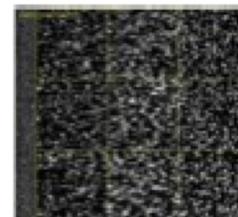
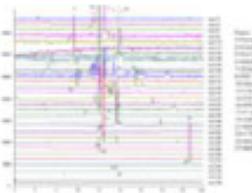
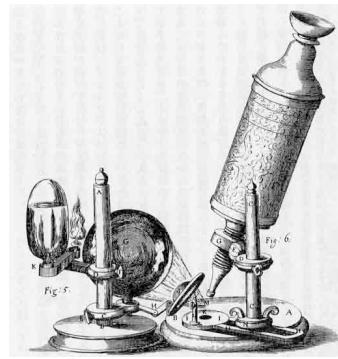
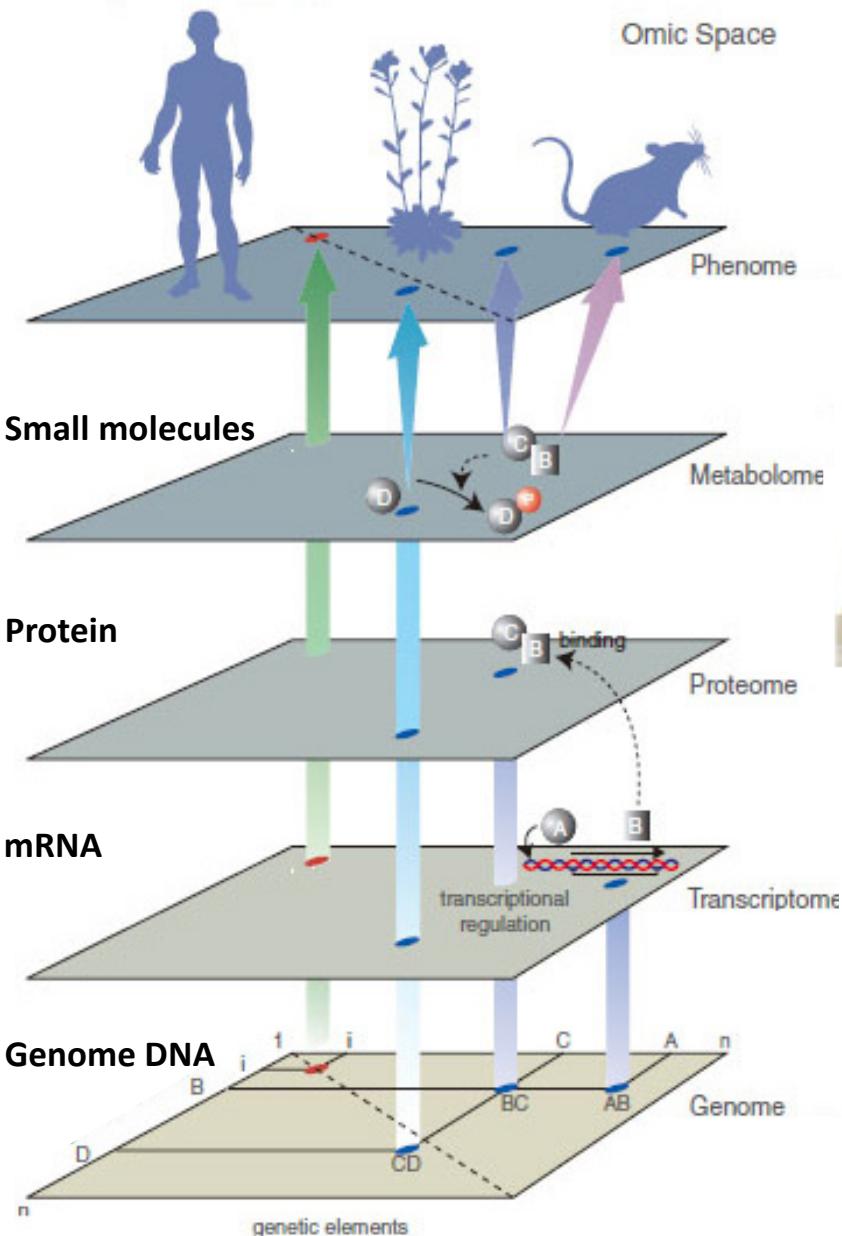


Data-driven analysis of the mechanism of animal development

Shuichi Onami, RIKEN Center for Biosystems Dynamics Research
Koji Koyamada, Kyoto Univ, Academic Center for Computing and Media Studies



Bottleneck in multi-omics analysis

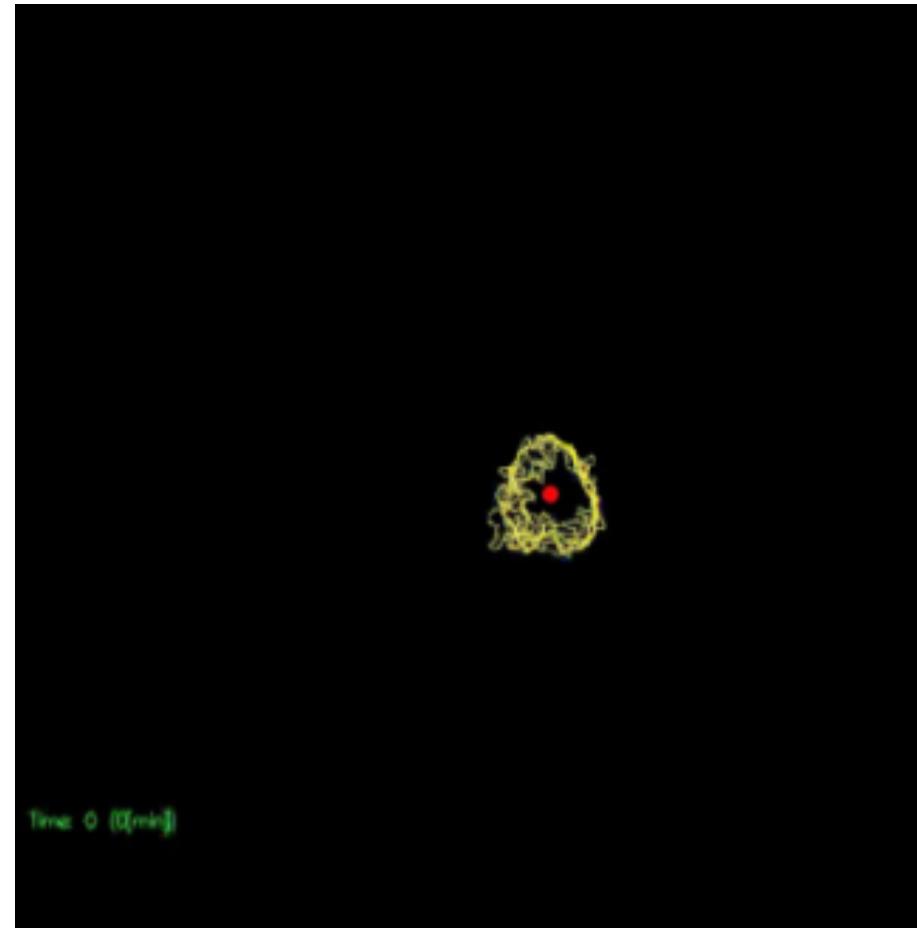
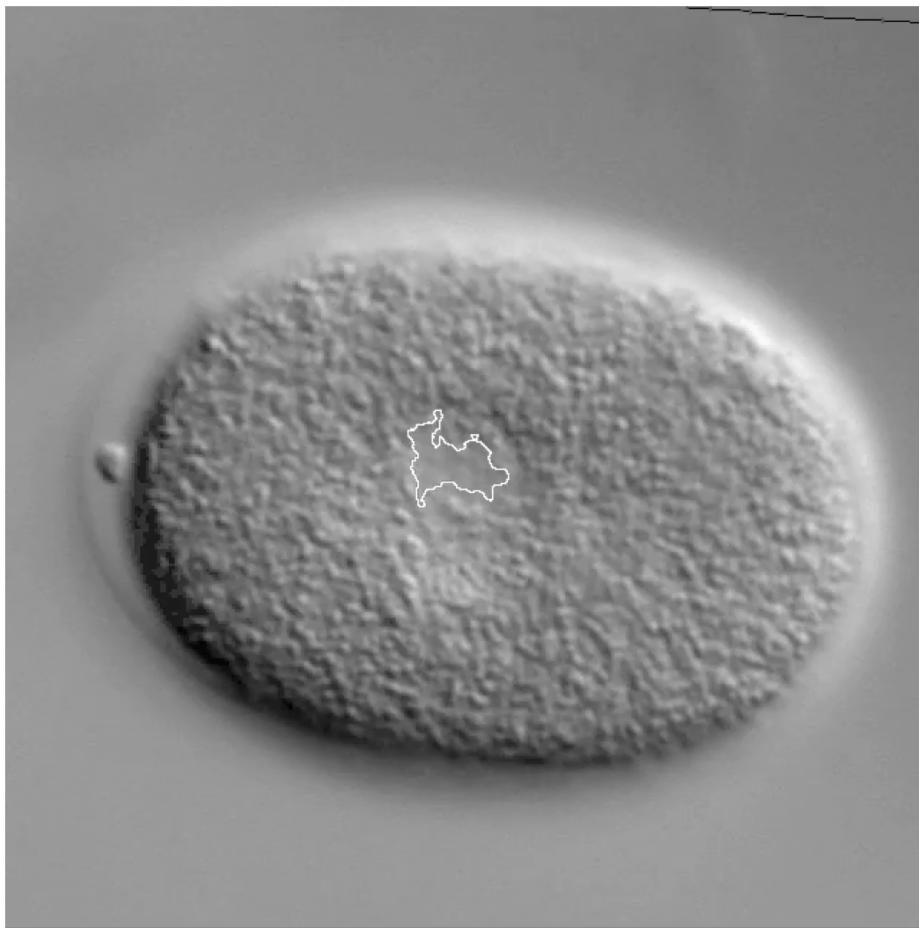


ataa	60
gtt	120
ttt	180
ttt	240
ttt	300
ttt	360
ttt	420
ttt	480

Needs “trained” human
Poorly automated,
subjective
low throughput, qualitative

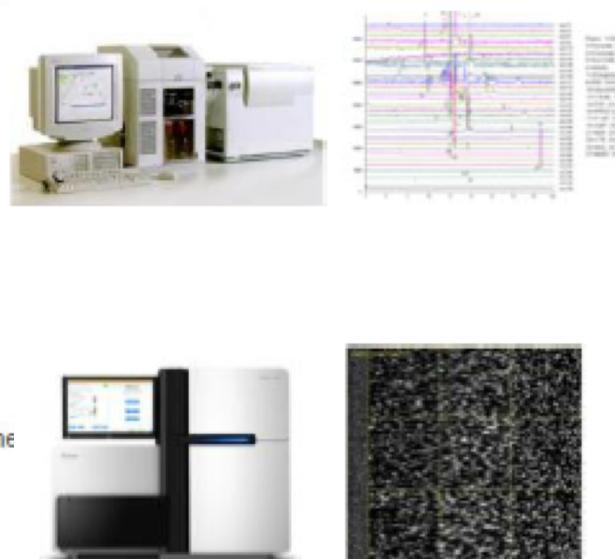
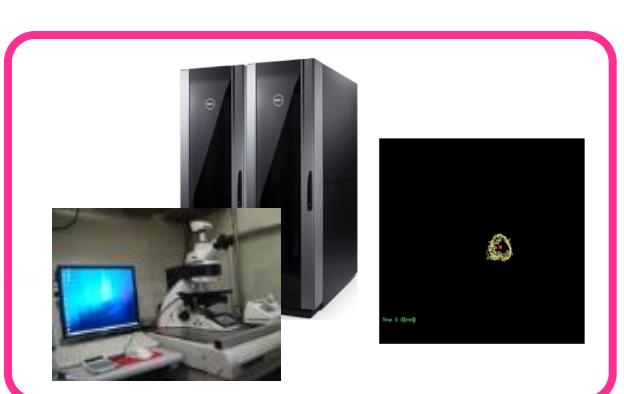
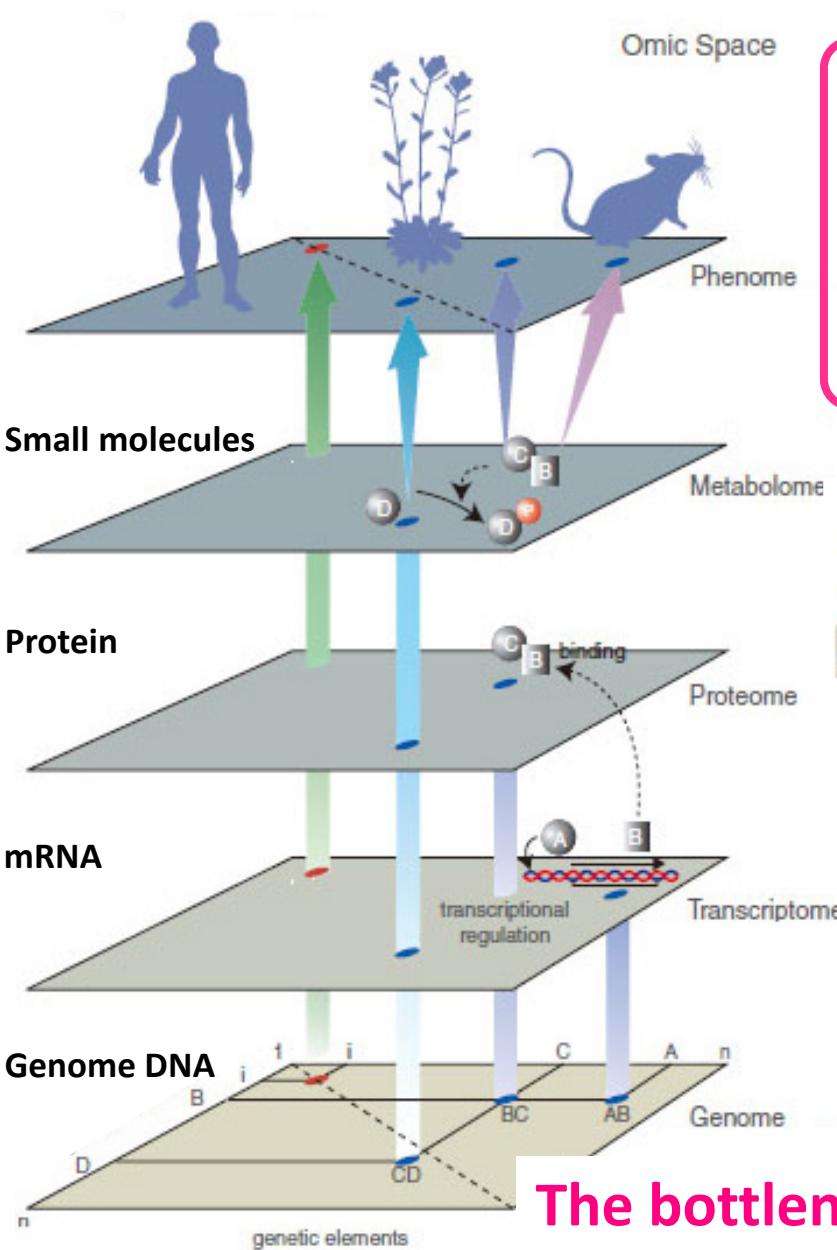
Highly automated
Objective
High throughput
Quantitative

Combination of 4D imaging and image recognition



3D information of nuclei for every 20 sec

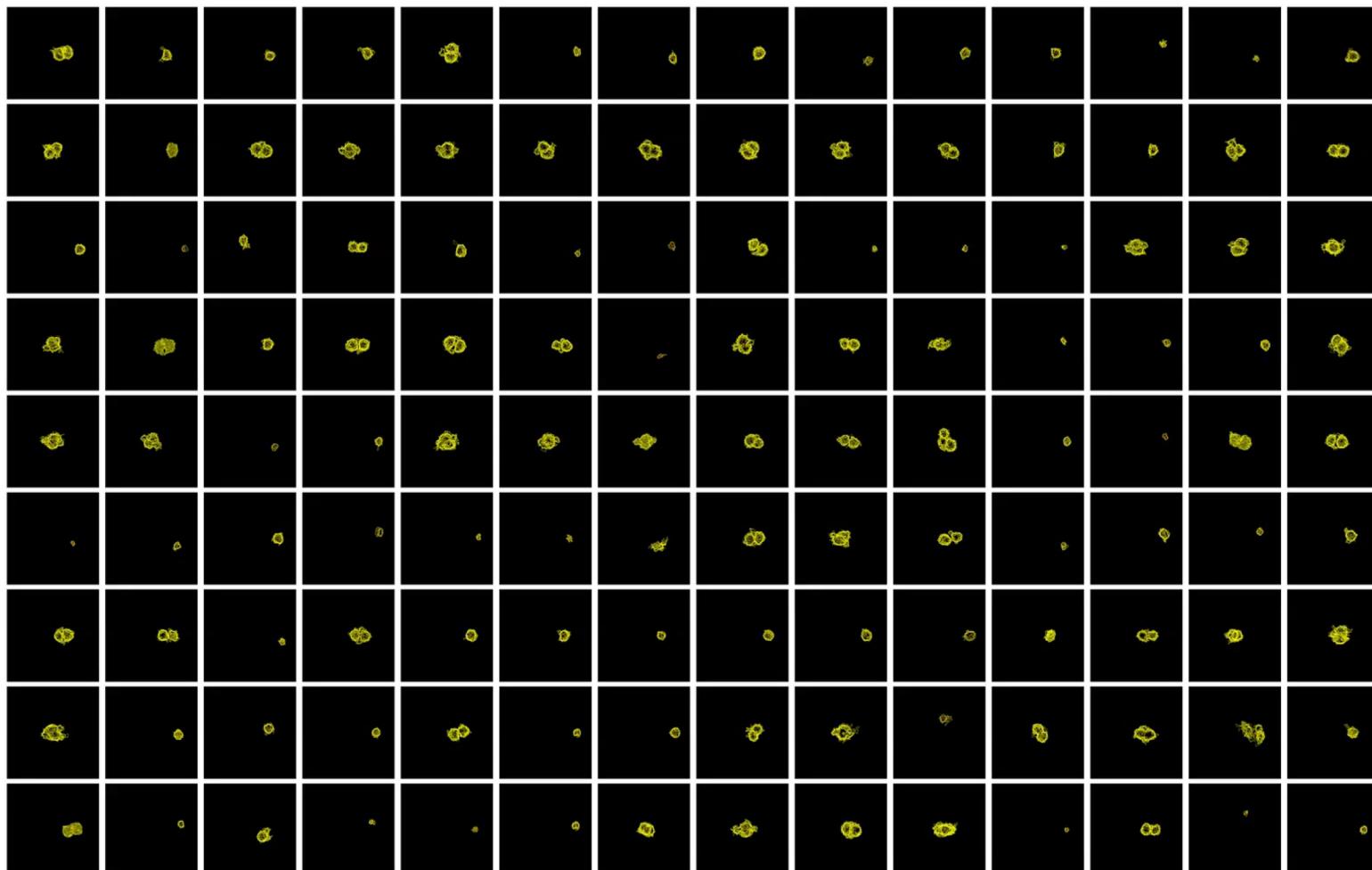
Data-driven modeling



**Highly automated
Objective
High throughput
Quantitative**

The bottleneck has been resolved

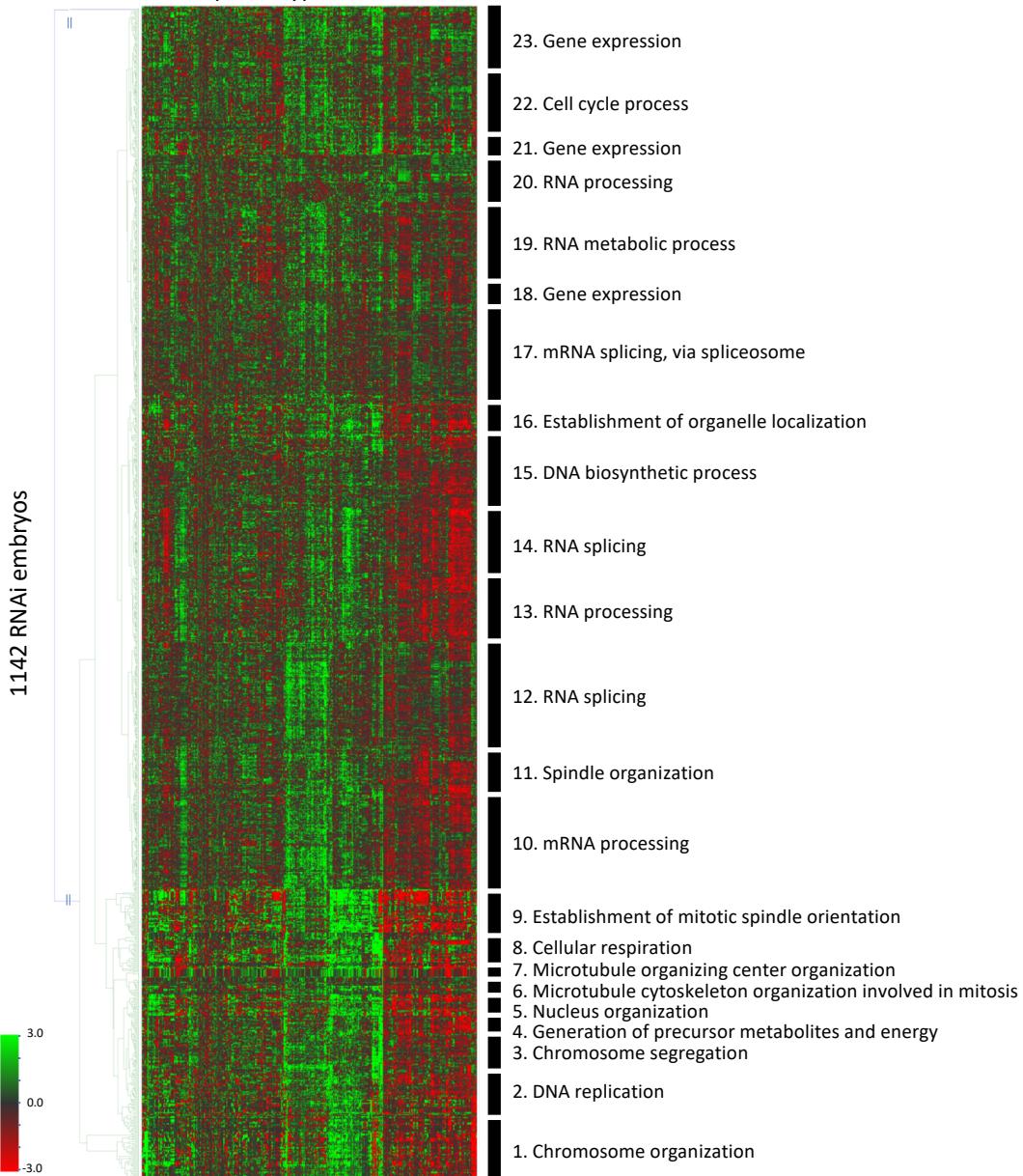
Collection of quantitative cell division dynamics data for gene knockdown embryos



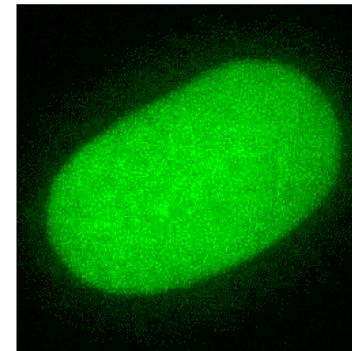
Single gene knockout for **all 351 essential embryonic genes** by RNAi
5 embryos / gene

Clustering of phenotypic expression combined with GO enrichment analysis

421 phenotypic characters

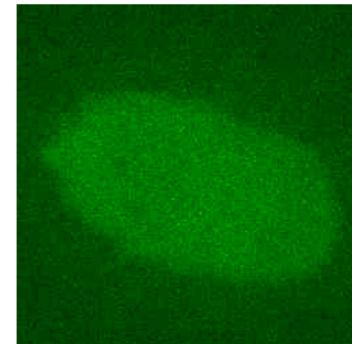


Chromosome segregation

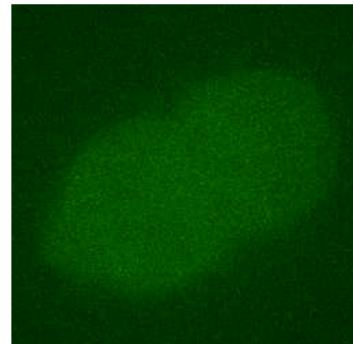


Y23H5A.3

RNA processing



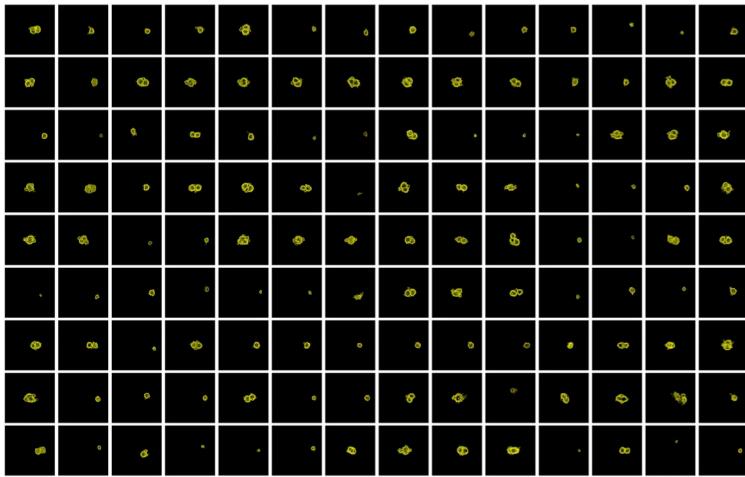
R08D7.1



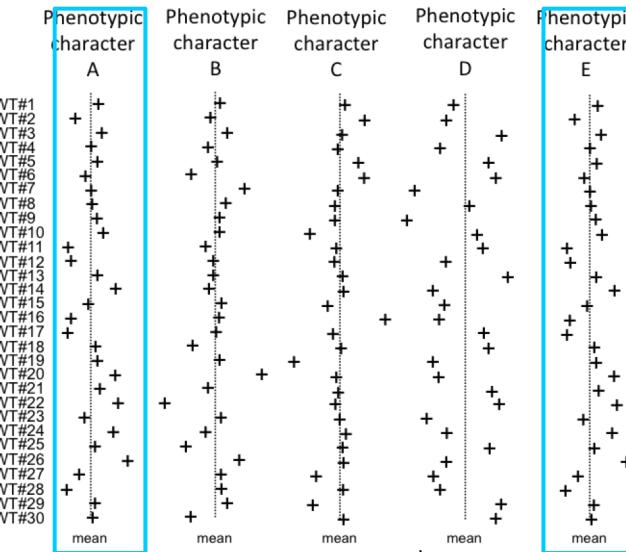
C32E8.5

Elucidation of the sequence of phenotype expression

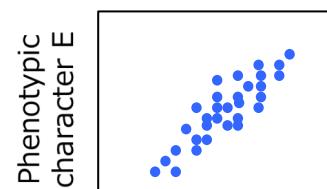
4D quantitative cell division data



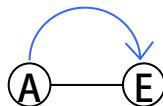
Correlation between phenotypic characters



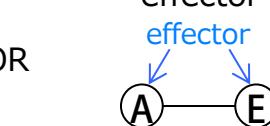
Extraction of causal relationship



Causal relationship

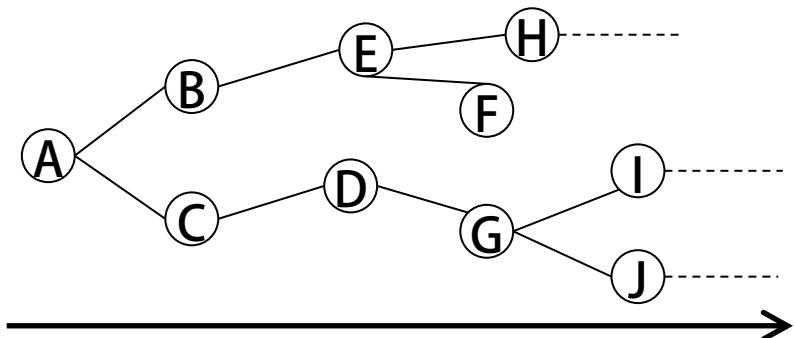


Common upstream effector

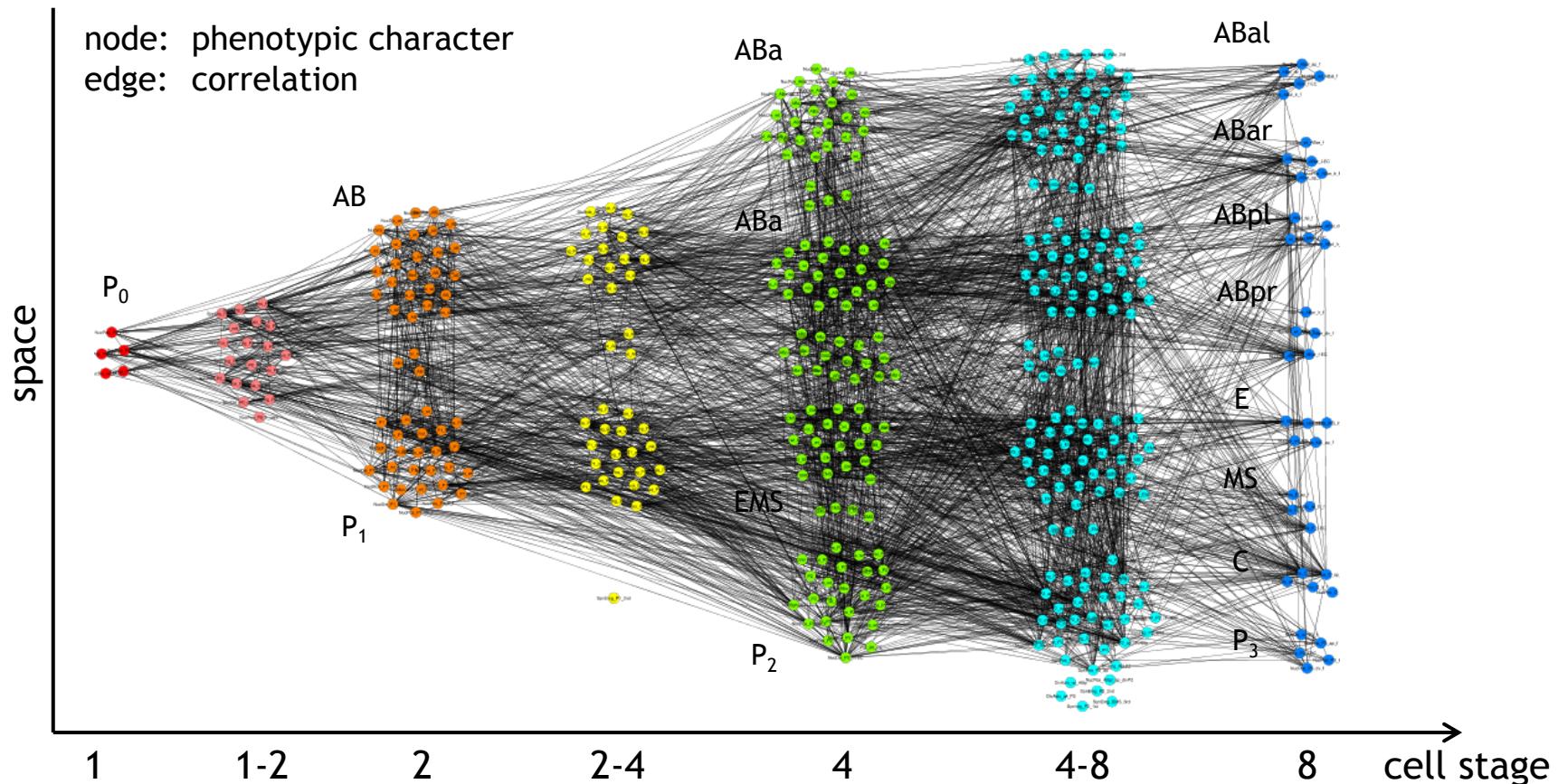


OR

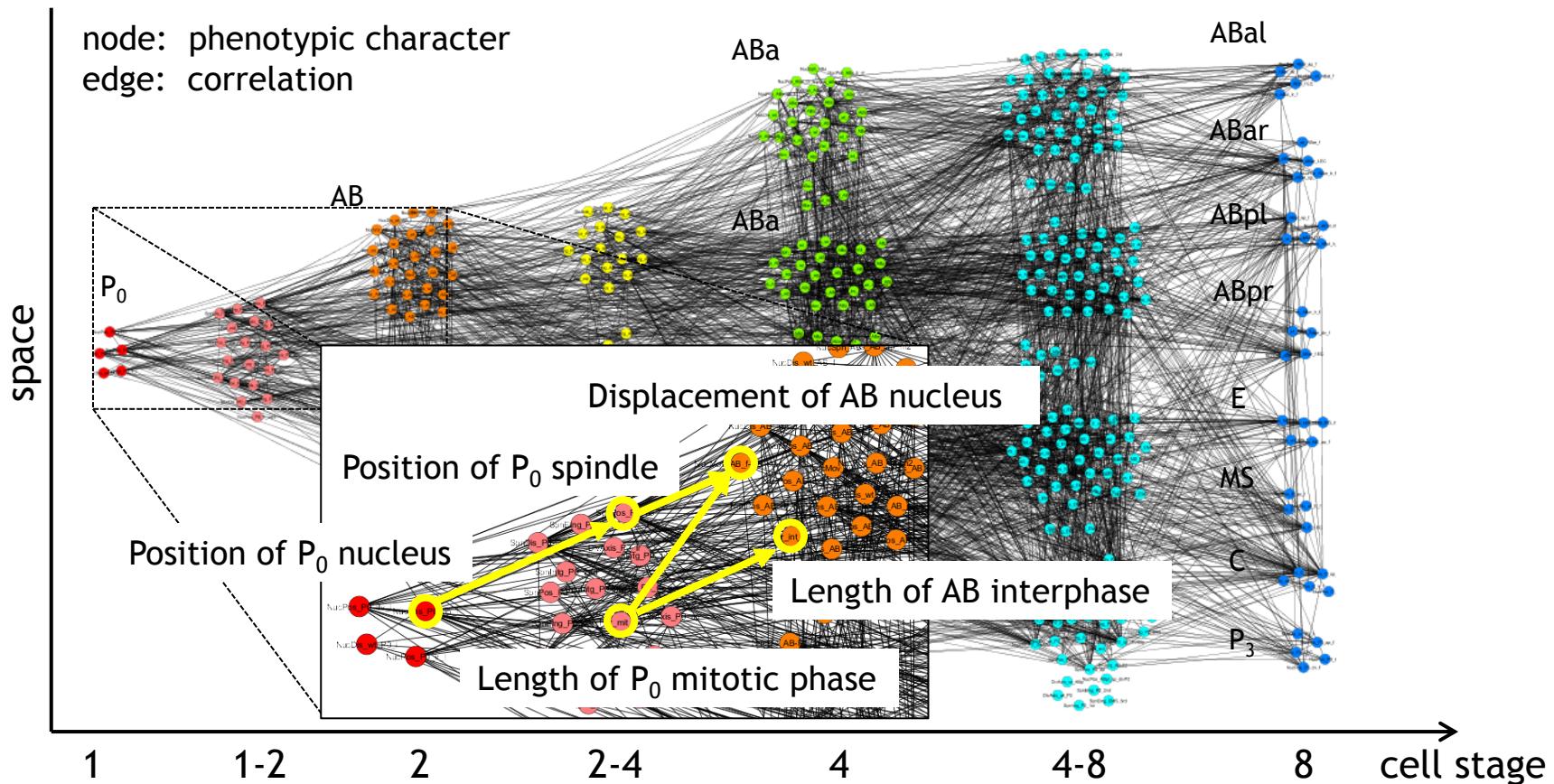
Sequence of phenotype expression



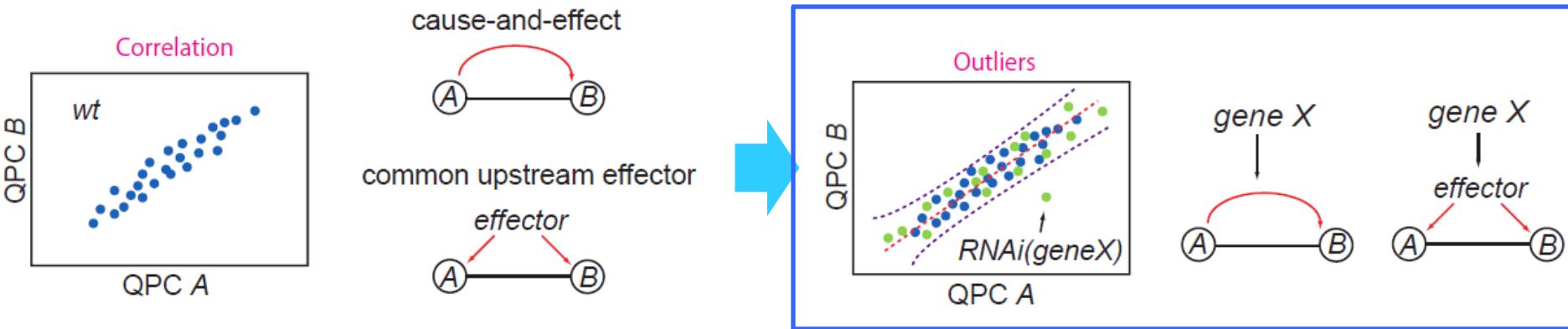
Phenotype expression network



Phenotype expression network



Inference of genes involved in the phenotypic network



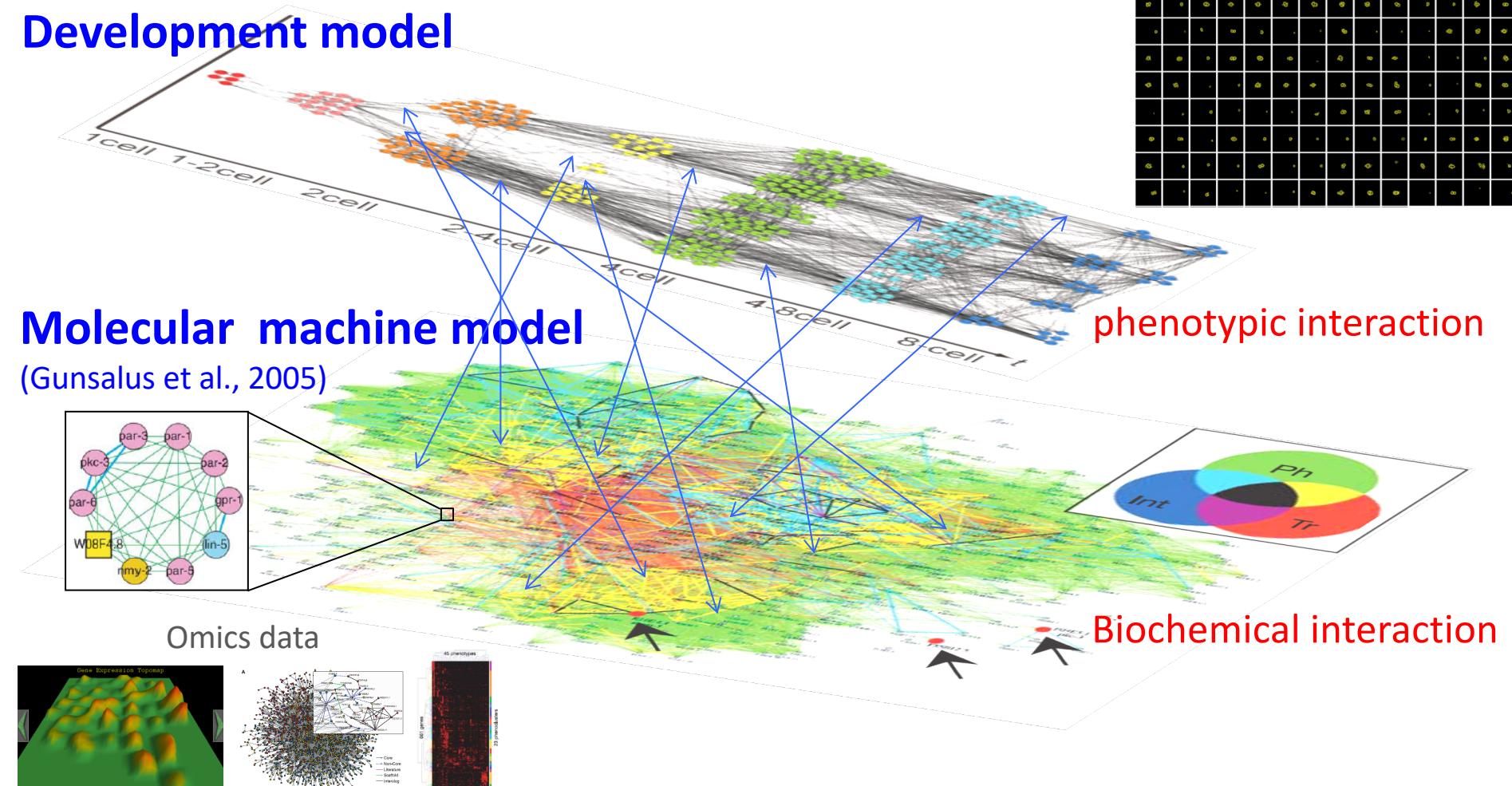
17,129 gene functions were inferred

Highly correlated pairs of phenotypic characters (correlation > 0.5) and genes that produced outliers in the correlation ($P < 0.001$) are shown. Correlation coefficients between phenotypic characters and prediction intervals for the correlated distribution were calculated by using CDD information from 33 wild-type embryos. QPC: quantitative phenotypic character; Corr: correlation coefficient between QPC1 and QPC2.

#	QPC1	QPC2	Corr	Corr	outlier-producing genes
1	NucPos_P1_ap_f	NucDis_P1_f-EC	0.9998	0.9998	R107.6 R08D7.2 C05D11.1 Y49E10.19 F54E7.3 T20H4.5 F58B8.3 F56A8.6 B0361.10 R07E5.14 B0464.7 Y66A7.8 R12B2.4 F01F1.7 F58A4.3 C07A9.3
2	NucPos_P1_ap_divAB	NucDis_P1_divAB-EC	0.998872	0.998872	Y49E10.19 F58B8.3 C26E6.4 C23G10.8
3	NucPos_ABa_ap_m4	NucPos_ABa_m4-EC	-0.99867	0.99867	F58B8.3 C34C12.8 B0361.10 F56D2.1 R08D7.2 Y49E10.19
4	NucPos_P1_ap_m2	NucDis_P1_m2-EC	0.99819	0.99819	C05D11.11 F58B8.3 R08D7.2 Y49E10.19
5	NucPos_AB_ap_l	NucDis_AB_l-EC	-0.99798	0.99798	R107.6 F11H8.4 Y49E10.19 F58A4.3 F56D2.1 C34C12.8
6	NucPos_ABa_ap_m	NucDis_ABa_m-EC	-0.99682	0.99682	R107.6 F58B8.3 Y71H2.378.C34C12.8 F56D2.1 F58A4.3 T20H4.5 B0361.10 C38D4.3 T08A11.2
7	SpnPos_P0_ap	SpnDis_P0-EC	0.996124	0.996124	F58B8.3 Y49E10.14 R07E5.14 C29F9.7 R107.6 F54E7.3 Y37D8A.14 H38K22.2 T20D8.7 T20G5.1 T20H4.5 Y49E10.19 F11H8.4 C34E10.2 F01F1.7 C05D11.11 C07A9.2 C34C12.8
8	NucPos_P2_ap_f	NucDis_P2_f-EC	0.995519	0.995519	F58B8.3 R12B2.4 F11H8.4
9	NucPos_ABa_ap_l	NucDis_ABa_l-EC	-0.9952	0.995203	R144.2 F58B8.3 C07A9.3 F01F1.7
10	SpnPos_ABa_ap	SpnDis_ABa-EC	-0.99515	0.995152	F58B8.3 Y37D8A.14 R107.6 T20G5.2 R10E4.4 C38D4.3 C29F9.7 F01F1.7
11	NucPos_P2_ap_l	NucDis_P2_l-EC	0.994835	0.994835	R107.6 Y37D8A.14 F58B8.3 F11H8.4 C23G10.8 F56D2.1 T20G5.2 R08D7.2 F54E7.3 Y47D3A.d C34E10.2 Y49E10.14 C38D4.3 Y49E10.19 W07B3.2
12	NucPos_AB_ap_f	NucDis_AB_f-EC	-0.99405	0.99405	R107.6 R08D7.3 F58A4.3 F56A8.6 Y49E10.19 C05D11.11 T20H4.5 Y66A7.8 F26F4.11 C29F9.7
13	NucPos_P2_ap_m4	NucDis_P2_m4-EC	0.99325	0.99325	F58B8.3
14	NucPos_AB_ap_m	NucDis_AB_m-EC	-0.99321	0.993214	C34C12.8 Y49F4B.6 C07A9.2 R08D7.3 R107.6 C05D11.11 R13F6.1 C26E6.4 Y66A7.8 R08D7.2 C34E10.2 Y111B2D.h F56D2.1 R12B2.4 T20H4.5 W07B3.2 H38K22.2 C29F9.7 F58A4.3 F26F4.11 Y49E10.14 C35D10.13 C34E10.2 T20H4.5 R144.2 R12B2.4 W07B3.2 H38K22.2 C29F9.7
15	NucPos_AB_ap_m2	NucDis_AB_m2-EC	-0.98992	0.989923	C34C12.8 Y49F4B.6 C07A9.2 R107.6 C05D11.11 R13F6.1 Y111B2D.h Y66A7.8 C26E6.4 R08D7.2 Y49E10.14 C35D10.13 C34E10.2 T20H4.5 R144.2 R12B2.4 W07B3.2 H38K22.2 C29F9.7
16	SpnPos_P2_ap	SpnDis_P2-EC	0.989669	0.989669	R107.6 F58B8.3 C07A9.3 B0361.10 F35G12.8 R08D7.2 R13F6.1 W07B3.2 T20G5.2 C16C10.6
17	NucPos_P2_ap_m	NucDis_P2_m-EC	0.989519	0.989519	F58B8.3 Y37D8A.14 R107.6 F11H8.4 C55D10.13 C07A9.3
18	NucAng_ABa_p2	NucDis_ABa_p2-EC	0.989119	0.989119	F58B8.3 F54E7.3 R107.6 B0361.10 F58A4.3 C23G10.8 T08A11.2 R08D7.2
19	NucPos_P2_ap_m4	NucDis_P2_m4-EC	0.988783	0.988783	F58B8.3 F54E7.3 R107.6 C07E5.14 C07A9.3
20	NucPos_AB_ap_f	NucDis_AB_f-EC	-0.987766	0.987766	R107.6 Y66A7.8 F58B8.3 Y49E10.19 F56D2.1 Y71H2.378.F56A8.6 T20H4.5 F58A4.3 R08D7.2
21	NucPos_AB_ap_m	NucDis_AB_ap_m	-0.98772	0.98772	R107.6 C35D10.13 T26G10.1 C34C12.8 R13F6.1 F26F4.11 C38D4.6 R02A9.6 Y71H2.378.Y111B2D.h Y49E10.14 F54E7.3
22	NucPos_P2_ap_divBp	NucDis_P2_divBp-EC	0.986458	0.986458	F58B8.3 R07E5.14
23	NucPos_ABp_ap_f	NucDis_ABp_f-EC	-0.9783	0.978301	T26G10.1 F56D2.1 Y37D8A.14 R107.6 Y71H2.378.F54E7.3 F58B8.3 C05D11.11 C07A9.2 C34E10.2 F02A9.6 Y47D3A.d F01F1.7 R08D7.1 B0464.7 F56A8.6 C34C12.8 H38K22.2 R144.2 Y49E10.19 C29F9.7
24	NucPos_AB_ap_m	NucDis_AB_ap_m	0.976845	0.976845	R107.6 C34C12.8 F02A9.6 C05D11.11 C35D10.13 Y111B2D.h T20G5.1 R144.2 T20H4.5
25	NucPos_AB_ap_P2	NucDis_AB_ap_P2-EC	-0.976823	0.976823	E107.6 C05D11.11 C35D10.13 Y111B2D.h T20G5.1 R144.2 T20H4.5
26	NucDis_AB_m-EC	NucPos_AB_ap_m	-0.97655	0.976546	C34C12.8 Y49F4B.6 C07A9.2 R107.6 R08D7.3 R08D7.2 F02A9.6 C05D11.11 Y66A7.8 R13F6.1 C35D10.13 C34C10.2 W07B3.2 T20G5.1 F26F4.11
27	NucPos_P2_divAbA	NucPos_P2_divAbA	0.975727	0.975727	C23G10.8 Y70D8A.14 T08A11.2 F58B8.3 R107.6 Y43F4B.6 F56D2.1 R13F6.1 C38D4.6 Y66A7.8 C34C12.8 Y49E10.14 T20G5.2 C16C10.6 R08D7.2 B0361.10 W07B3.2 T20G5.1 R07E5.14 F58A4.3 T20H4.5
28	NucPos_AB_l_m	NucPos_AB_l_m	0.975014	0.975014	C34C12.8 R107.6 R13F6.1
29	NucPos_ABal_divEMS	NucDis_ABal_divEMS-EC	-0.97393	0.97392	F56D2.1 R107.6 F58A4.3 C26E6.4
30	NucPos_P1_ap_m	NucDis_P1_m-EC	0.972349	0.972349	
31	NucPos_ABal_f	NucDis_ABal_f-EC	-0.97233	0.972331	F56D2.1 R107.6 R08D7.2 R08D7.1 Y71H2.378.a

Integrated model of *C. elegans* embryogenesis

Bridging biochemical network and phenotypic network.



CREST Team

Shuichi Onami, RIKEN Center for Biosystems Dynamics Research

Systems biology

- Measurement system
- Basic idea of new analysis method
- Database

Koji Kawakami, Department of Pharmacoepidemiology, Kyoto University

Applied statistics

- Generalized structural equation modeling
- LASSO and LASSO variants

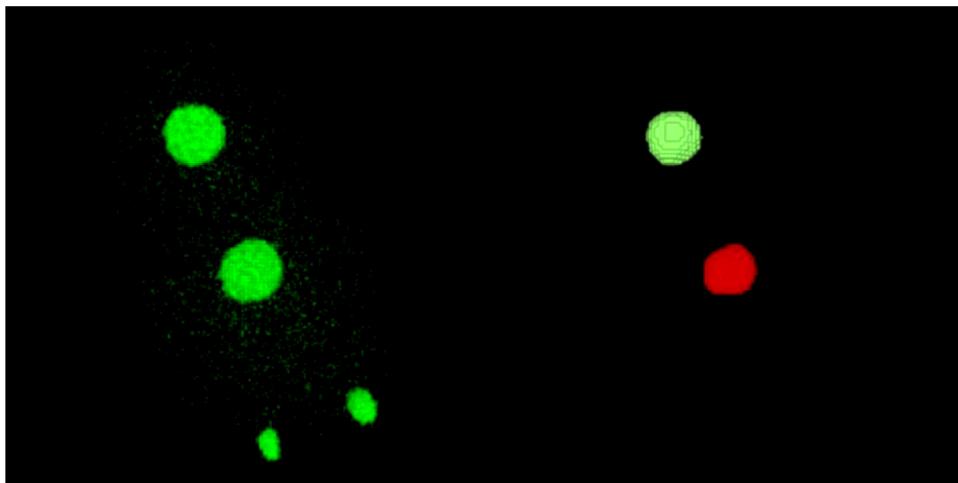
Koji Koyamada, Academic Center for Computing and Media Studies, Kyoto University

Scientific visualization

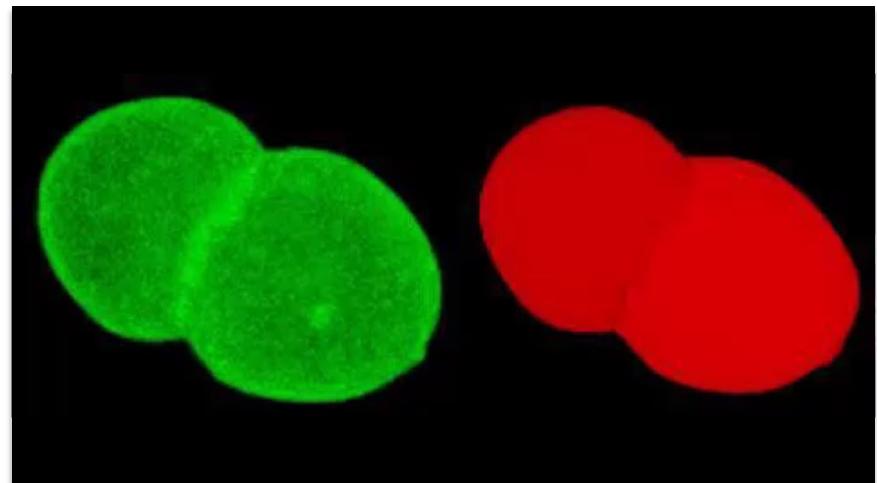
- Edge concentration
- Empirical Dynamic Modeling
- Natural language processing

New measurement system

Nucleus

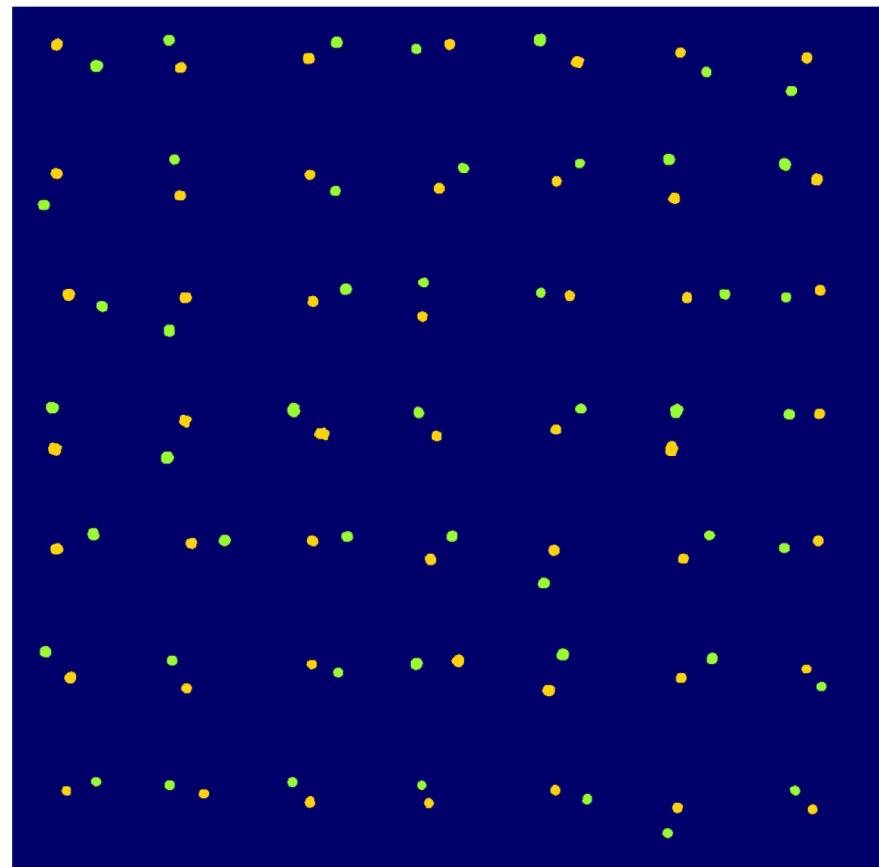


Cell membrane

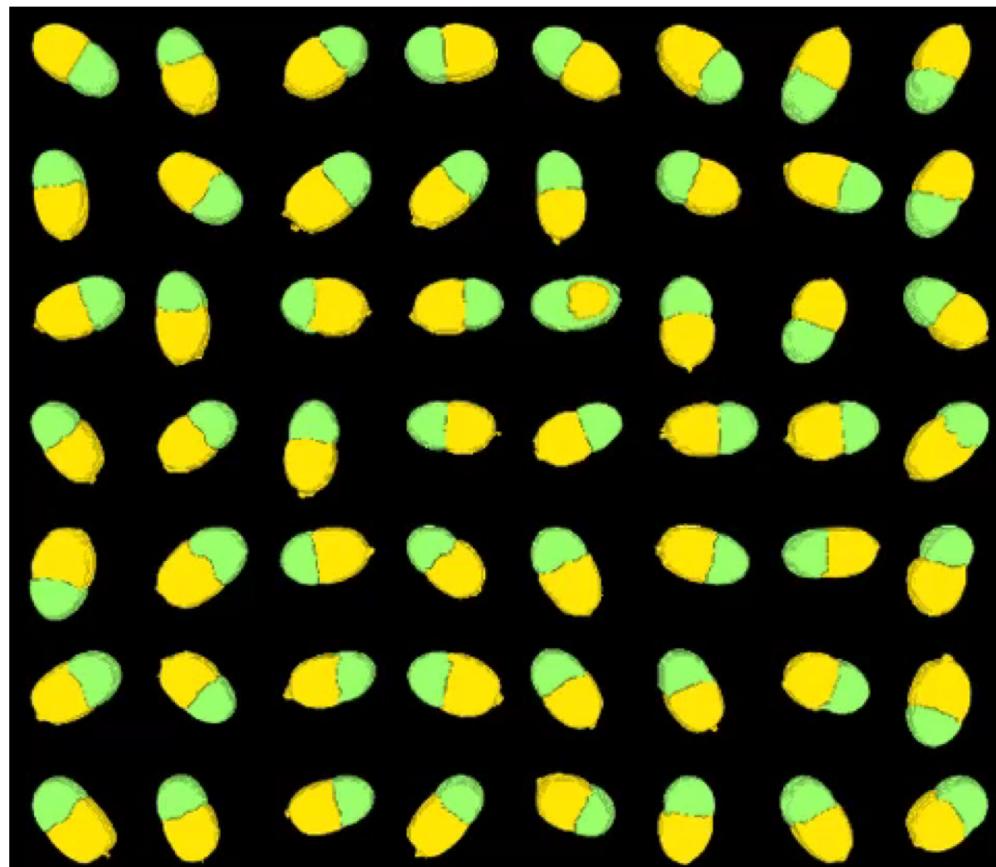


New data set of nuclear and cell shape dynamics

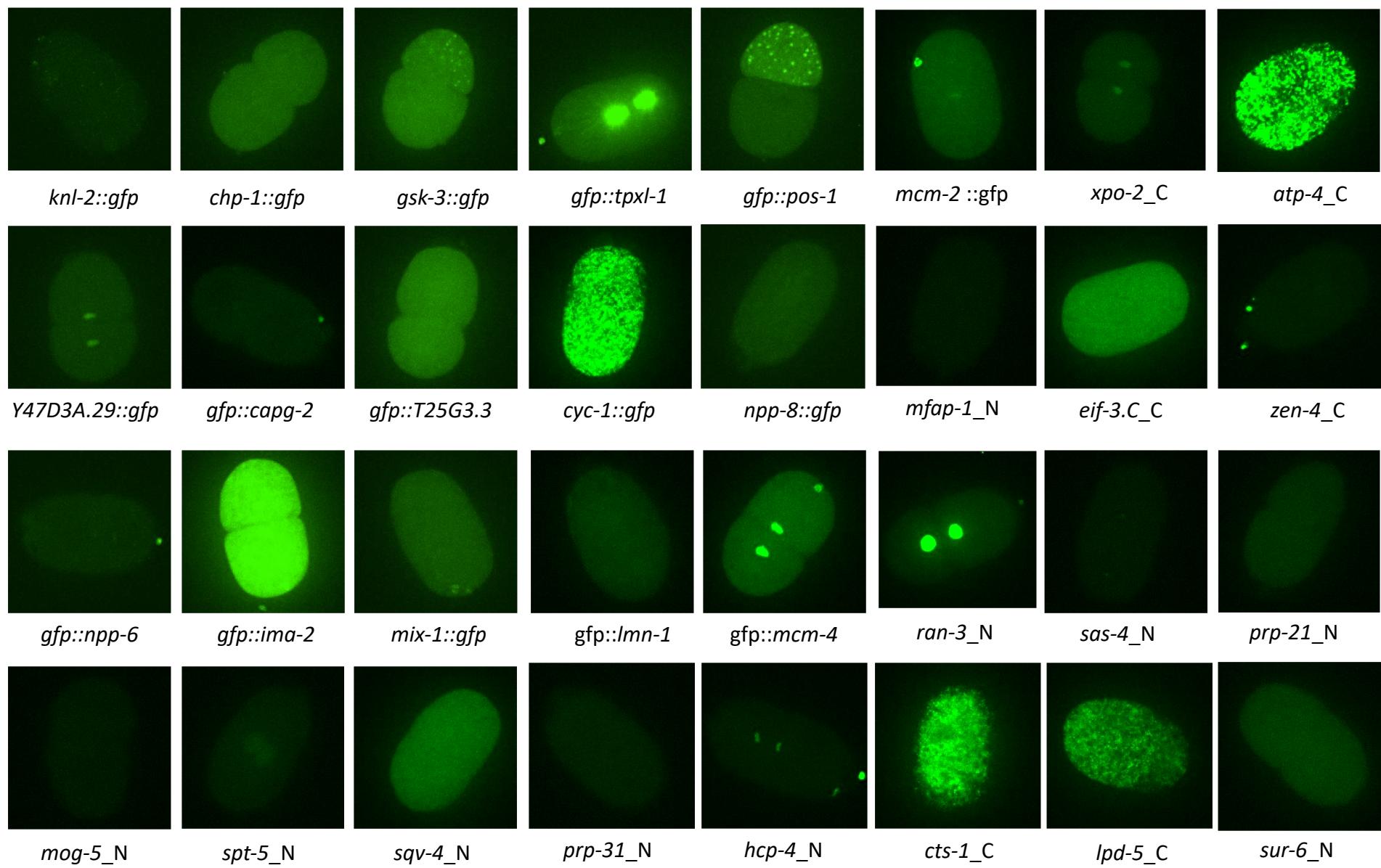
Nucleus



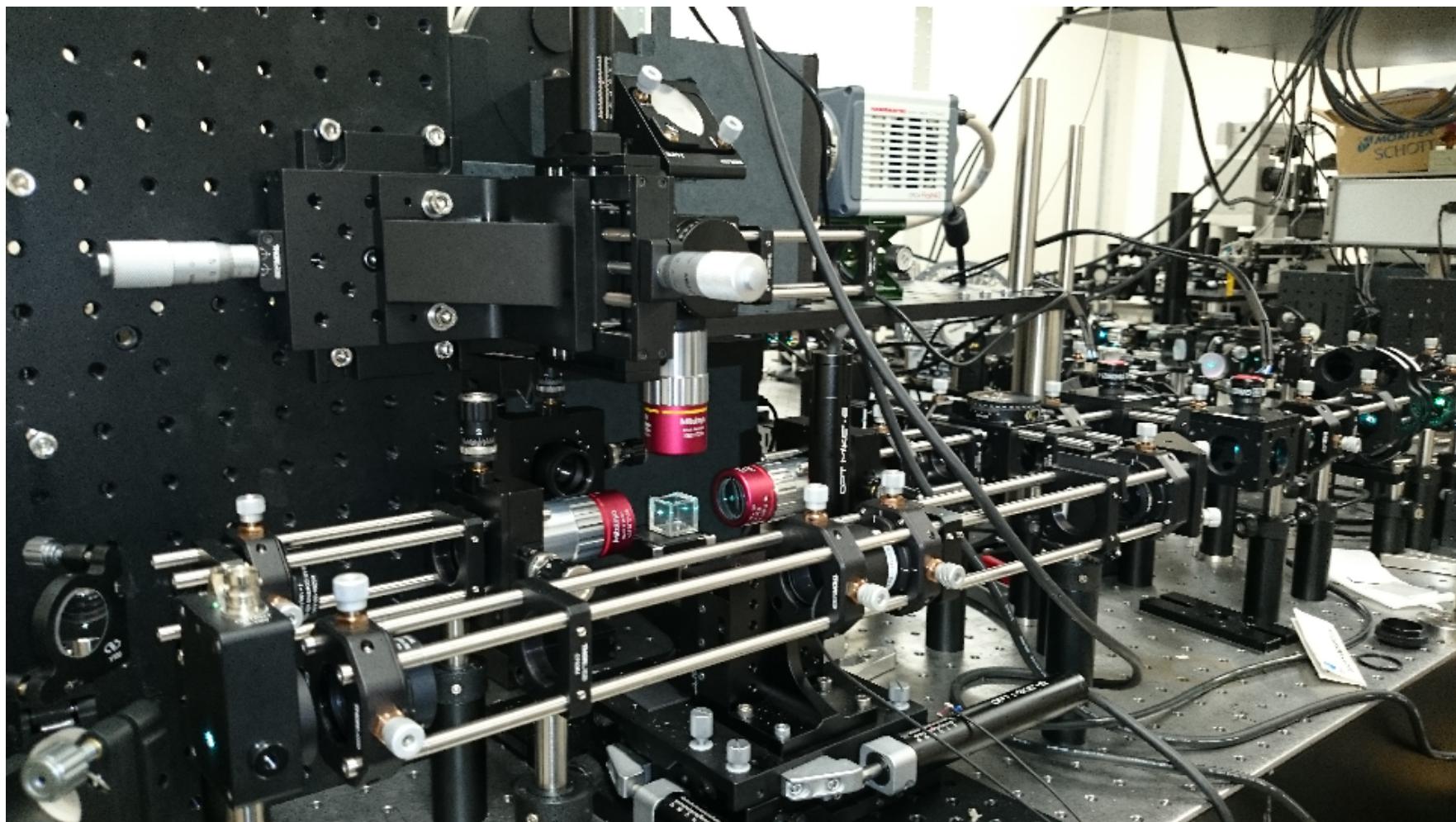
Cell membrane



4D gene expression dynamics data



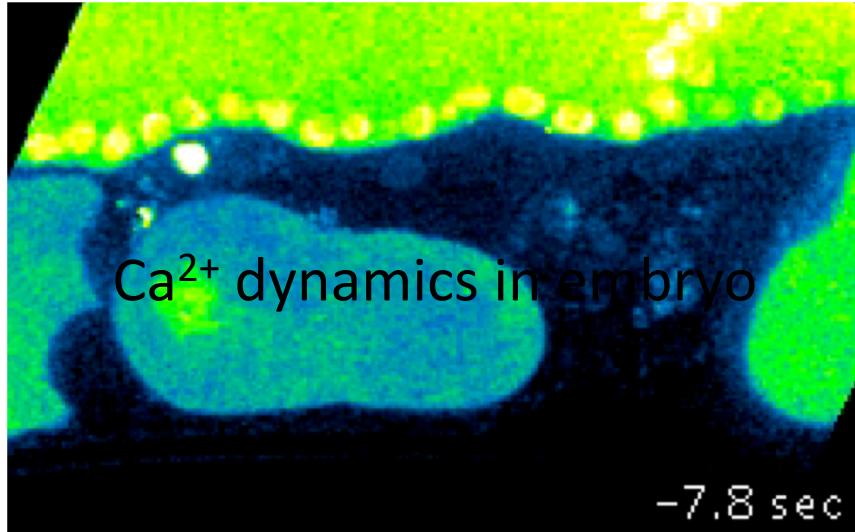
New microscopy for mouse embryo and organoid



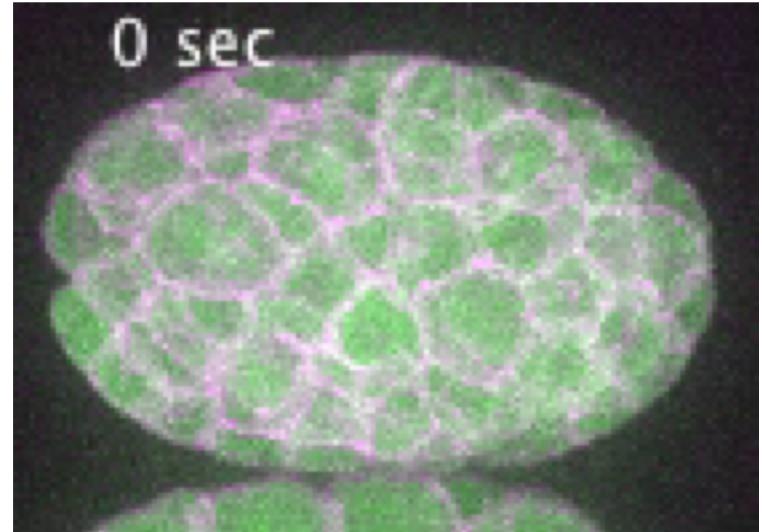
Collaboration with T. Watanabe T and Y. Fufuta (RIKEN)

Developmental dynamics data

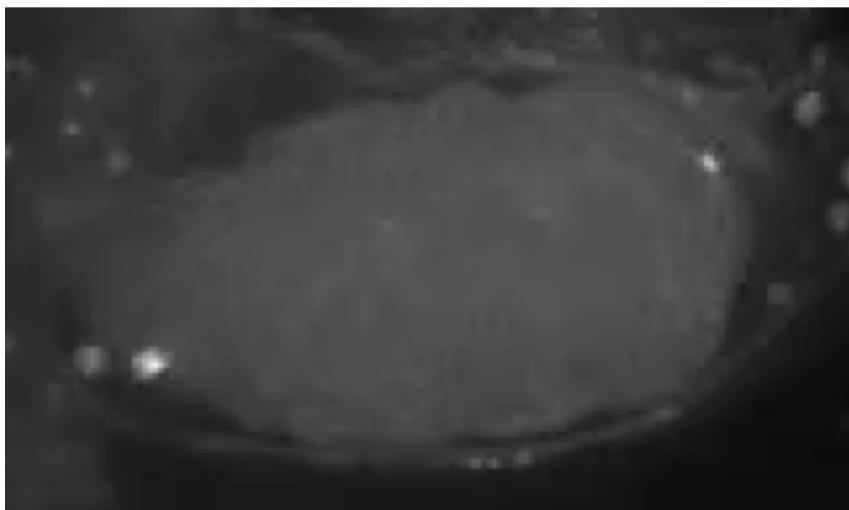
Ca^{2+} dynamics upon fertilization



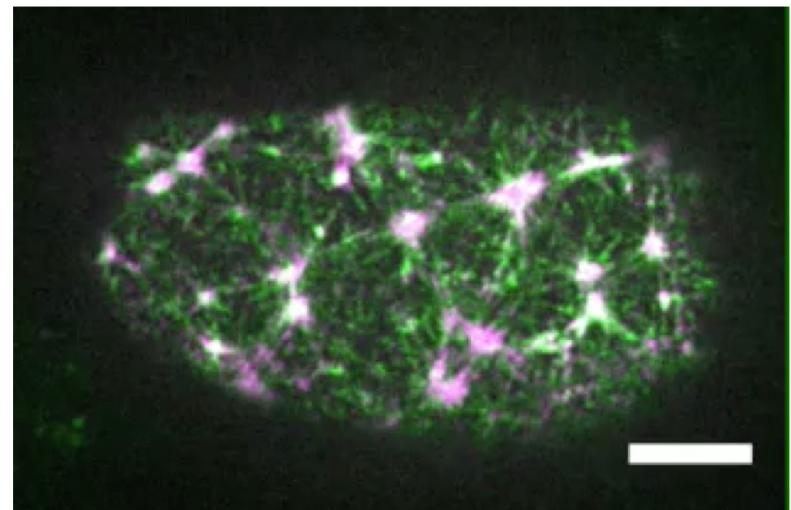
Ca^{2+} dynamics in embryo

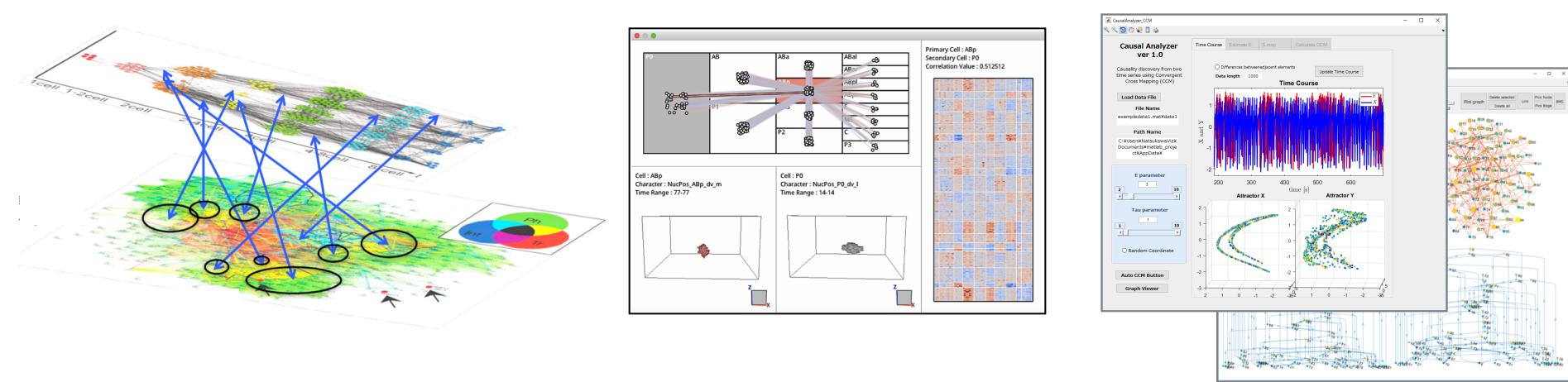


Nuclear dynamics in embryo

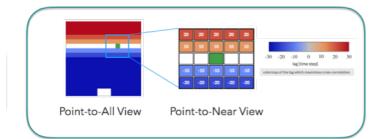


Cell cortex dynamics in embryo

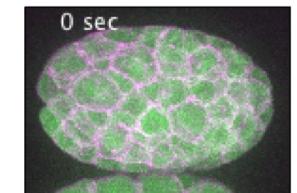




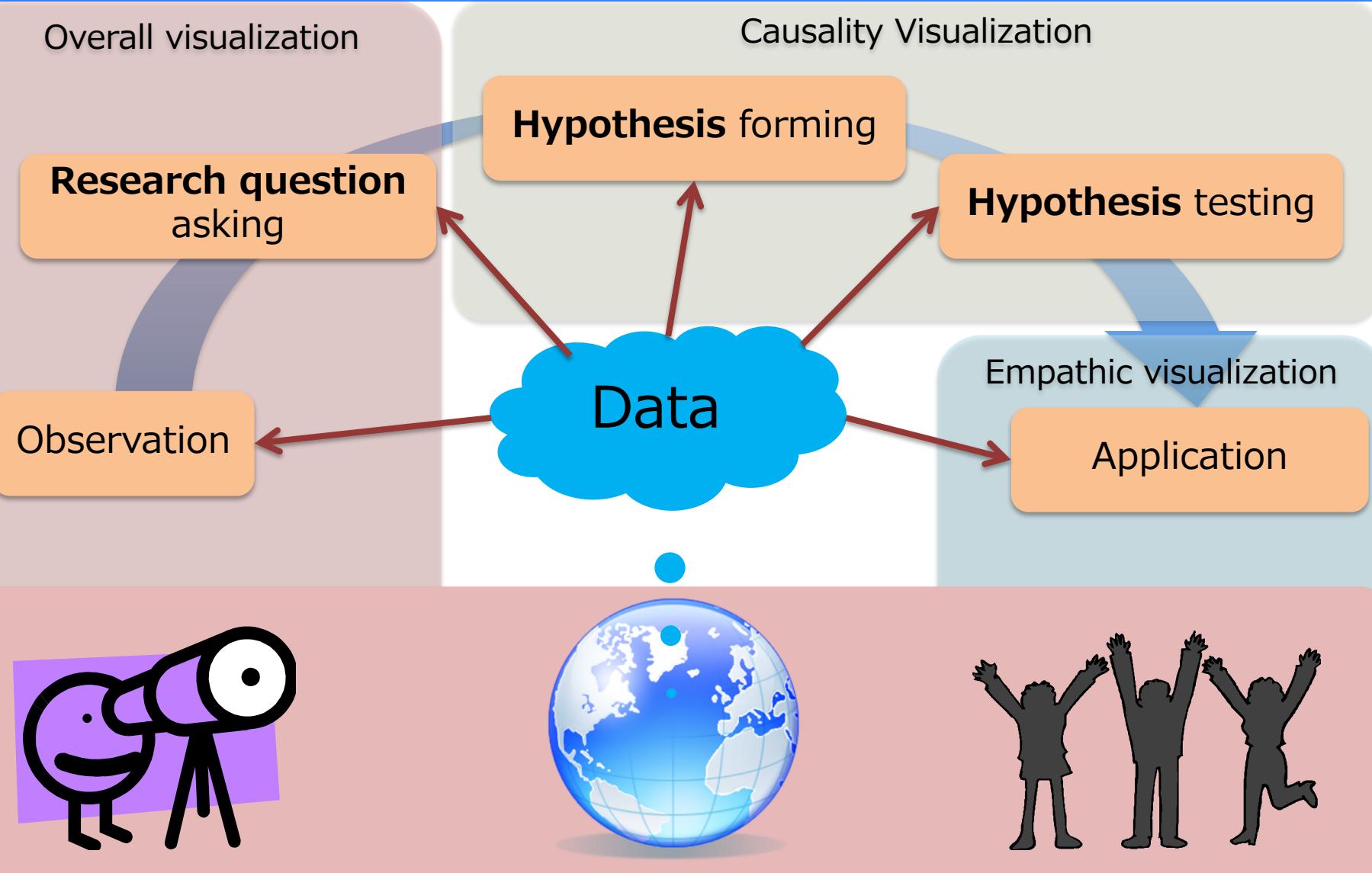
Visual data science and its applications to *C. elegans* live imaging data



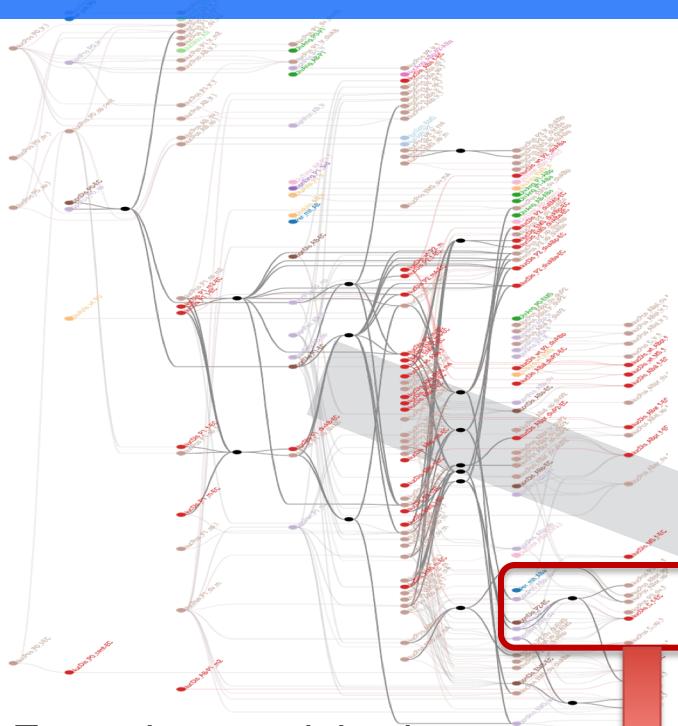
July 11, 2018
Kyoto University
Koji Koyamada



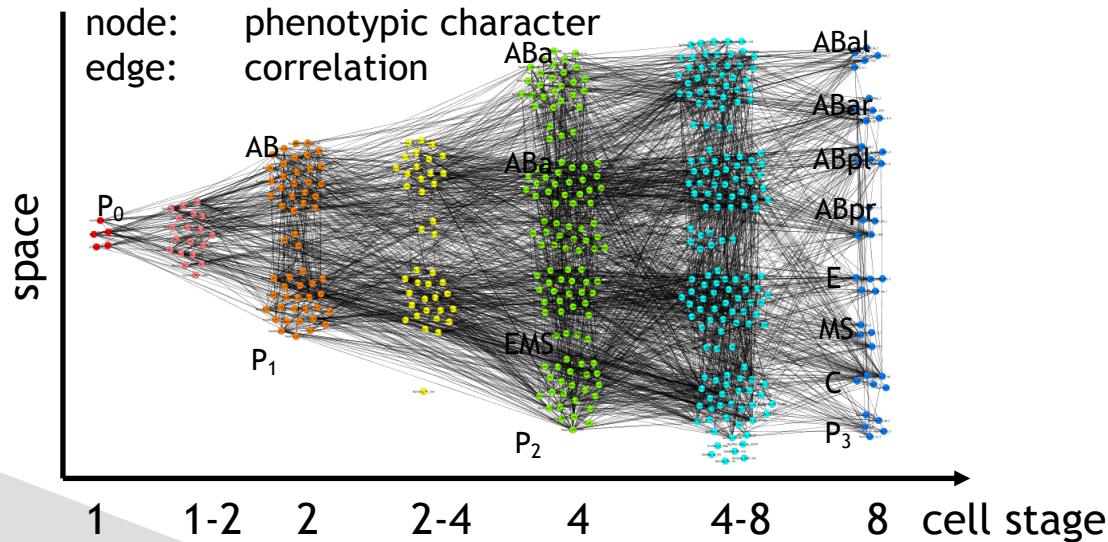
Visual data science



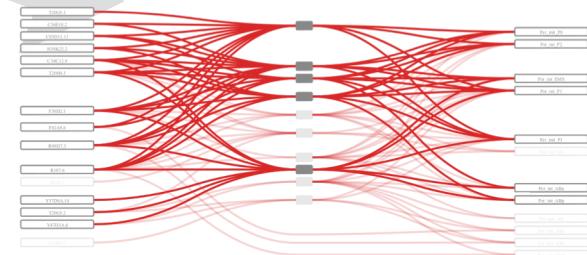
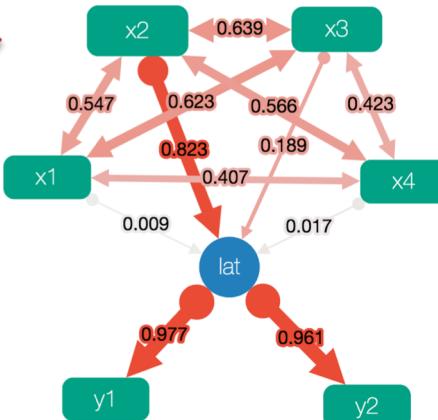
Causality exploration in the phenotypic network



Extracting special sub-structure
of phenotypic character network



Validating latent factors using
structural equation modeling (SEM)

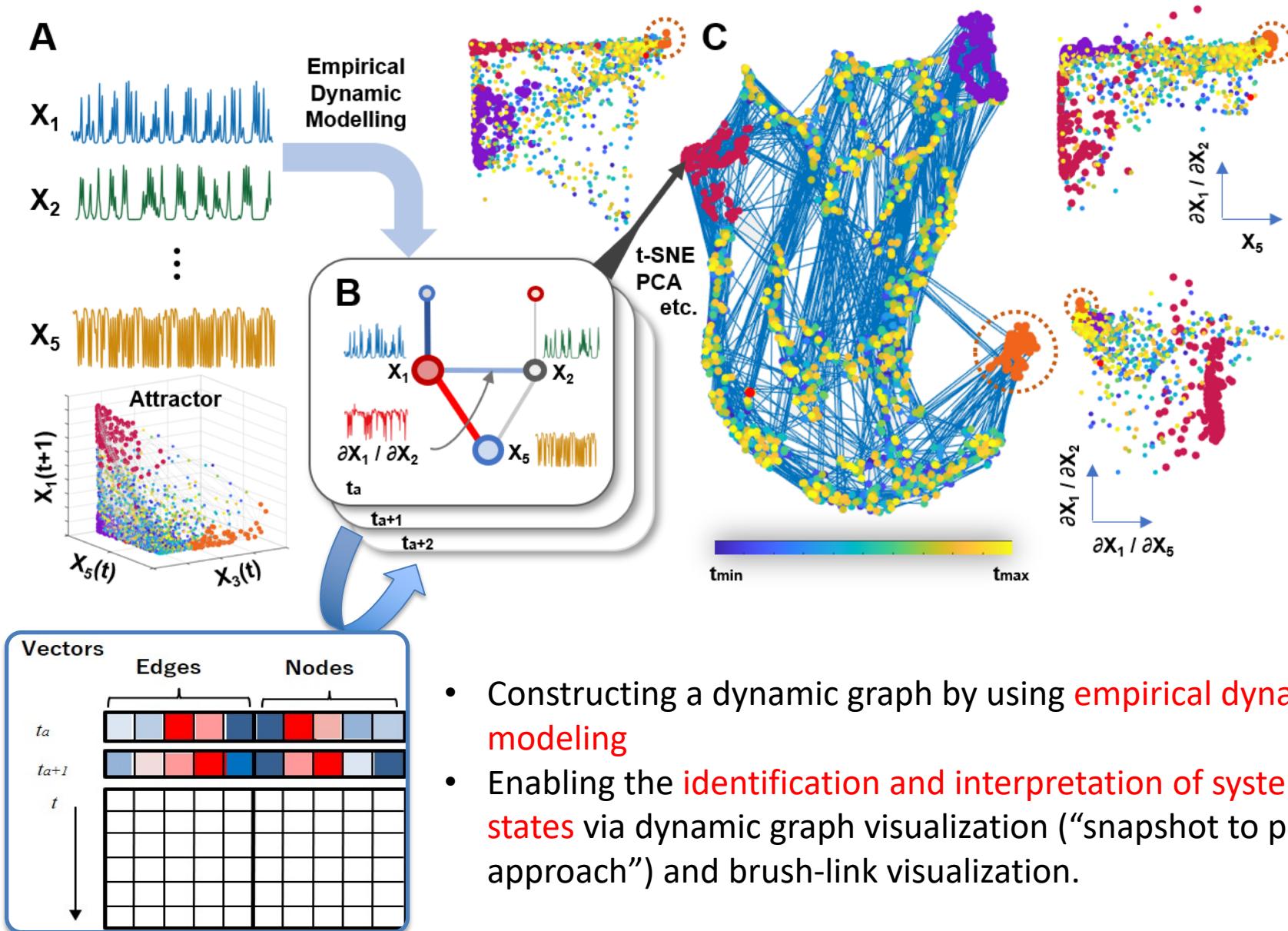


Connecting genes and
phenotypic characters
using biclustering

Publications

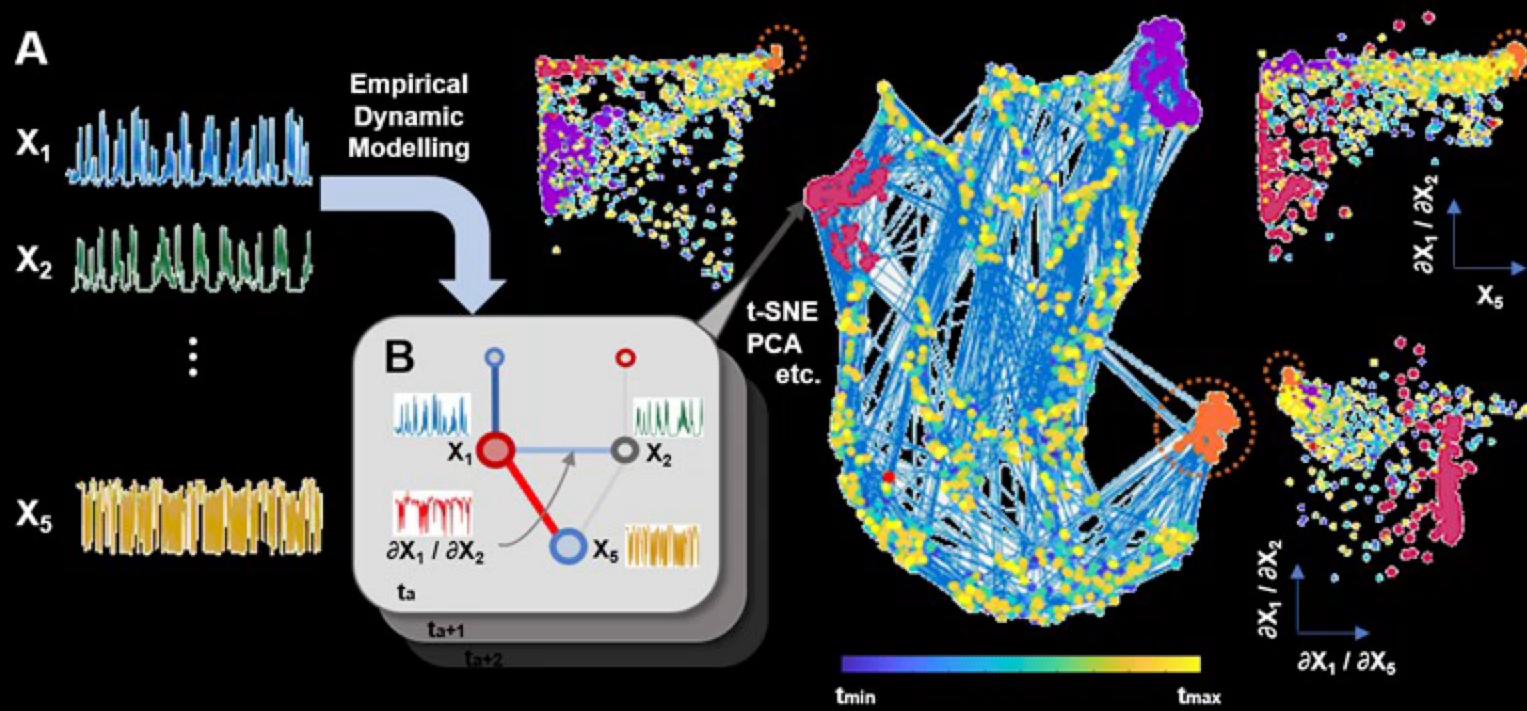
- Onoue, Y., & Koyamada, K. (2017). Quasi-biclique Edge Concentration : A Visual Analytics Method for Biclustering. In *Proceedings of IEEE Pacific Visualization 2017* (pp. 215–219).
- Onoue, Y., Ashida, Y., & Koyamada, K. (2017). Interactive Model Building and Visualization for Structural Equation Modeling. In *The 14th Asian Symposium on Visualization*.

Exploration of system states in time-series data





A Visual Analytics Approach for the Identification of System States based on Empirical Dynamic Modeling

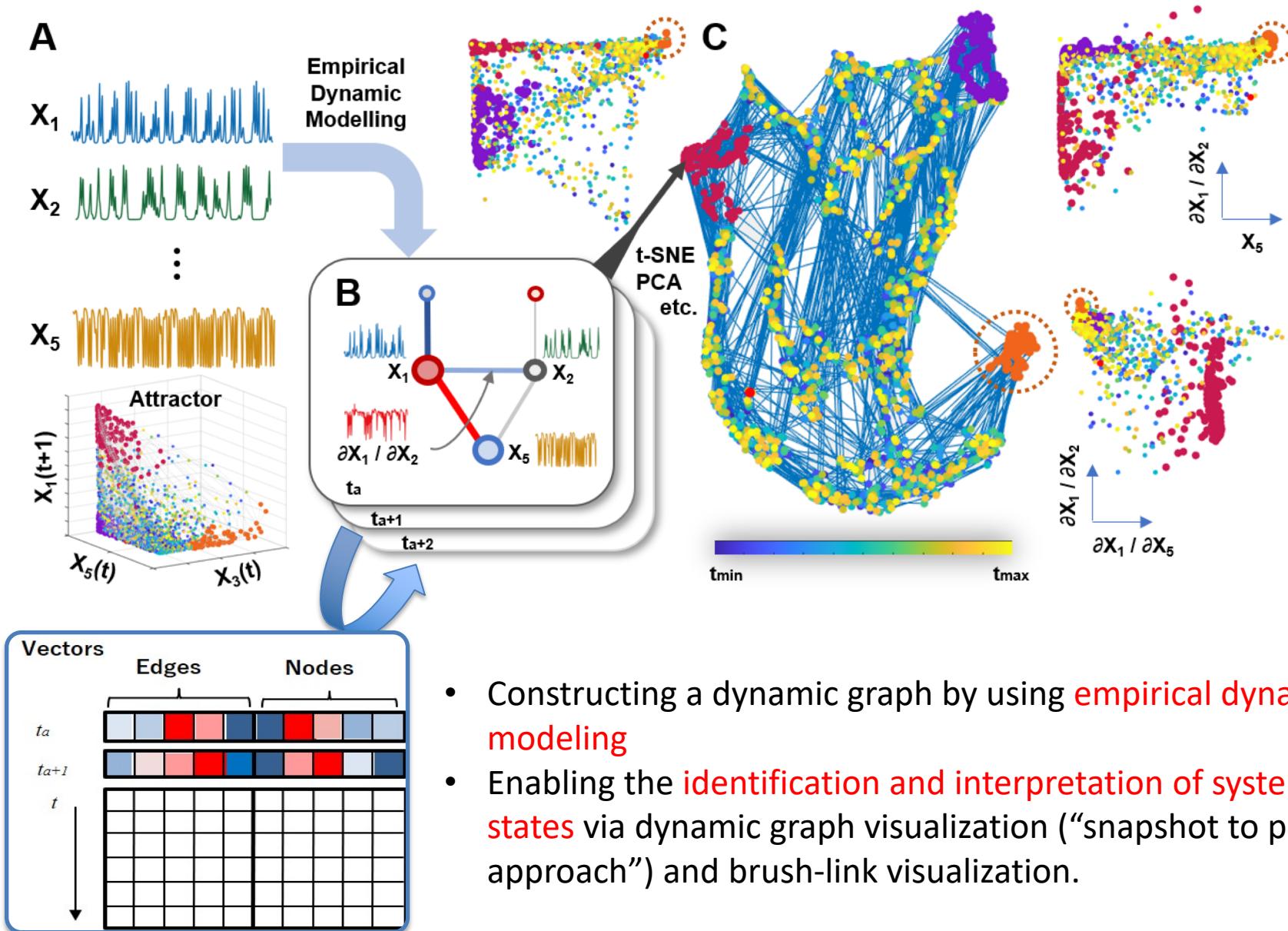


Hiroaki NATSUKAWA*, Ethan DEYLE**, Koji KOYAMADA*, George SUGIHARA**

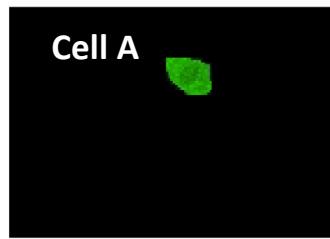
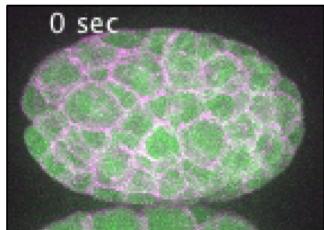
*Kyoto University, Academic Center for Computing and Media Studies

**UC SanDiego, Scripps Institution of Oceanography

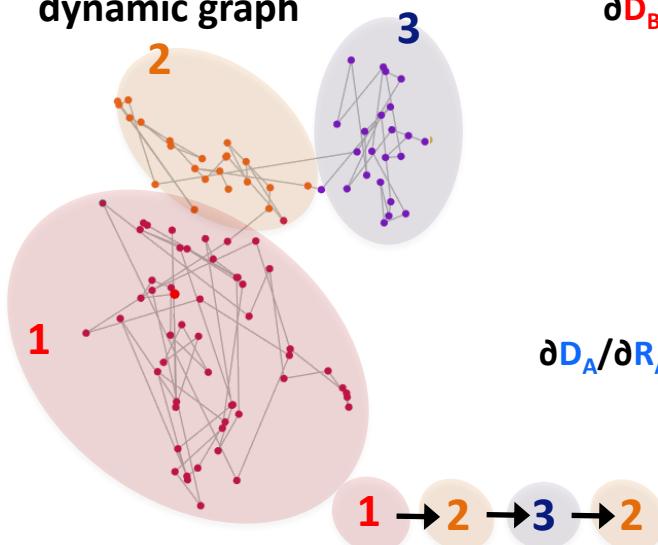
Exploration of system states in time-series data



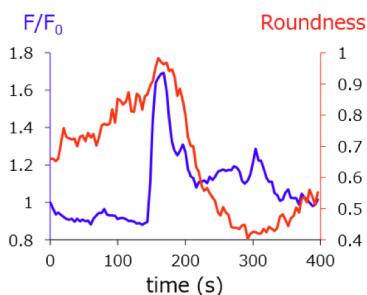
Calcium dynamics in early cell division phase



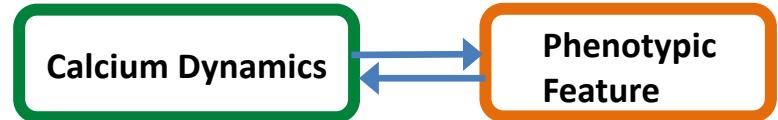
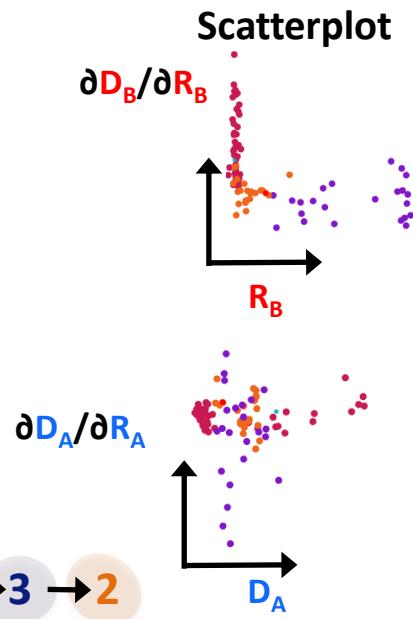
2D mapping of dynamic graph



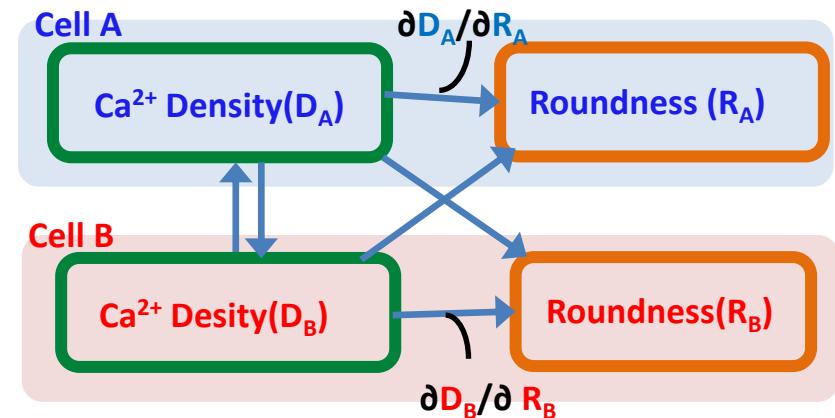
150918-4
Bin: 2x2 (=256x256)
EM: 300x
G: 25 ms, 20% laser
R: 20 ms, 50% laser
z: 1 μ m x 20 planes
t: 4 sec interval



Scatterplot



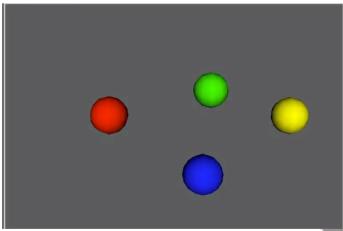
Time varying relationships between Ca^{2+} density and roundness of the two cells are analyzed by our visual analytics tool.



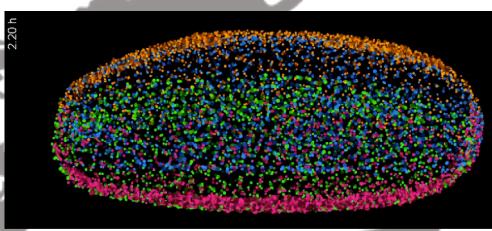
- The independent increases of interaction between Ca^{2+} density and roundness in each cell
- State transition in cell division phase

Quantitative biological dynamics data world-wide

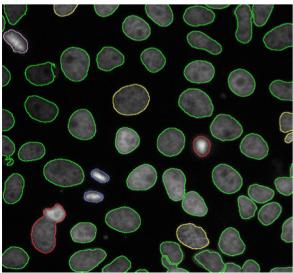
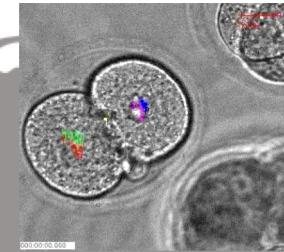
(Bao et al., 2006)



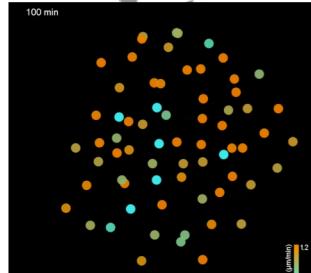
(Keller et al., 2010)



(Kurotaki et al., 2007)



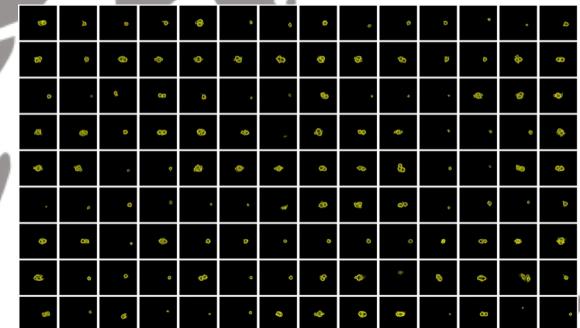
(Heldet et al., 2010)



(Keller et al., 2008)



(Yemini et al., 2013)



(Kyoda et al., 2013)

SSBD Database

[» Japanese](#)

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[Data Search](#)

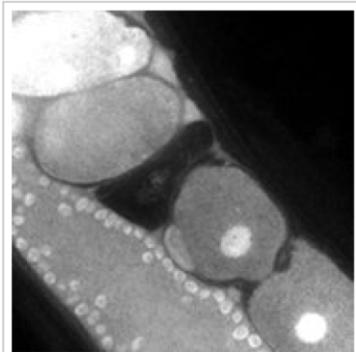
[Image Search](#)

Introduction of SSBD

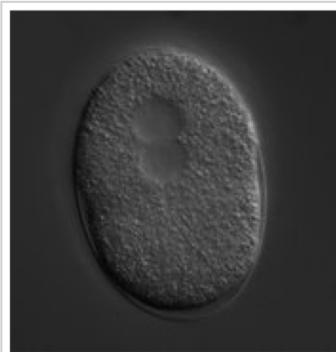
Systems Science of Biological Dynamics (SSBD) database provides a rich set of open resources for analyzing quantitative data and microscopy images of biological objects, such as single-molecule, cell, gene expression nuclei, etc. Quantitative biological data and microscopy image are collected from a variety of species, sources and methods. These include data obtained from both experiment and computational simulation.

Samples

Microscopy images



Calcium response and shape changes in oocyte of *C. elegans*

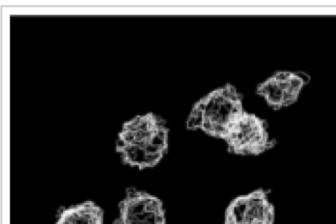
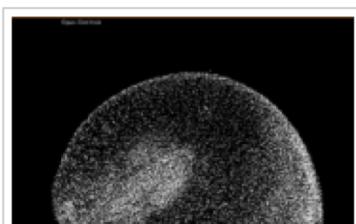


Nuclear division dynamics in *C. elegans* wild-type embryo



ERK activity in rat kidney epithelial (NRK-52E) cells

Quantitative data



News and Events

Jul. 10, 2017: System maintenance notice (Date: July 10 (JST))
SSBD will not be available on 10 July 2017 due to unscheduled maintenance

May. 20, 2017: SSBD API notice
SSBD REST API full service is now available.

[Older news ...](#)

Information

OMERO: Images can be viewed on [OMERO.web](#). If you have problem viewing the images on the website, please click on the drop-down arrow on the right of 'public data' on the bar above the data tree, select 'Public' group and 'public data' to view the images (click [here](#) for more details).

OMERO session ID: None

Introducing SSBD Database



Introducing the

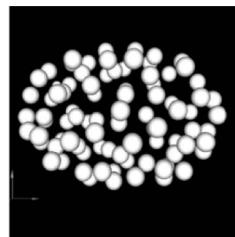
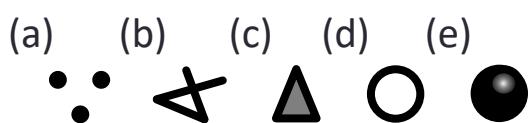
SSBD Database
Systems Science of Biological Dynamics



BDML: Biological Dynamics Markup Language

Unified format for representing quantitative biological dynamics data

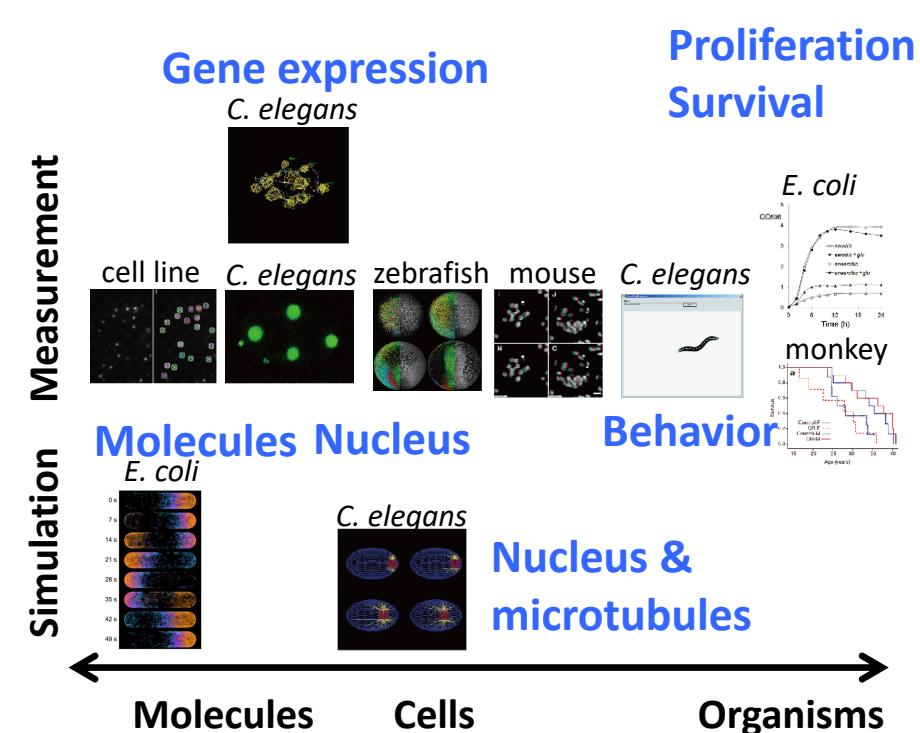
- Unified way to represent spatial temporal information



- Based on XML
 - High extensibility
 - High readability

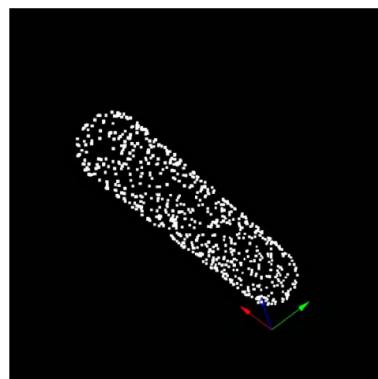
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  <measurement>
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    <point>
      <xyz>
        <x>10</x>
        <y>30</y>
        <z>18</z>
      </xyz>
    </point>
  </measurement>
</component>
```

- From molecules to cells and organisms



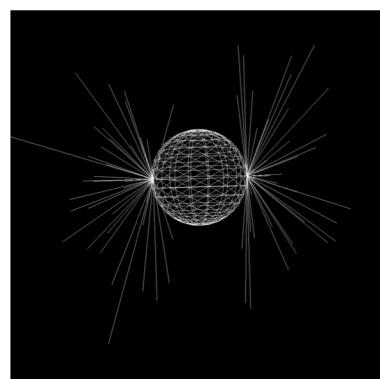
Biological dynamics data in SSBD

E. coli



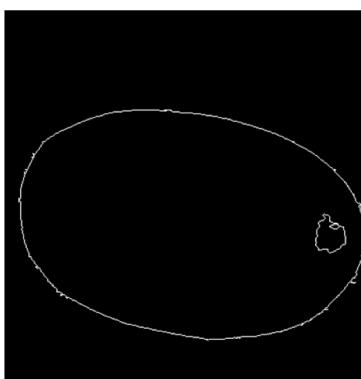
(Arjunan & Tomita 2007)

C. elegans



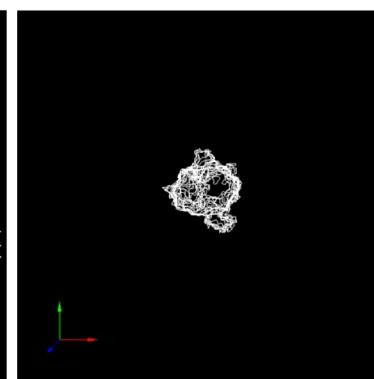
(Kimura & Onami 2005)

C. elegans



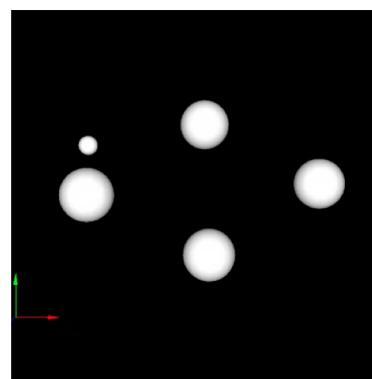
(Tohsato et al., submitted)

C. elegans



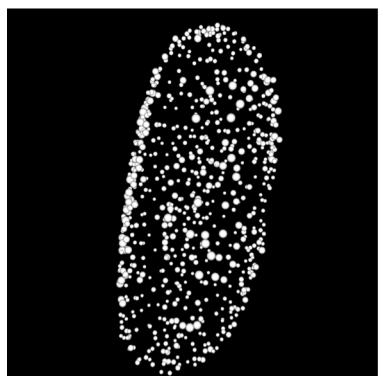
(Kyoda et al. 2013)

C. elegans



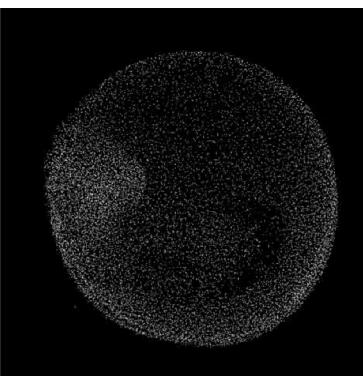
(Bao et al. 2006)

D. melanogaster



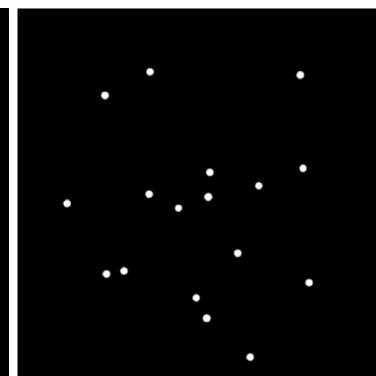
(Keller et al. 2010)

Zebrafish



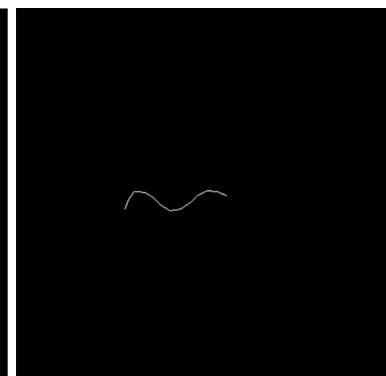
(Keller et al. 2008)

mouse



(Bashar et al. 2012)

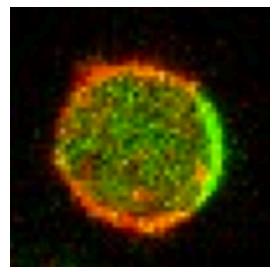
C. elegans



(Cronin et al. 2005)

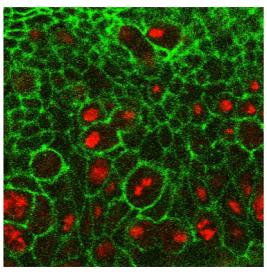
SSBD has started collecting/sharing microscopy images that have not been image processed

Dictyostelium



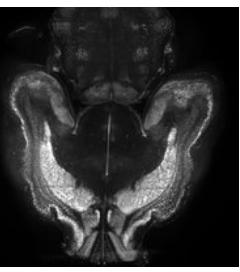
(Watabe et al. 2015)

D. melanogaster



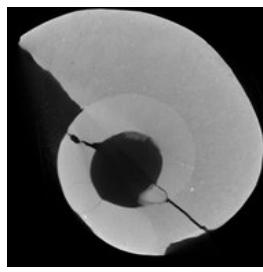
(Kondo & Hayashi 2013)

M. musculus



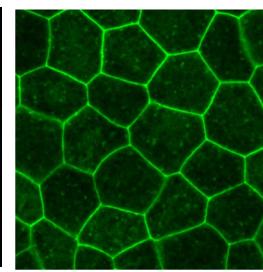
(Susaki et al. 2014)

D. cf. damesi



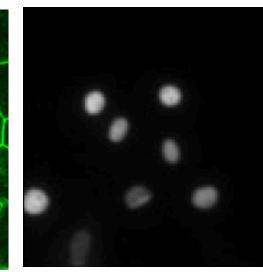
(Inoue & Kondo 2016)

X. laevis



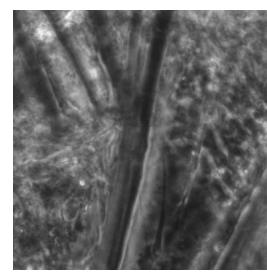
(Inomata et al. 2013)

Cultured cell



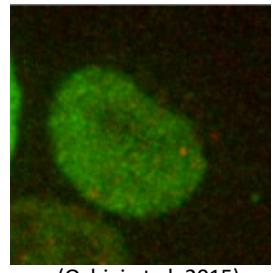
(Aoki et al. 2013)

Mouse derived iPS cell



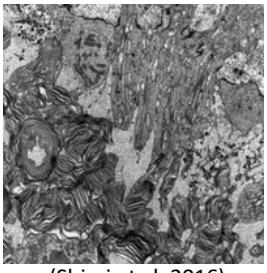
(Tanaka and Fujita 2015)

Mouse ES cell



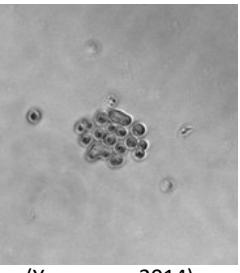
(Ochiai et al. 2015)

Human derived cultured cell



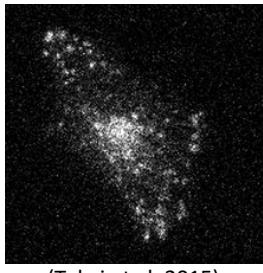
(Shirai et al. 2016)

Mouse derived cultured cell



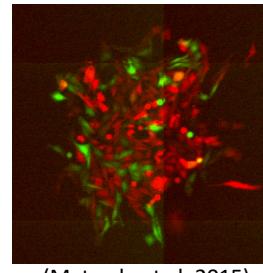
(Yonemura 2014)

Dog derived cultured cell



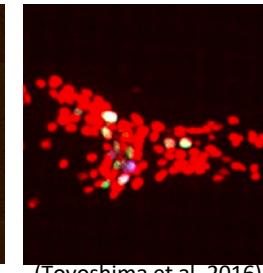
(Takai et al. 2015)

Hamster derived cultured cell



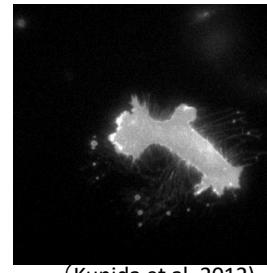
(Matsuda et al. 2015)

C. elegans Nerve cell



(Toyoshima et al. 2016)

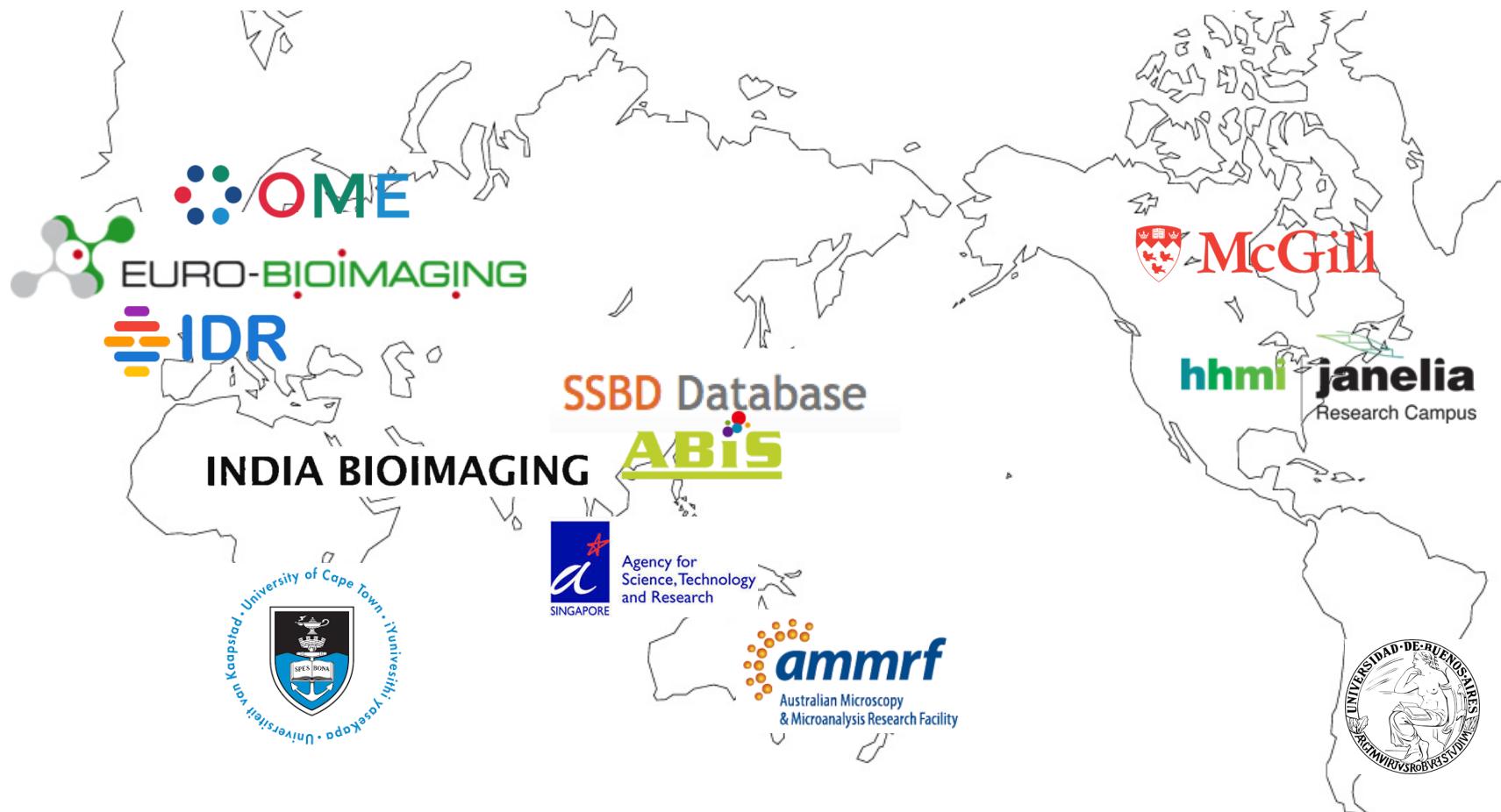
Cultured cell



(Kunida et al. 2012)

Global BioImaging Project

GLOBAL
BIOIMAGING
growing collaboration



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