WholeCellViz: data visualization for whole-cell models
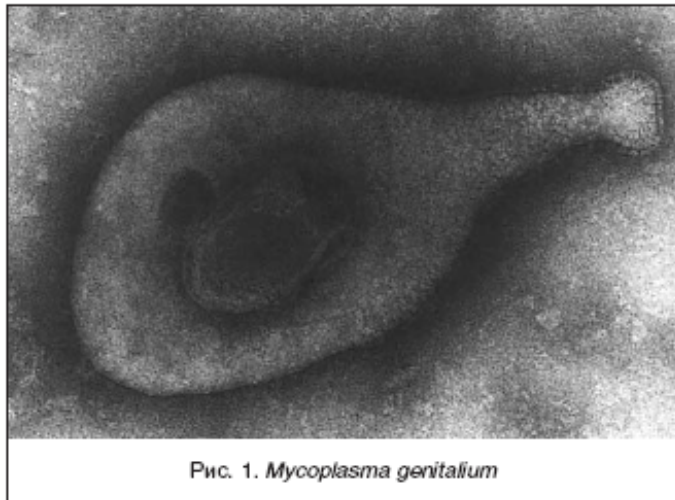
http://www.theatlantic.com/technology/archive/2012/07/to-model-the-simplest-microbe-in-the-world-you-need-128-computers/260198/

M. Genitalium

Рис. 1. *Mycoplasma genitalium*

Mycoplasma genitalium

- First isolated in 1981[1]
- Genital and reproductive tract disease
- Frequency
  - more common than *N. gonorrhoeae* but less common than *C. trachomatis*
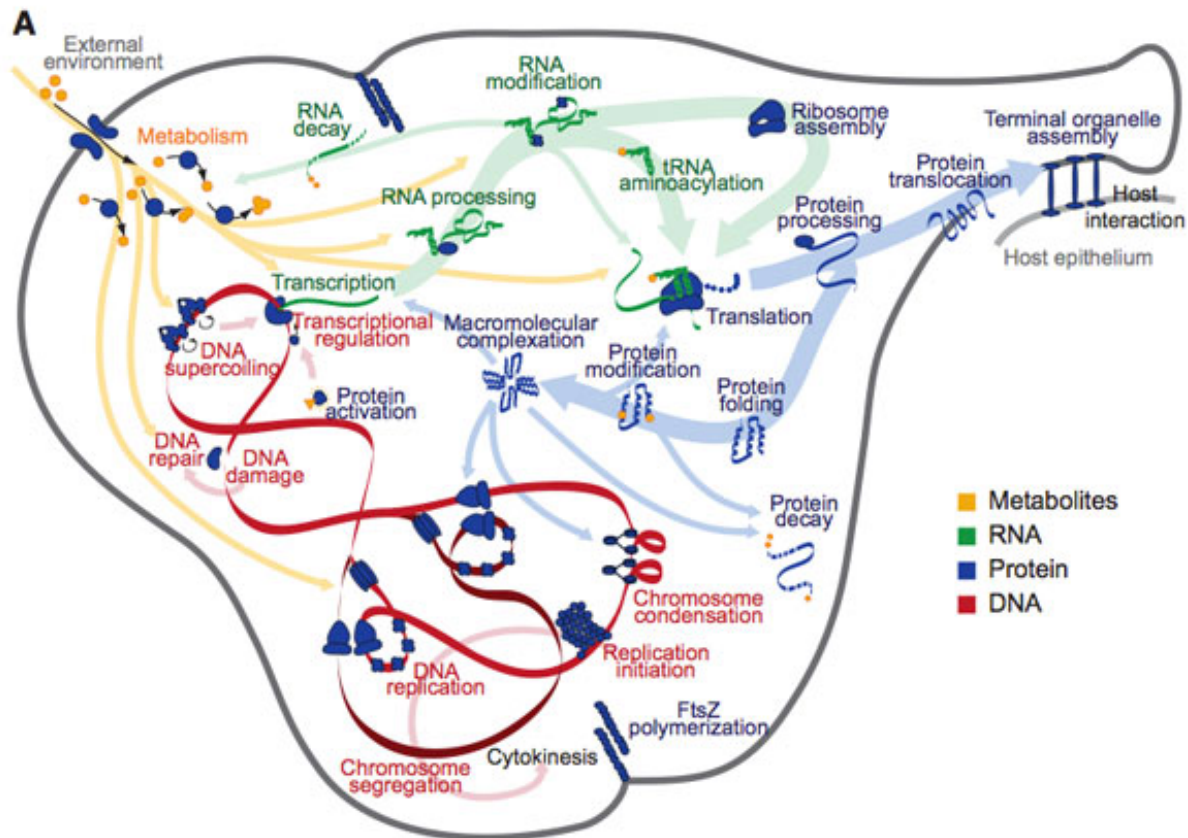 - coinfection with *C. trachomatis* not uncommon[1-3]

[1]Mena L, 2002; [2]Falk L, 2010; [3]Anagrius C, 2005

Small Genome

Mycoplasma pneumoniae
816394 bp

Mycoplasma genitalium
580070 bp
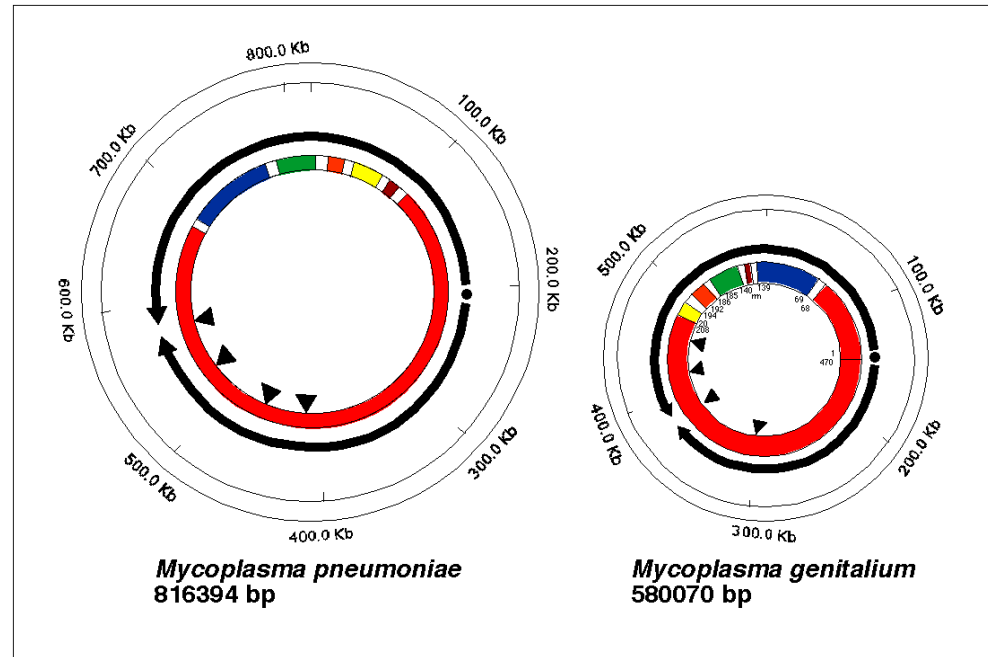
525 genes
(580 kb) nucleotide base pairs

Whole Cell Simulation

Simulation

A Whole-Cell Computational Model Predicts Phenotype from Genotype

Jonathan R. Karr,[1,4] Jayodita C. Sanghvi,[2,4] Derek N. Macklin,[2] Miriam V. Gutschow,[2] Jared M. Jacobs,[2] Benjamin Bolival, Jr.,[2] Nacyra Assad-Garcia,[3] John I. Glass,[3] and Markus W. Covert[2,*]
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http://dx.doi.org/10.1016/j.cell.2012.05.044

www.wholecellsimdb.org

WholeCellSimDB ✉

Publication release
March 9, 2014

This package provides all code for WholeCellDB. Please visit http://wholecelldb.stanford.edu to browse the database. Please see the user guide for usage instructions, and the developer's guide for installation instructions.

Download Links

Name	File Type	Platform	Updated
WholeCellDB			
WholeCellSimDB.html (URL)	binary	Any	Jun 16, 2014
Description: WholeCellSimDB			
Source code			
WholeCellSimDB-git-repo.html (URL)	code	Any	Jun 16, 2014
Description: WholeCellSimDB code (Git repository)			

Documentation Links

|			
User tutorial			
User tutorial.html (URL)			Jun 16, 2014
Description: User tutorial			
Developer's guide			
Developer's guide.html (URL)			Jun 16, 2014
Description: Developer's guide			
Source code documentation			
Source code documentation.html (URL)			Jun 16, 2014
Description: Source code documentation			
Data model			
Data model.png (URL)			Mar 20, 2014
Description: Data model			

Please cite these papers

- Karr JR*, Phillips NC*, Covert MW. WholeCellSimDB: a hybrid relational/HDF database for whole-cell model predictions. Database. (2014) [Download]

Data

https://simtk.org/project/xml/downloads.xml?group_id=714#package_id1307

Visualization

http://wholecellviz.stanford.edu/
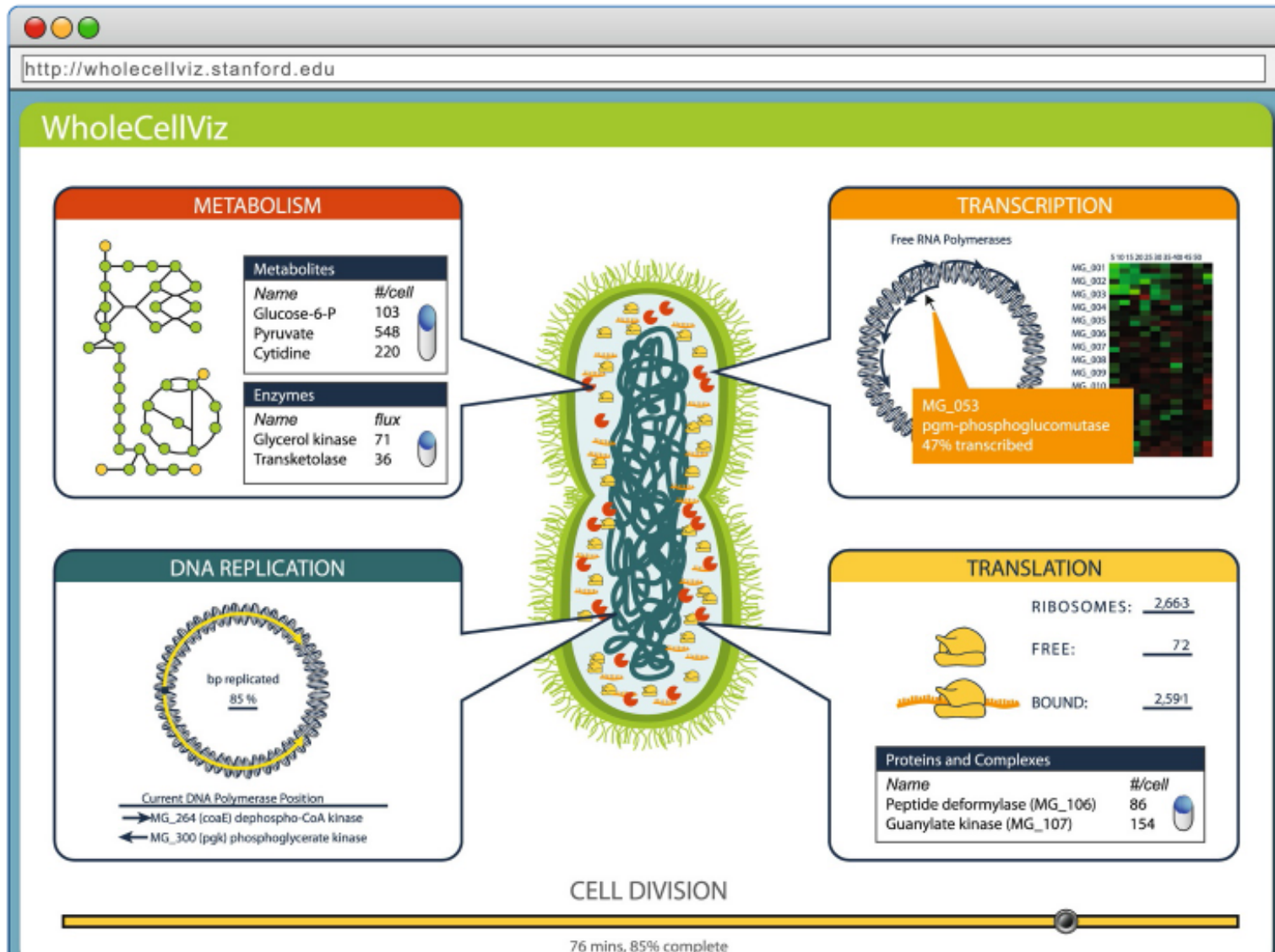
About

WholeCellViz is a web-based software program for visually analyzing whole-cell simulations. WholeCellViz enables visual analysis of several all aspects of cell physiology including:

- The cell mass, volume, and shape,
- The copy number of every metabolite, RNA, and protein,
- The flux of every metabolic reaction,
- The status of every molecular machine – DNA polymerase, RNA polymerase, ribosome, FtsZ ring, and
- The copy number, superhelicity, integrity, and DNA binding status of every chromosome.
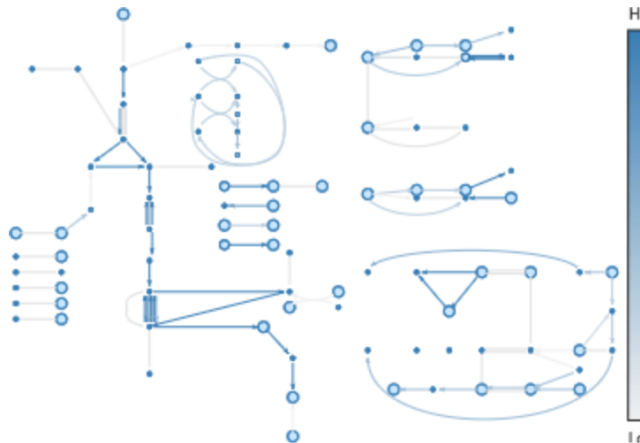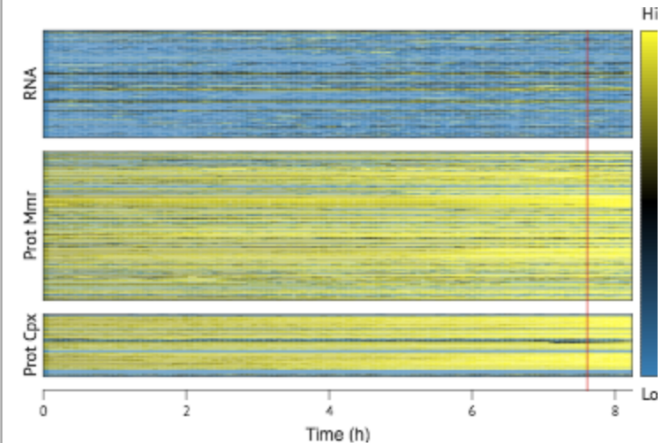
Cell shape
Simulation: Wild-type #1
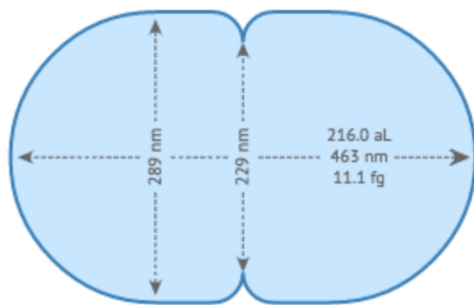
Metabolism
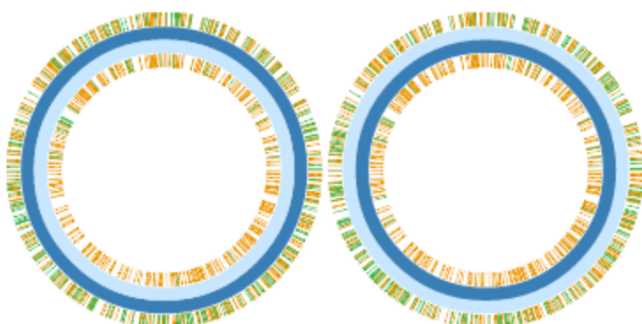Simulation: Wild-type #1

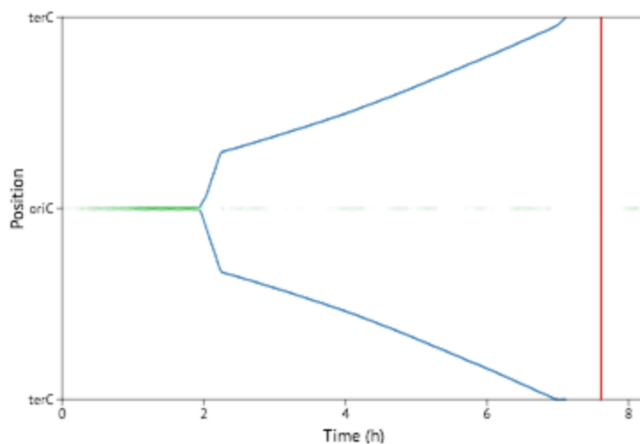## Gene expression
Simulation: Wild-type #1

DNA replication, protein occupancy, methylation, & damage
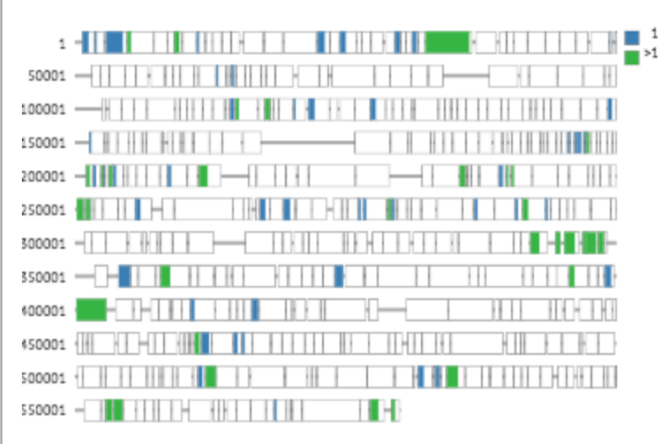Simulation: Wild-type #1
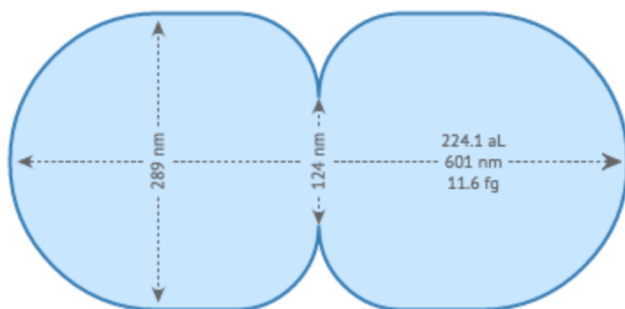

DNA replication
Simulation: Wild-type #1

Translation
Simulation: Wild-type #1

Mycoplasma genitalium

WholeCellViz

Home | Edit | Download | Help

Cell shape
Simulation: Wild-type #1

289 nm
124 nm
224.1 aL
601 nm
11.6 fg

DNA replication, protein occupancy, methylation, & damage
Simulation: Wild-type #1

Chromosome 1
1
100001
200001
300001
400001
500001

Chromosome 2
1
100001
200001
300001
400001
500001

Mother
Daughter
ssDNA
dsDNA
Methylation
Protein
Strand brea

Talking to server …

Retrieving data for panel 2. This may take a few minutes over slow connections. Please be patient …

Metabolites: dNTP count
Simulation: Wild-type #1

4x105
3x105
3x105
2x105
2x105
1x105
5x104
0

dNTP count

0   2   4   6   8
Time (h)
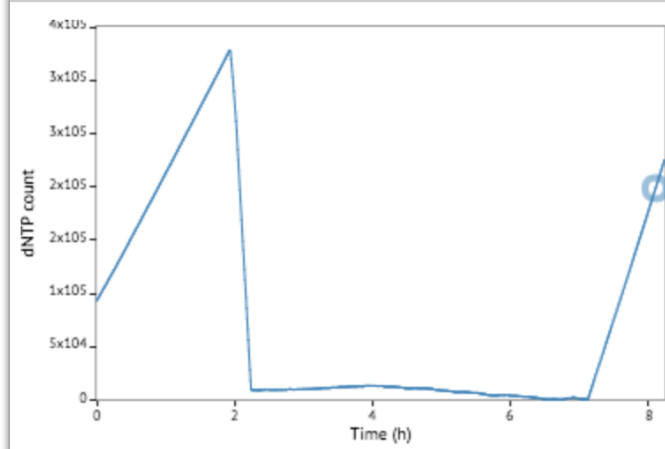
FtsZ contractile ring
Simulation: Wild-type #1

oriC   R5   R4   R3   R2   R1

Superhelicity
Simulation: Wild-type #1

-0.054
-0.056
-0.058
-0.060
-0.062
-0.064
-0.066

Superhelicity

0   2   4   6   8
Time (h)

Example

Chromosome 1
- Mother
- Daughter
- Methylation
- Strand break
- ssDNA
- dsDNA
- Protein
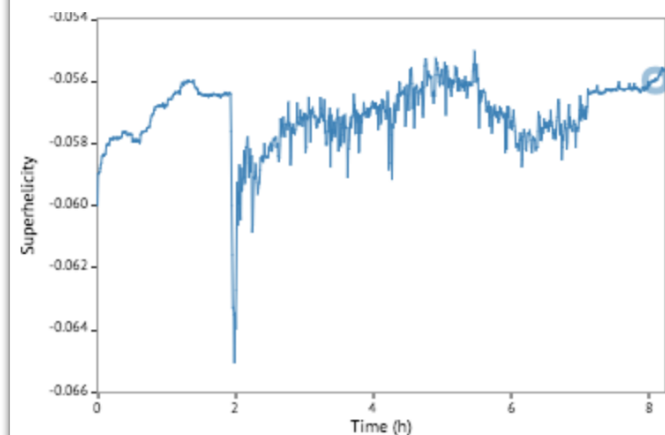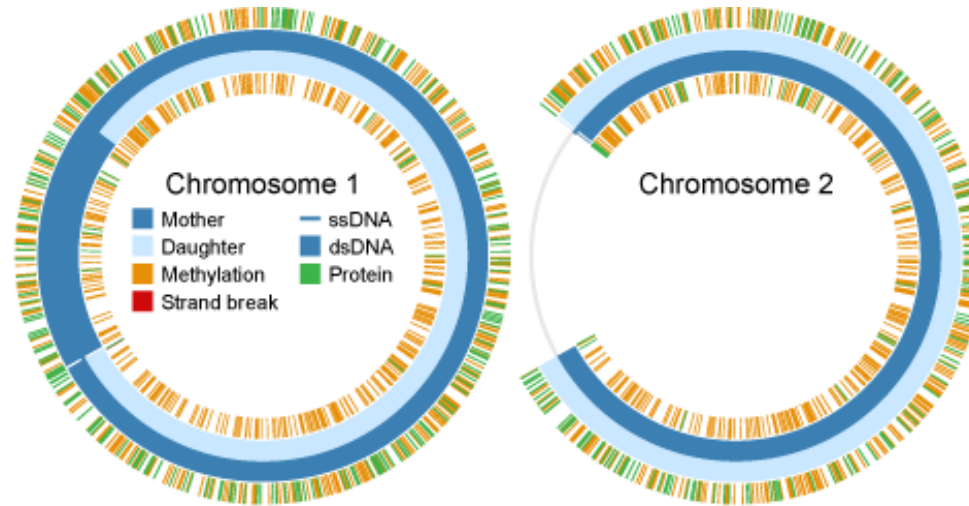
Chromosome 2

DNA replication, protein occupancy, methylation, & damage.

This visualization displays the polymerization (blue), protein DNA binding (green), methylation (orange), and strand break (red) status of the M. genitalium chromosomes.

Mother DNA is colored dark blue. Daughter DNA is colored light blue.

Example
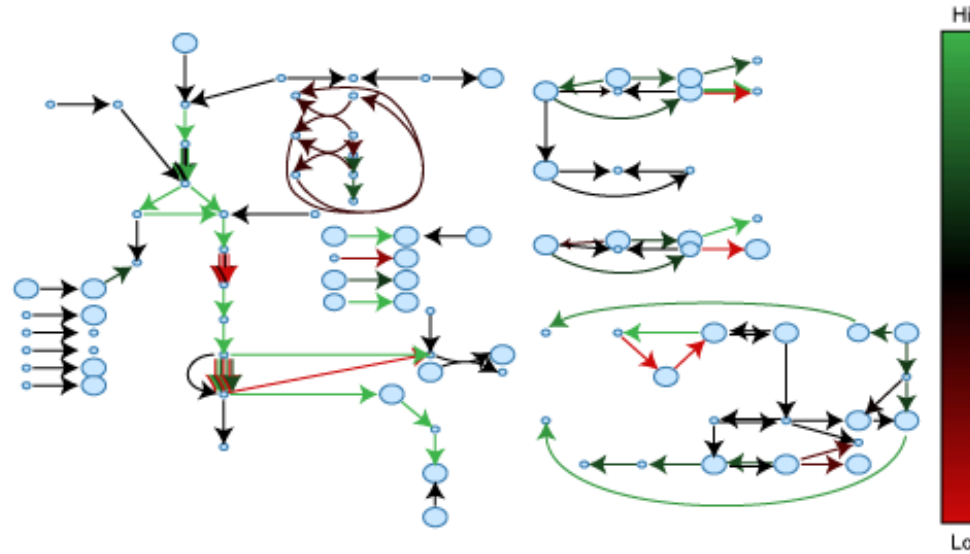
Metabolism

This visualization depicts the fluxes of several metabolic reactions (green indicates high flux, red indicates low flux) and the concentrations of several metabolites (node size)

Example

Gene expression

This visualization displays the expression of every RNA and protein gene product. High expression is colored yellow; low expression is colored blue.

What Else ?

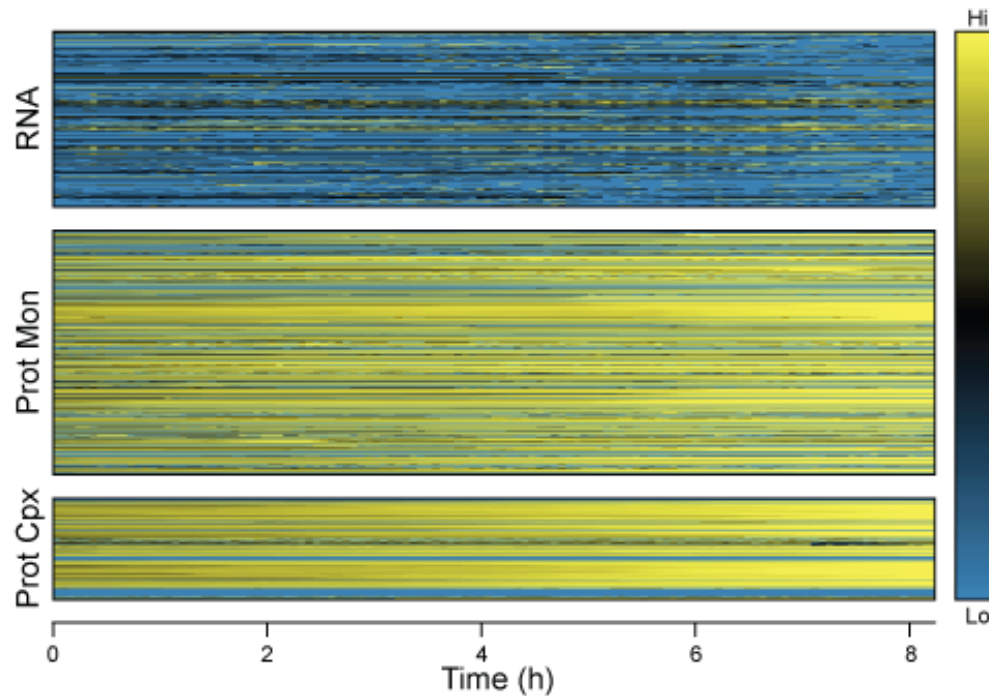**Example views**

Cell growth | Cell cycle | Replication
Omics | Synthesis | Population | Knockouts

Table 1 WholeCellViz visualizations

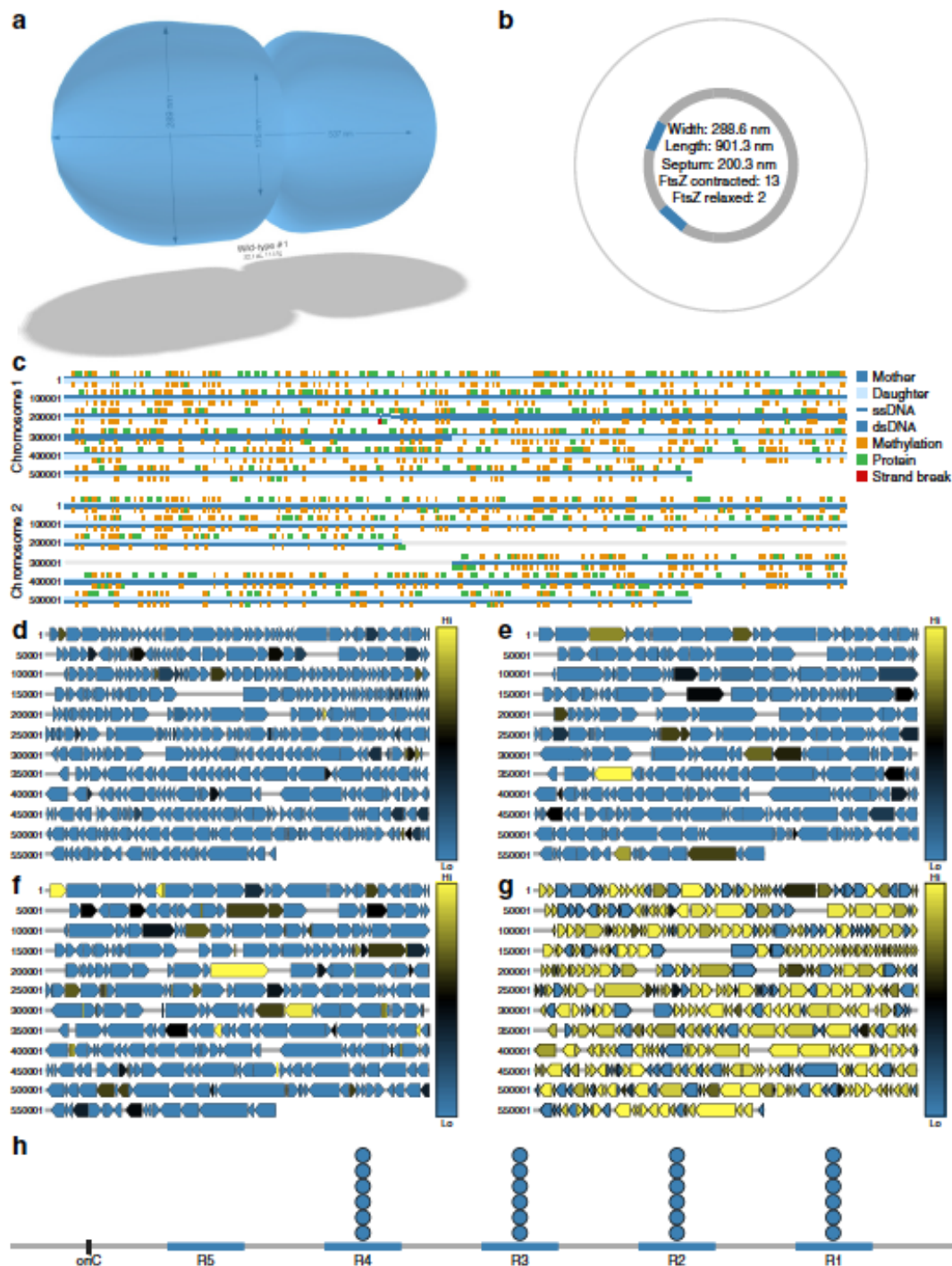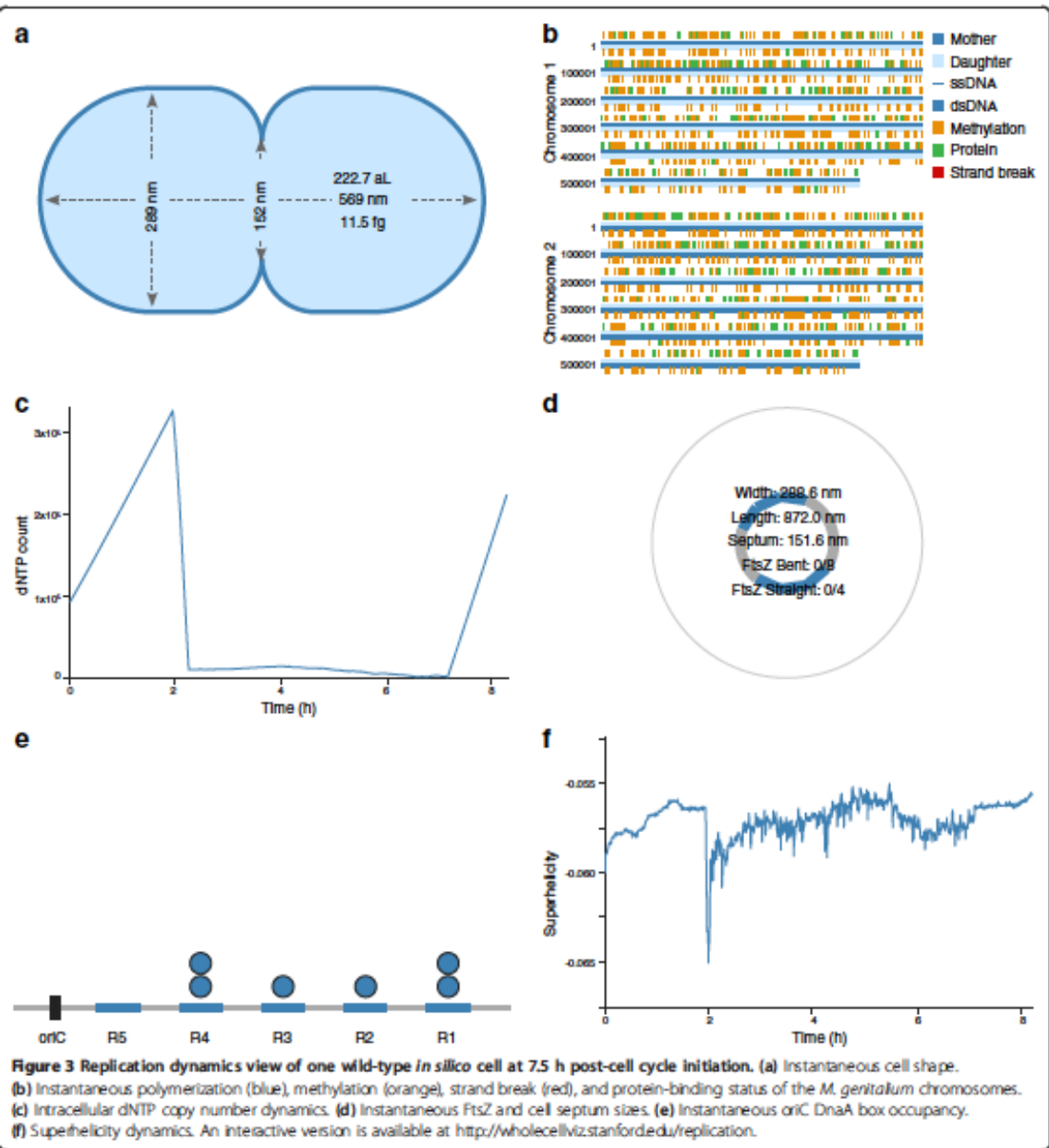| Visualization	Figure	URL
Cell shape	1a	http://wholecellviz.stanford.edu/CellShape
Cell shape (3D)	2a	http://wholecellviz.stanford.edu/CellShape3D
Chromosome (linear)	2c	http://wholecellviz.stanford.edu/Chromosome1
Chromosome (circular)	1d	http://wholecellviz.stanford.edu/Chromosome2
Chromosome (space-time)	1e	http://wholecellviz.stanford.edu/ChrSpaceTime
Cytokinesis	2b	http://wholecellviz.stanford.edu/Cytokinesis
Gene expression	1c	http://wholecellviz.stanford.edu/GeneExp
Immature protein expression	2d	http://wholecellviz.stanford.edu/NascentProtExp
Immature RNA expression	2e	http://wholecellviz.stanford.edu/NascentRnaExp
Metabolism	1b	http://wholecellviz.stanford.edu/Metabolism
Mature protein expression	2f	http://wholecellviz.stanford.edu/MatureProtExp
Mature RNA expression	2g	http://wholecellviz.stanford.edu/MatureRnaExp
Replication initiation	2h	http://wholecellviz.stanford.edu/RepInit
Translation	1f	http://wholecellviz.stanford.edu/Translation
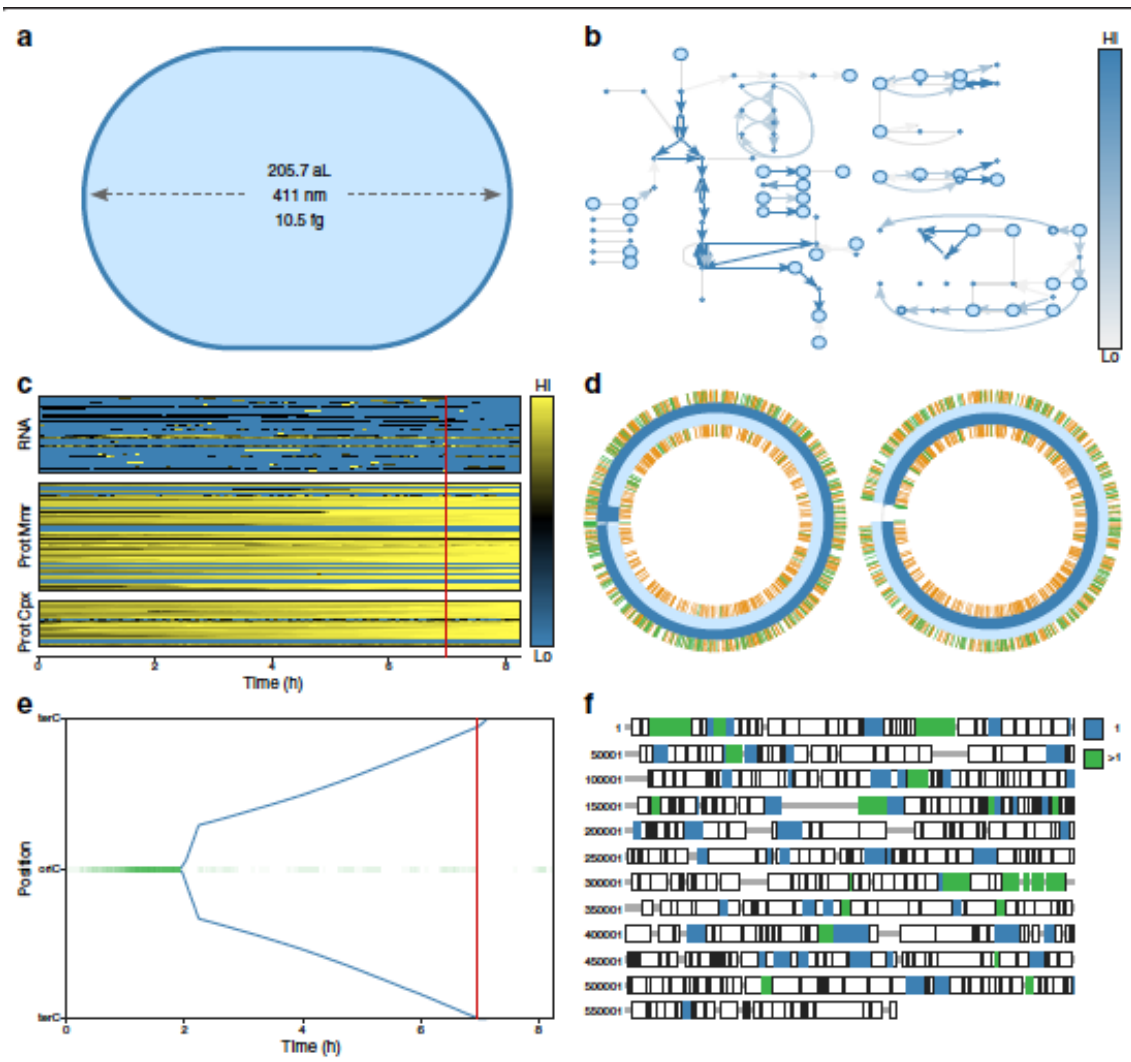
Figure 1 Cell cycle dynamics view of one wild-type *in silico* cell at 7 h post-cell cycle initiation. This view includes six animations which highlight the dynamics of the predicted metabolic fluxes and RNA and protein expression over the cell cycle. In particular, the view shows the onset of DNA replication, and the subsequent bidirectional movement of DNA polymerase on the chromosome. The view also highlights the onset of cytokinesis following the completion of DNA replication. **(a)** Instantaneous shape of *M. genitalium* as it initially elongates and later pinches at the septum, forming two daughter cells. **(b)** Metabolic map illustrating metabolite concentrations and reaction fluxes. Each metabolite is normalized to its mean concentration, and each reaction is normalized to its mean flux. Dark blue arrows indicate high reaction flux; light blue arrows indicate low reaction flux. Large circles indicate high metabolite concentrations; small circles indicate low metabolite concentrations. **(c)** Heatmap of the copy number of each RNA, protein monomer, and protein complex species. Each gene product is normalized to its mean copy number. Yellow indicates high expression; blue indicates low expression. **(d)** Instantaneous polymerization (blue), methylation (orange), strand break (red), and protein-binding status of the *M. genitalium* chromosomes. **(e)** Space-time plot illustrating the instantaneous chromosomal locations of the replication initiator DnaA and DNA polymerase. **(f)** Map of the protein-coding genes indicating protein synthesis. Each gene is colored according to the length of its longest nascent polypeptide. Green represents genes with one active ribosome; blue represents genes with multiple active ribosomes. An interactive version is available at http://wholecellviz.stanford.edu/cellCycle.

a

Wild-type #1

b

Width: 288.6 nm
Length: 901.3 nm
Septum: 200.3 nm
FtsZ contracted: 13
FtsZ relaxed: 2

c

Chromosome 1

Chromosome 2

- Mother
- Daughter
- ssDNA
- dsDNA
- Methylation
- Protein
- Strand break

d

e

f

g

h

oriC   R5   R4   R3   R2   R1

Figure 2 Additional WholeCellViz visualizations. Visualizations highlight one wild-type *in silico* cell at various time points. **(a)** Instantaneous shape of *M. genitalium* as it initially elongates and later pinches at the septum, forming two daughter cells. **(b)** Instantaneous FtsZ contractile ring size. FtsZ rings iteratively contract at the cell septum to pinch the cell membrane during cytokinesis. **(c)** Instantaneous polymerization (blue), methylation (orange), strand break (red), and protein-binding status of the *M. genitalium* chromosomes. **(d–g)** Heatmaps of the copy number dynamics of immature proteins **(d)**, immature RNA **(e)**, mature proteins **(f)**, and mature RNA **(g)**. Each gene product is normalized to its maximal expression. Yellow indicates high expression; blue indicates low expression. **(h)** Occupancy of the oriC functional DnaA boxes which recruit DNA polymerase to the oriC to initiate replication.

Figure 2 (See legend on next page.)

Figure 3 Replication dynamics view of one wild-type *in silico* cell at 7.5 h post-cell cycle initiation. (a) Instantaneous cell shape.
(b) Instantaneous polymerization (blue), methylation (orange), strand break (red), and protein-binding status of the *M. genitalium* chromosomes.
(c) Intracellular dNTP copy number dynamics. **(d)** Instantaneous FtsZ and cell septum sizes. **(e)** Instantaneous oriC DnaA box occupancy.
(f) Superhelicity dynamics. An interactive version is available at http://wholecellviz.stanford.edu/replication.

The Project

It's About Time:

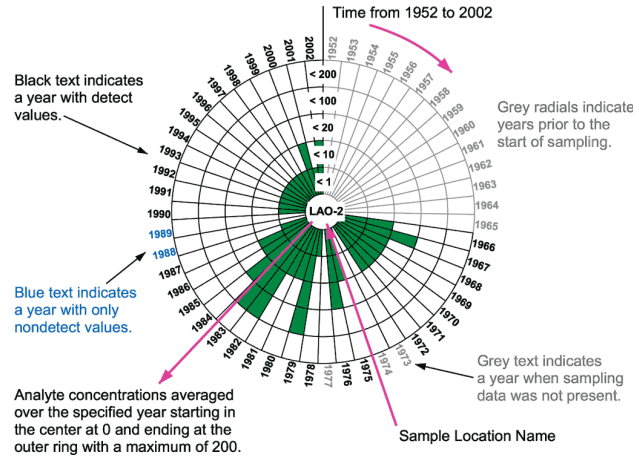Giving Data More Meaning & Context
with Temporal Visualization Approaches

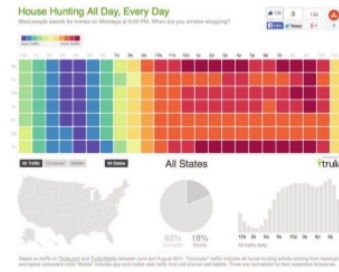"The Persistence of Memory". Via Wikipedia - http://en.wikipedia.org/wiki/

September 16, 2014

Temporal Data
value changes over time
events

TEMPORAL HEATMAP

Time from 1952 to 2002

Black text indicates a year with detect values.

Grey radials indicate years prior to the start of sampling.

Blue text indicates a year with only nondetect values.

Grey text indicates a year when sampling data was not present.

Analyte concentrations averaged over the specified year starting in the center at 0 and ending at the outer ring with a maximum of 200.

Sample Location Name
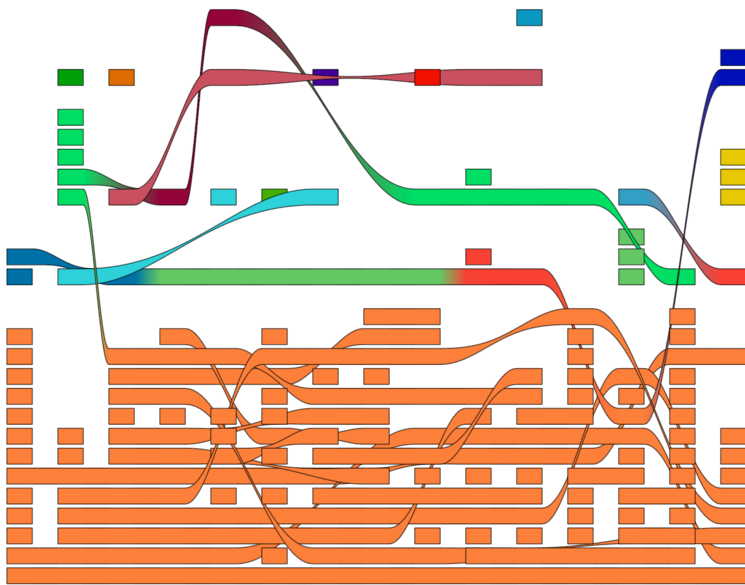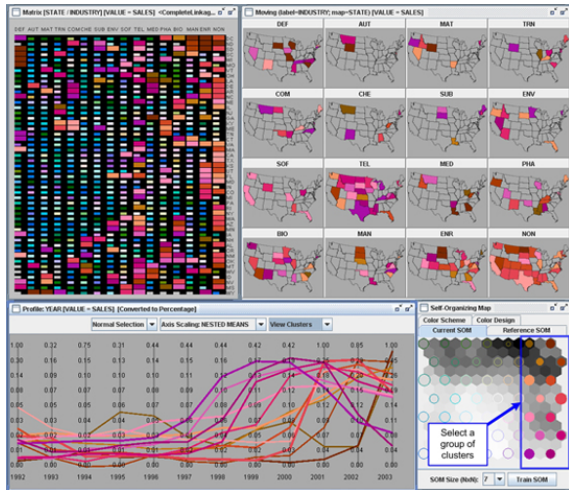
Data

https://simtk.org/project/xml/downloads.xml?group_id=714#package_id1307
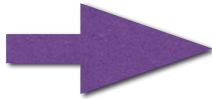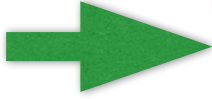
WholeCellViz ✉

Publication release
September 6, 2012

WholeCellViz is a web-based software program for visually analyzing whole-cell simulations.

Download Links

Name	File Type	Platform	Updated
WholeCellViz			
WholeCellViz.html (URL)	binary	Any	Jun 16, 2014
Description: WholeCellViz			
Source code (current)			
WholeCellViz-Git-repo.html (URL)	code	Any	May 23, 2013
Description: WholeCellViz code (current) (Git repo)			
Source code (publication release)			
SourceCode.zip (9338 kB)	code	Any	Jul 26, 2013
Description: Source code (publication release)			

Documentation Links

➡ **Tutorial**
    Tutorial.html (URL)   Jun 16, 2014
    Description: Tutorial

➡ **Developers' guide**
    DevelopersGuide.pdf (243 kB)   Jan 25, 2013
    Description: Developers' guide

MIT license
    license.txt (1 kB)   Jul 18, 2013
    Description: MIT license

Please cite these papers

- Lee R*, Karr JR*, Covert MW. WholeCellViz: Data visualization for whole-cell models. BMC Bioinformatics 14, 253 (2013) [Download]

Must Do

Option 1

With More Than 5 Views

And Again

User Studies & Usability Testing

To check effectiveness

Option 2

Choose 2 Views

- Pick any two

- Correlate

- Model

- Gambol :)

- Code and Create a New Visualization

- No second user study is needed.