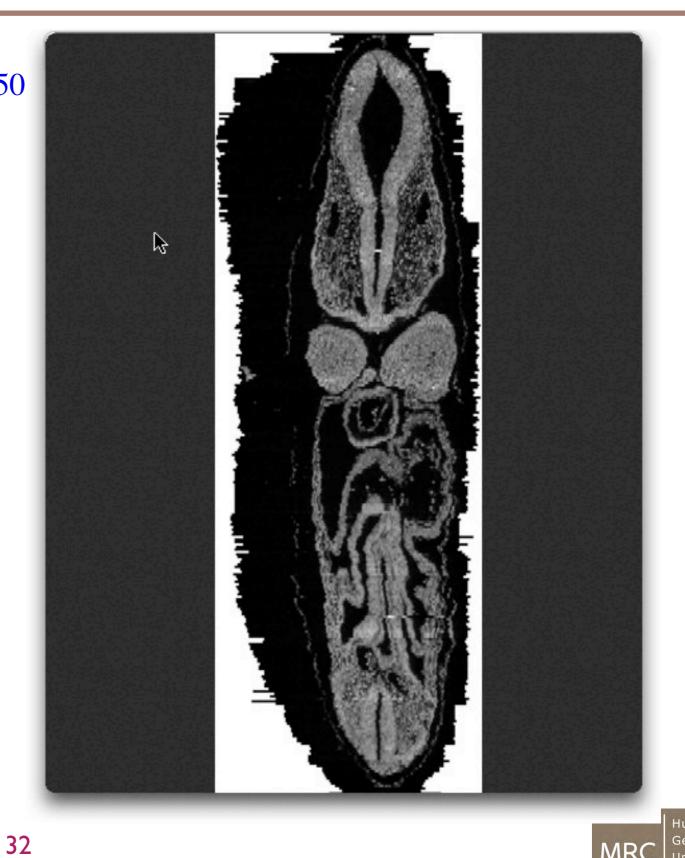
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SEL=0&MAP=LINEAR,0,255,255,0&QLT=50



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SEL=0&MAP=LINEAR,0,255,255,0&QLT=50&CVT=jpeg

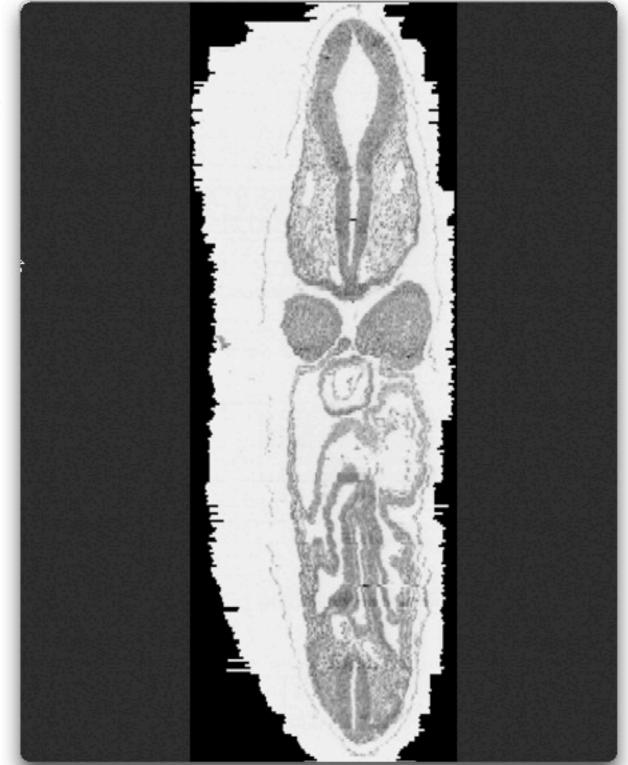
SEL=0&MAP=LINEAR,0,4096,0,255&QLT=50&CVT=jpeg











SEL=0&MAP=LINEAR,0,255,255,0&QLT=50 SEL=0&MAP=LINEAR,0,4096,0,255&QLT=5

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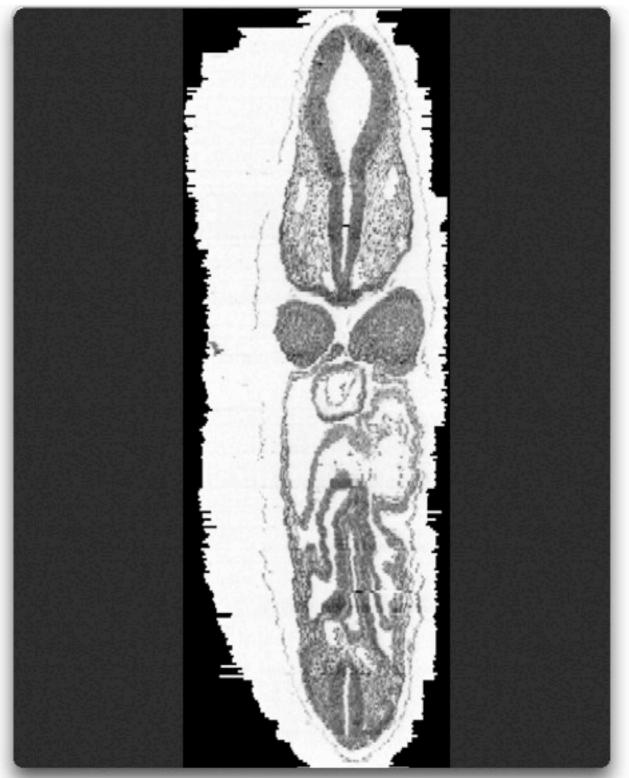
SEL=0&MAP=LINEAR,0,255,255,0&QLT=50&CVT=jpeg SEL=0&MAP=LINEAR,0,4096,0,255&QLT=50&CVT=jpeg

SEL=0&MAP=GAMMA,0,255,0,255,1.6&QLT=50&CVT=jpeg









SEL=0&MAP=LINEAR,0,255,255,0&QLT=50 SEL=0&MAP=LINEAR,0,4096,0,255&QLT=5 SEL=0&MAP=GAMMA,0,255,0,255,1.6&QLT







SEL=0&MAP=LINEAR,0,255,255,0&QLT=50&CVT=jpeg

- SEL=0&MAP=LINEAR,0,4096,0,255&QLT=50&CVT=jpeg
- SEL=0&MAP=GAMMA,0,255,0,255,1.6&QLT=50&CVT=jpeg

SEL=0&MAP=LINEAR,0,255,0,0,LINEAR,0,255,0,255,LINEAR,0,255,0,255&QLT=50&CVT=jpeg









SEL=0&MAP=LINEAR,0,255,255,0&QLT=50 SEL=0&MAP=LINEAR,0,4096,0,255&QLT=5 SEL=0&MAP=GAMMA,0,255,0,255,1.6&QL1 SEL=0&MAP=LINEAR,0,255,0,0,LINEAR,0,2





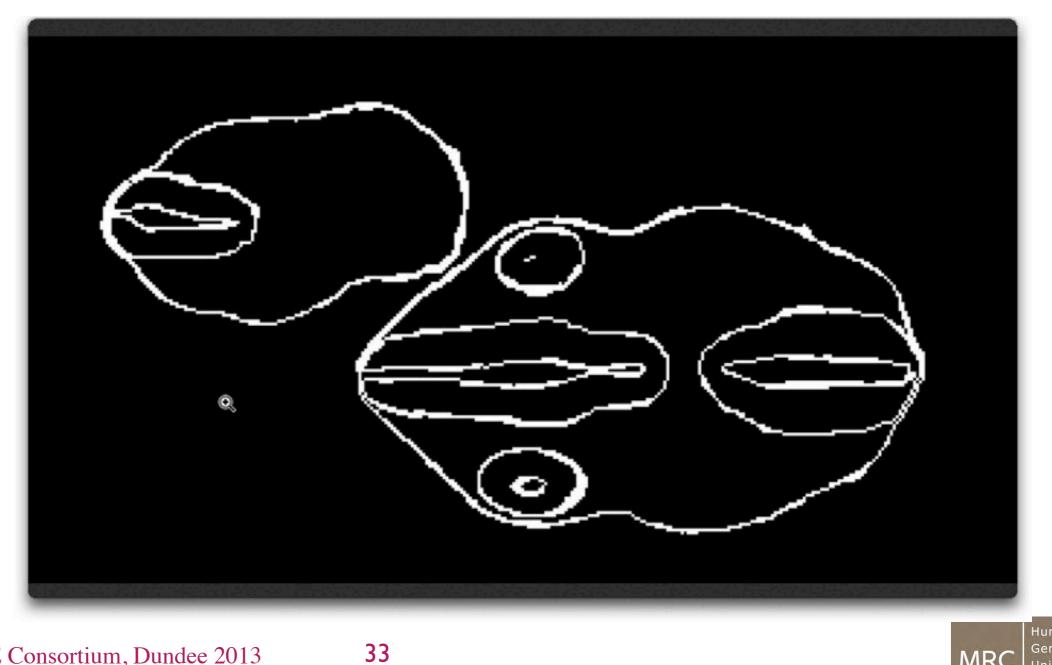
SEL=union(diff(dilation(2,1),2),diff(dilation(1,1),1))&QLT=50&CVT=jpeg

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SEL=union(diff(dilation(2,1),2),diff(dilation(1,1),1))&QLT=50&CVT=jpeg







SEL=union(diff(dilation(2,1),2),diff(dilation(1,1),1))&QLT=50&CVT=jpeg

SEL=diff(dilation(erosion(threshold(0,250,lt),3),3),2), 0,255,0,255&QLT=50&CVT=jpeg

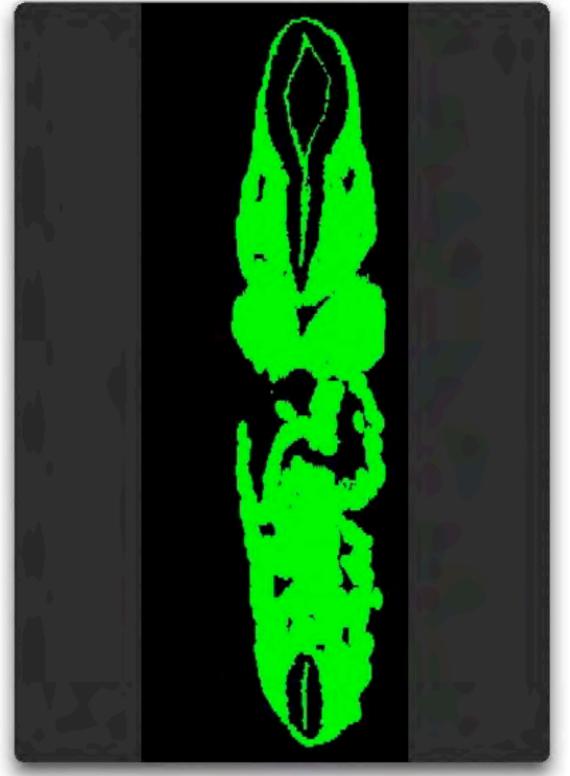




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SEL=union(diff(dilation(2,1),2),diff(dilation(1,1),1)

SEL=diff(dilation(erosion(threshold(0,250,lt),3),3), 0,255,0,255&QLT=50&CVT=jpeg



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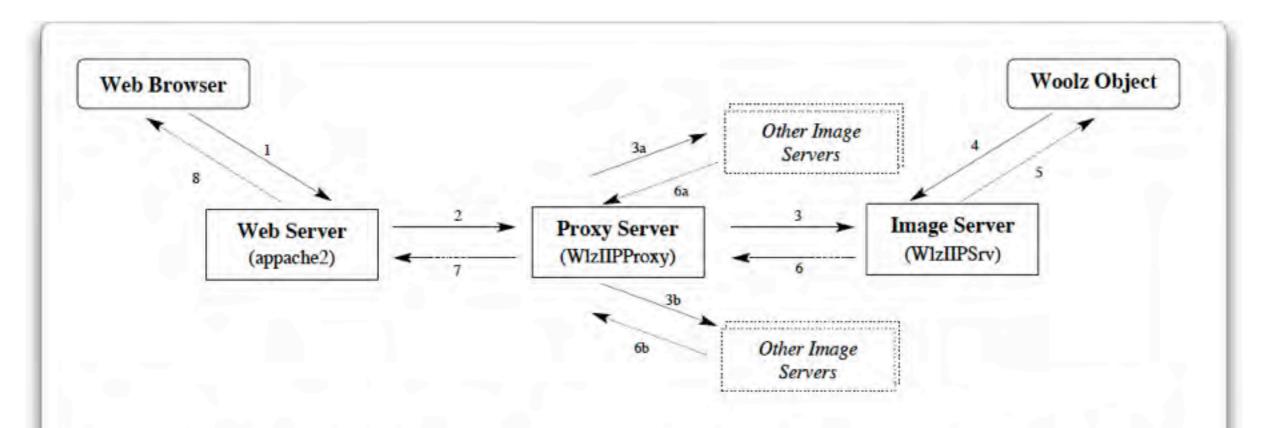


Figure 4: Architecture of IIP3D server using a proxy server. The web server passes the user requests to the proxy, which forwards them to individual IIP servers. These servers have direct access to the Woolz Object and return the requested data. The numbered lines show the order of the requests (continuous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

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€map

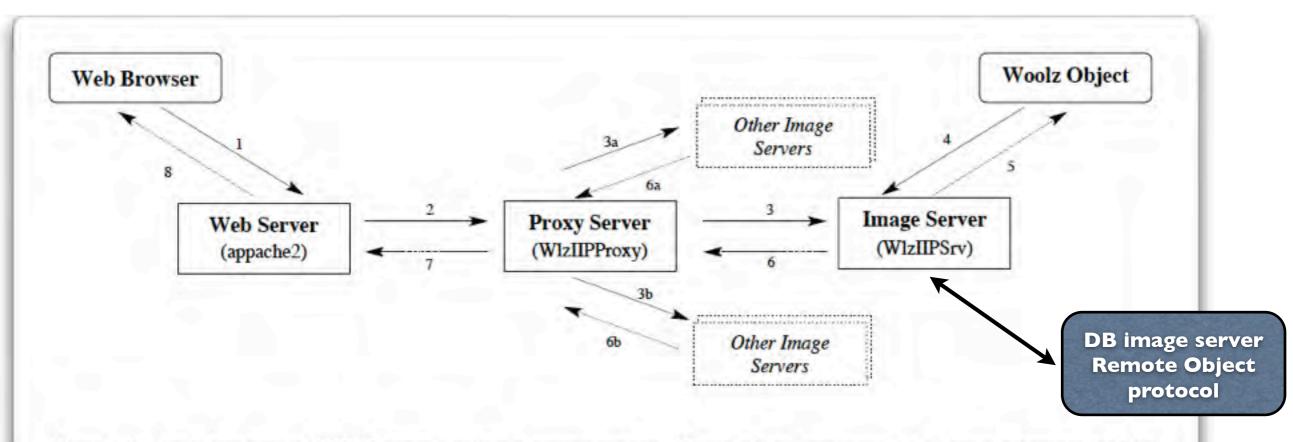


Figure 4: Architecture of IIP3D server using a proxy server. The web server passes the user requests to the proxy, which forwards them to individual IIP servers. These servers have direct access to the Woolz Object and return the requested data. The numbered lines show the order of the requests (continuous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

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€map

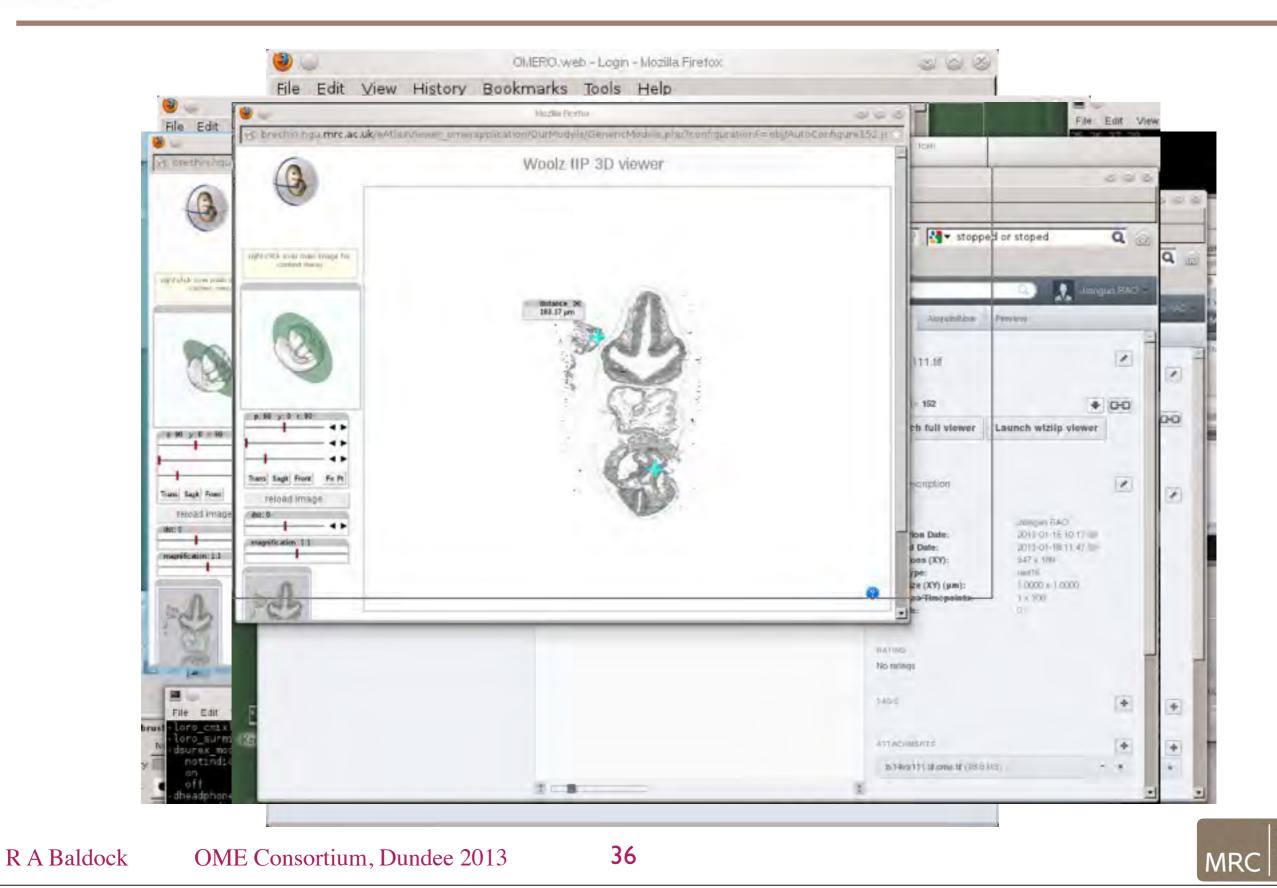


- Javascript
 - Ajax
 - MVC design, uses MooTools & Yahoo Widgets
- Multi-section at high resolution
- Volume overlays
- Anatomy & gene-expression overlays
- Controls
 - viewing angles virtual sections
 - > zoom
 - distance, fixed point
 - section locator & view angle feedback
 - distance measurement, query by image value
 - contrast, grey-slicing and mapping
 - thresholding, domain processing



€map

IIP3D and OMERO



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- 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

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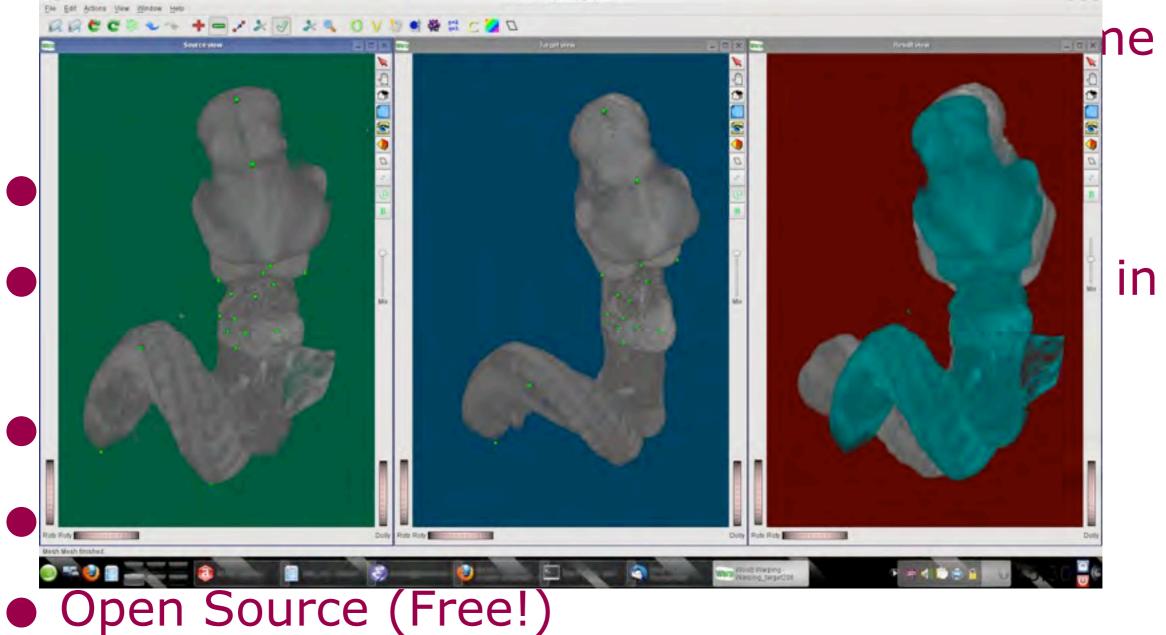
- Woolz, Qt, Coin3D(+SIMVoleon)
- Linux, OS X, Windoes
- Open Source (Free!)





3D mapping - WlzWarp

Allows placement of landmarks (points of



37



3D mapping - WlzWarp



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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

Jackson Laboratory

Martin Ringwald



Institute of Human Genetics, Newcastle University

> Susan Lindsay Janet Kerwin

University of Edinburgh

University of Dundee

Douglas Armstrong Nestor Milyeav Jason Swedlow

Other

Jonathan Bard Matt Kaufman

Funding

MRC, BBSRC, EU FP5,6,7, NIH, Wellcome Trust



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