The Mouse Atlas Database: An Atlas-Based IMage Resource

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Credits

- Bill Hill
- Jianguo Rao
eMouseAtlas - Development and Gene-Expression

Carol Wicking, University of Queensland

R A Baldock           OME Consortium, Dundee 2013
eMouseAtlas Framework
Atlas-Based Infrastructures

Basic research  Clinical practice

Population
Organism
Tissue
Cell
Organelle
Molecule

emage
Hudsen
Visible Human
Virtual Patient
Personal Atlas

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eMouseAtlas

WELCOME to EMAP
The e-Mouse Atlas Project

- EMA, the e-Mouse Atlas. A 3-D anatomical atlas of mouse embryo development including detailed histology. EMA includes the EMAP ontology of anatomical structure.
  More about EMA

- EIMAGE, the e-Mouse Atlas of Gene Expression. A database of mouse gene expression where, uniquely, the gene expression is mapped into the EMA 3-D space and can be queried spatially.
  More about EIMAGE.

All news items

All atlas links

All gallery images
eMouseAtlas

These are the original images of 7μm wax sections stained with Haematoxylin and Eosin. They are the images from which the 3D reconstruction was built.
eMouseAtlas
eMouseAtlas
EMAGE - current status

~22K submissions
Range Theiler 7-25

Repository DB: 38.4K entries

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

- ~22K submissions
- Range Theiler 7-25
- MGI/GXD (~1,300)
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Repository DB: 38.4K entries
EMAGE Embryo Space

Paint a region using your cursor

Retrieve gene expression detected in the region.
Retrieve data for both the left-hand and right-hand sides of the embryo.
Retrieve data over a range of stages: TS17 - 0 - 0 - 0
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
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 Mapping - Wnt signalling pathway
3D Mapping - Wnt signalling pathway

Wnt1

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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)
  - Multi-layer
  - Interactive overlays
  - WebGL
OME Project Objectives

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.
- IGMM imaging - archiving and analysis
A fast interval processor


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 microcell. The high pixel data rate (8 MHz peak) easily saturates most computer configurations. The linkage procedure used to reconstitute contiguous object descriptions is of the order of 1 ms.

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

Pattern Recognition

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

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

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

Piper J, MRC Hum Genet Ctr

Abstract
A fluorescent metaphase finder was adapted to a stand developed for a standard positive control. The method for preparing metaphase spreads was refined. Pre-existing scoring criteria were revised. The process was automated. Cells and metaphases were scored more efficiently. Positive control scores were added to a database and metaphase scores were assisted by the user. The efficiency of the process was increased. Scores were obtained from a database.

cuboid volume = 14M
domain volume = 5M
Woolz images

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

- Domain
  - Rectangle based
  - Interval based
  - 3D planewise domains
Woolz Images

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  - Rectangle based
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Values
  • Rectangle based
  • Ranged and interval based
  • Tiled
Woolz Images

- Domain
  - Rectangle based
  - Interval based
  - 3D planewise domains

Values
  - Rectangle based
  - Ranged and interval based
  - Tiled

20,225  25,225  27,225  29,225

20-25, 27-27, 29-29, ...
Woolz Images

- Domain
  - Rectangle based
  - Interval based
  - 3D planewise domains

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

- Domain
  - Rectangle based
  - Interval based
  - 3D planewise domain

- Values
  - Rectangle based
  - Ranged and interval based
  - Tiled
Values

- Rectangle based
- Raged and interval based
- Tiled
Woolz Images

- 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 image objects

- Polylines, boundary lists
- Histograms
- Meshes - 2D & 3D
- Transforms
  - Affine
  - Basis function
  - Mesh
  - Conforming mesh
Polylines, boundary lists

histograms

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

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Woolz image objects

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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
- to be continued....
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.
- 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

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

Pseudo Wholemount Mapping to Emap - done
3D Mapping to emap

1. Rigid body registration
2. Extract body part
3. Stack them up
4. Insert empty sections
5. Flip rotate to matching the model

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3D Mapping to emap
3D Mapping to emap

[Images of 3D mappings and emap representations]

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3D Mapping to emap
3D Mapping to emap
Serial Section Reconstruction

• 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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ITK based registration
Serial Section Reconstruction

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ITK based registration

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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

Sectioning Parameters

- **Angles:**
  - Pitch, Yaw, Roll

- **Position:**
  - Fixed point (f) & distance

- **Scale**

- **Tiling depends on orientation & scale**
### IIP3D - Extensions

#### Table 1: Extended command overview

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

#### Table 2: Extended object overview

<table>
<thead>
<tr>
<th>Object</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIP-server</td>
<td>Identify if WLZ-IIP is running</td>
</tr>
<tr>
<td>Max-size</td>
<td>The size of the section</td>
</tr>
<tr>
<td>Tile-size</td>
<td>The size of a tile</td>
</tr>
<tr>
<td>Wlz-true-voxel-size</td>
<td>The voxel size of the object</td>
</tr>
<tr>
<td>Wlz-volume</td>
<td>The volume of the object</td>
</tr>
<tr>
<td>Wlz-distance-range</td>
<td>The range of the sectioning plane distance</td>
</tr>
<tr>
<td>Wlz-sectioning-angles</td>
<td>The pitch, yaw and roll angles of the sectioning plane</td>
</tr>
<tr>
<td>Wlz-3d-bounding-box</td>
<td>The first and last plane, line and column number of the object</td>
</tr>
<tr>
<td>Wlz-coordinate-3D</td>
<td>The 3D coordinates defined in 2D by the PRL command</td>
</tr>
<tr>
<td>Wlz-grey-value</td>
<td>The grey or RGB value of a point specified either the PRL or the PAB commands</td>
</tr>
</tbody>
</table>
IIP3D Examples
IIP3D Examples

3D Model (EMA:80): TS23(14.5 dpc)

WHS Mouse

Electronic Atlas of the Developing Human Brain CS17

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IIP3D Examples
IIP3D Examples

3D Model (EMA:80): TS23(14.5 dpc)

WHS Mouse

Electronic Atlas of the Developing Human Brain CS17

Juvenile zebrafish - 2011-10-sam29-33-10mm, Juvenile-wt-pta, Zebrafish Atlas

Thursday, 28 February 2013
Image Processing IIP3D extensions

<table>
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<tr>
<th>Operator</th>
<th>Description</th>
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<tr>
<td><code>diff(exp, exp)</code></td>
<td>The difference between the two given domains.</td>
</tr>
<tr>
<td><code>dilation(exp, radius)</code></td>
<td>The dilation of the domain by <code>radius</code> voxels.</td>
</tr>
<tr>
<td><code>domain(exp)</code></td>
<td>The domain of an object.</td>
</tr>
<tr>
<td><code>erosion(exp, radius)</code></td>
<td>The erosion of the domain by <code>radius</code> voxels.</td>
</tr>
<tr>
<td><code>intersect(exp list)</code></td>
<td>The intersection of the domains in the given lists.</td>
</tr>
<tr>
<td><code>threshold(exp, value, comparison)</code></td>
<td>Creates an object where the image values satisfy the given <code>value</code> and <code>comparison</code>. Here the value is floating point and valid comparisons are (1\lt) (less than), (1\le) (less than or equal), <code>eq</code> (equal), <code>ge</code> (greater than or equal) and <code>gt</code> (greater than). The union of the domains in the given lists.</td>
</tr>
<tr>
<td><code>union(exp list)</code></td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Descriptions of morphological operators

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

Table 3: Syntax for morphological expressions.
## Image Processing IIP3D extensions

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### MAP

- **Purpose**: Defines a colour or grey value mapping. Grey values outside the mapped region are clamped to the minimum and maximum output colour component or grey values. There may be 1, 2, 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 four an RGBA mapping.

- **Syntax**:
  
  ```
  MAP=mspec[,mspec[,mspec[,mspec]]]
  where mspec=t, t1, t1u, t1u, t0, p0, p1
  ```

- **Input Parameters**:
  - `t` ∈ `IDENTITY | LINEAR | GAMMA | SIGMOID`
  - The mapping function:
    - `FLOAT t1`
    - Input lower grey value
    - `FLOAT t1`
    - Input upper grey value
    - `FLOAT t0`
    - Output lower colour component or grey value
    - `FLOAT t0`
    - Output upper colour component or grey value
    - `FLOAT p0`
    - Gamma (\(\gamma\)) or first sigmoid parameter (\(\mu\))
    - `FLOAT p1`
    - Second sigmoid parameter (\(\sigma\))

- **Response Example**:

  ```
  ⇒ MAP=LINEAR, 0, 4095, 0, 255
  ```

  Input grey values in the range 0-4095 are mapped to output values with the range 0-255

- **Default value**: `IDENTITY`

### Table 3: Syntax for morphological expressions.
Image Processing IIP3D extensions

SEL=0&MAP=LINEAR,0,255,255,0&QLT=50&C VT=jpeg
SEL=0&MAP=LINEAR,0,255,255,0&QLT=50
Image Processing IIP3D extensions

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
Image Processing IIP3D extensions

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
Image Processing IIP3D extensions

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
Image Processing IIP3D extensions

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,0,255,0,0,LINEAR,0,255&QLT=50&CVT=jpeg
SEL=union(diff(dilation(2,1),2),diff(dilation(1,1),1))&QLT=50&CVT=jpeg
SEL=\text{union}(\text{diff}(\text{dilation}(2,1),2),\text{diff}(\text{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
SEL=union(diff(dilation(2,1),2),diff(dilation(1,1),1))
SEL=diff(dilation(erosion(threshold(0,250,lt),3),3),3)
SEL=0,255,0,255&QLT=50&CVT=jpeg
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).
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
- contrast, grey-slicing and mapping
- thresholding, domain processing
IIP3D and OMERO
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, Windows
- Open Source (Free!)
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Woolz, Qt, Coin3D (+SIMVoleon)

Linux, OS X, Windows

Open Source (Free!)

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

Duncan Davidson
Richard Baldock

NIH GUDMAP:
Simon Harding
Bernard Haggerty
Koosum Roochum

BBSRC:
Mike Wicks

FP7 RICORDO:
Xu Gu

Wellcome OME:
Jianguo Rao

Colin Semple
Pedro Coutinho
Ian Overton

Heriot Watt University
Albert Burger

Jackson Laboratory
Martin Ringwald

Institute of Human Genetics,
Newcastle University
Susan Lindsay
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