CG020 Genomika
Bi7201 Základy genomiky

High throughput approaches Systems biology

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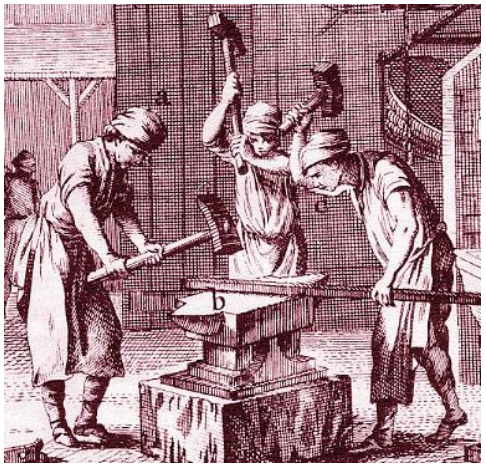
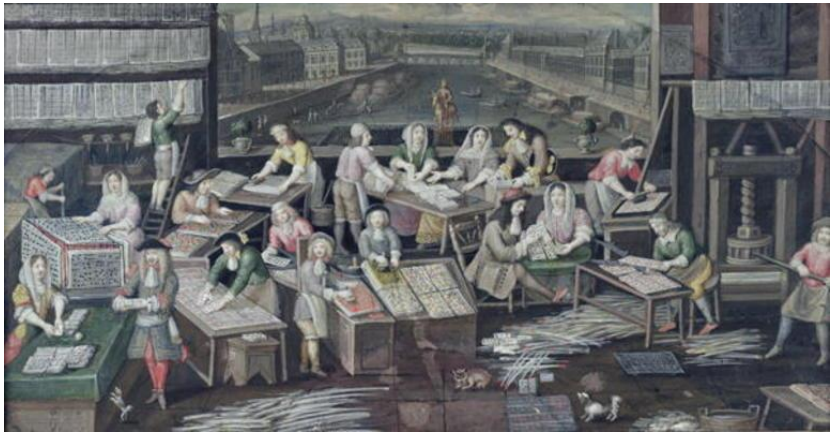
Přehled

- High throughput biology
  - Automation
  - Omics
  - Transcriptomics and high throughput transcriptomics
  - High throughput interactomics and how to read it
  - High throughput of anything
  - 1000(+1) genomes, GWAS
  - ENCODE
- Little about Systems biology
  - Omics
  - Holism and modules
  - Gene regulation in E. coli
  - Negative autoregulatory loops
  - Robustness of negative autoregulatory networks
  - Positive autoregulatory networks

Examples of automation in human history



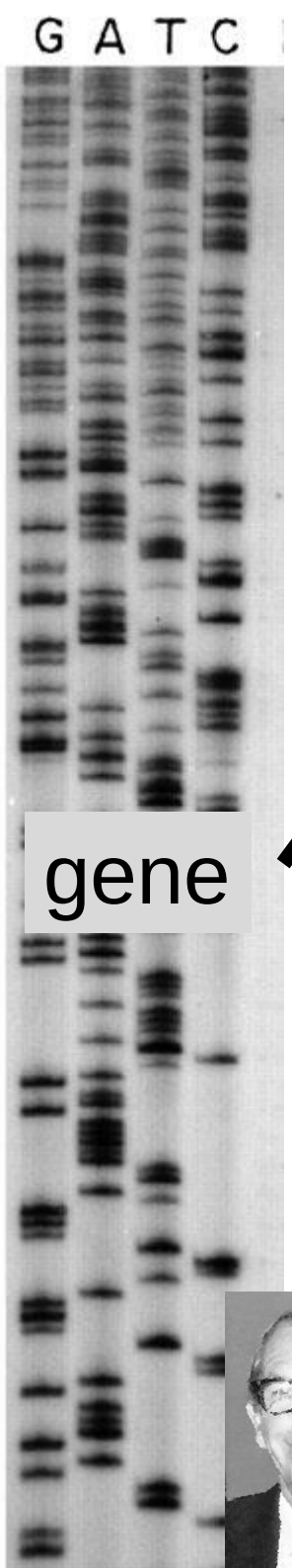
blacksmith



manufacture

assembly line

robotic automation

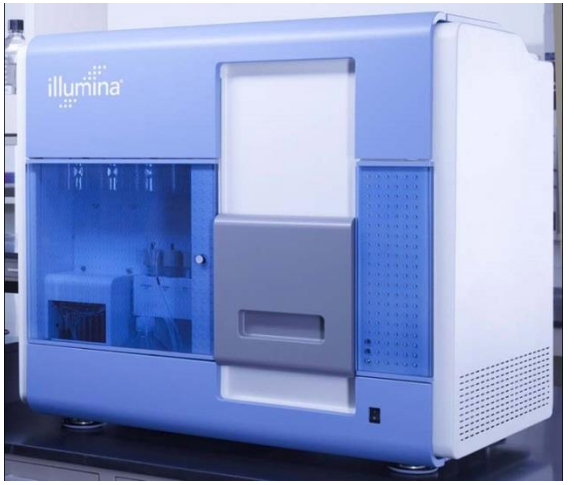


High throughput sequencing

gene

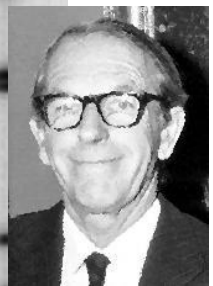
genes

genome

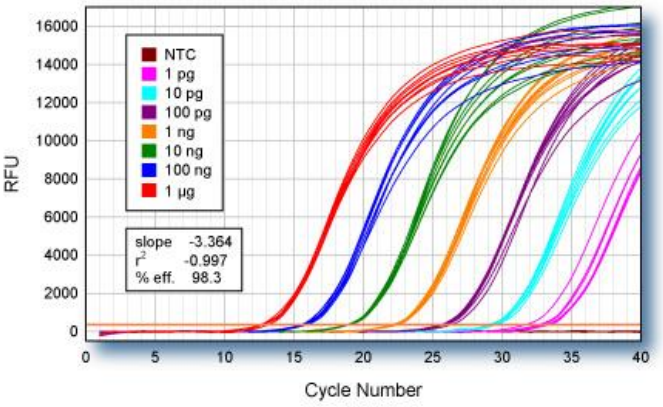


genomes

populations?



Automation in transcriptomics

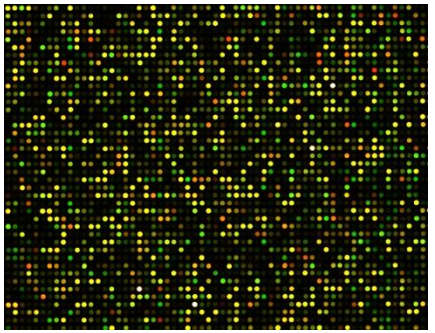


qRT-PCR

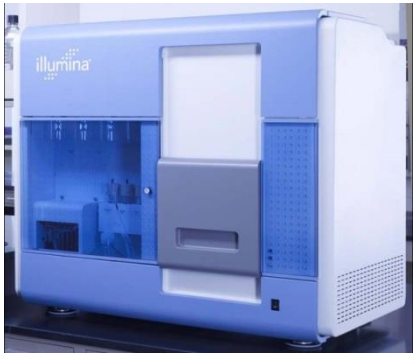
multichannel pipette

bigger multichannel pipette

pipetting robot

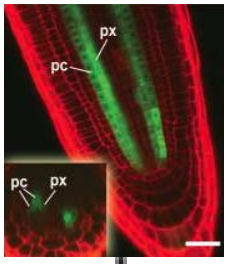


microarray



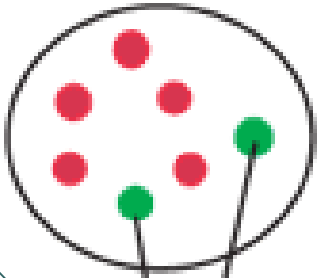
deep sequencing

Protoplasting/cell sorting

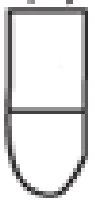


Cell-specific GFP line

Protoplast cells

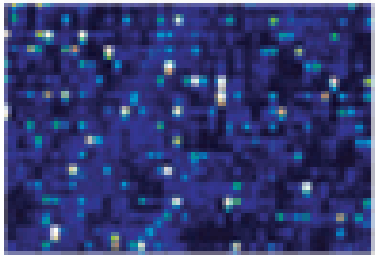


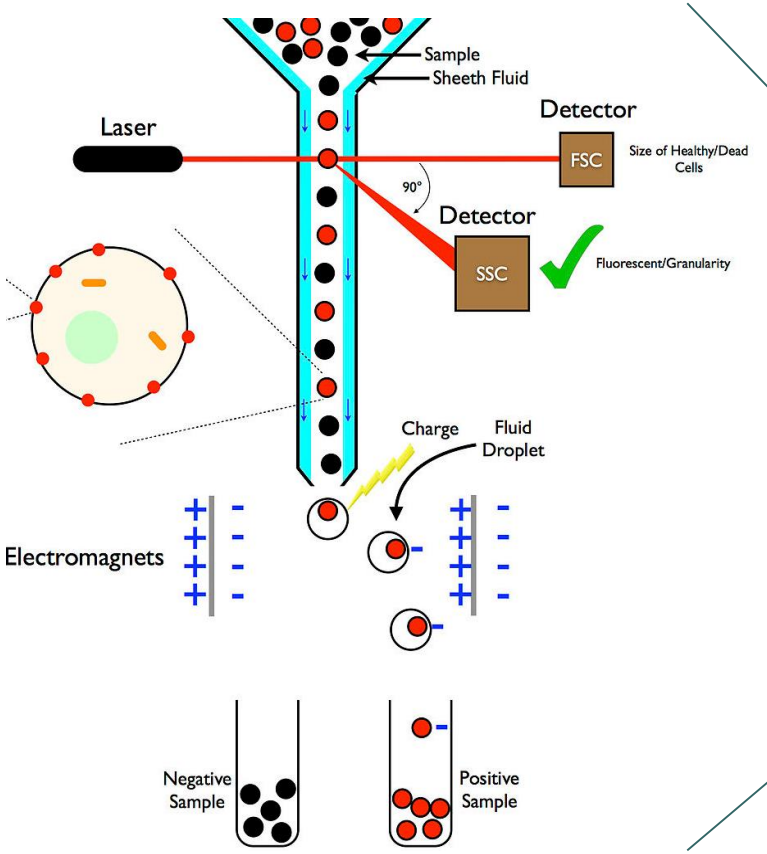
Sort GFP-positive protoplasts



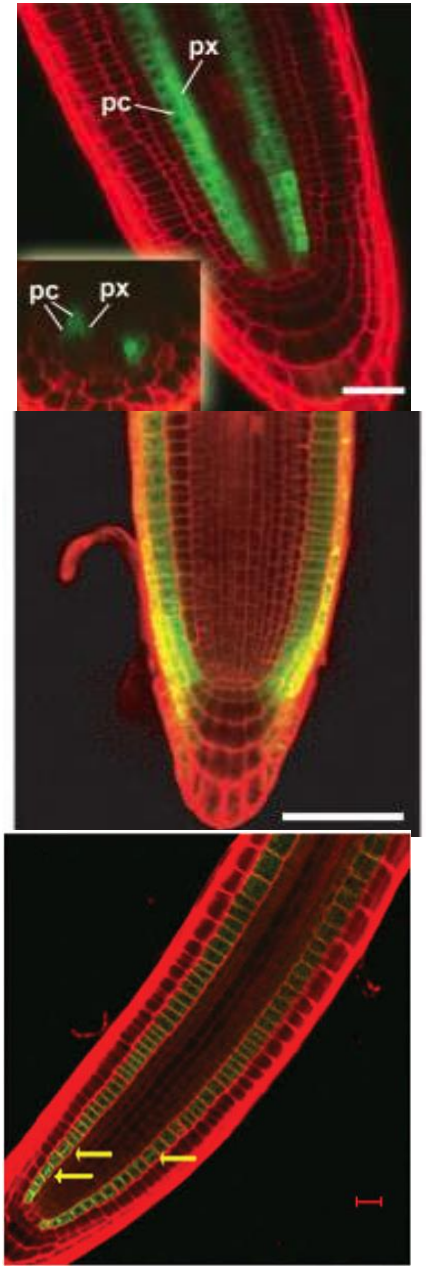
Extract and label mRNA

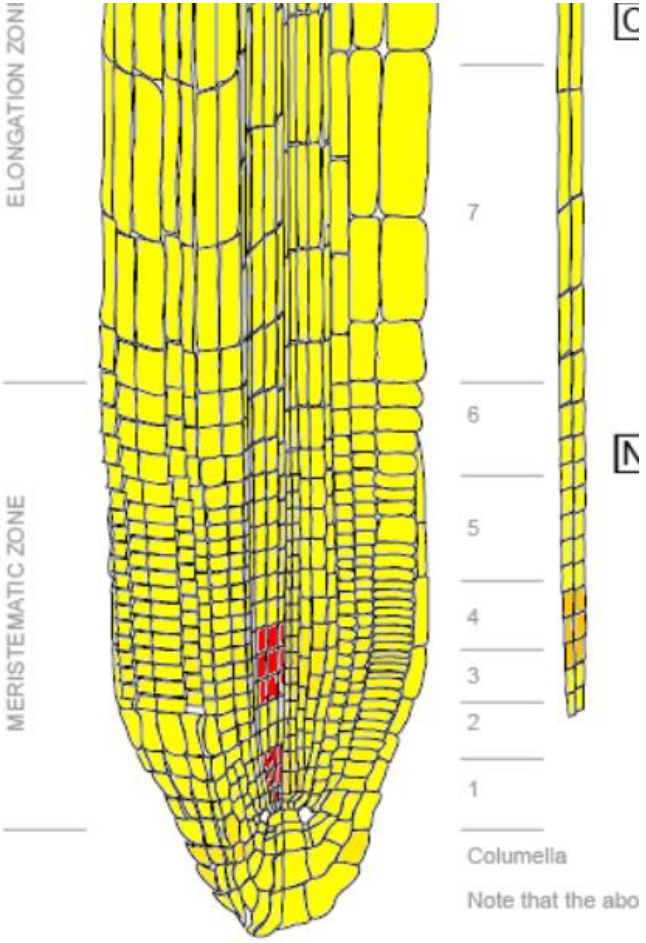
Apply to microarray

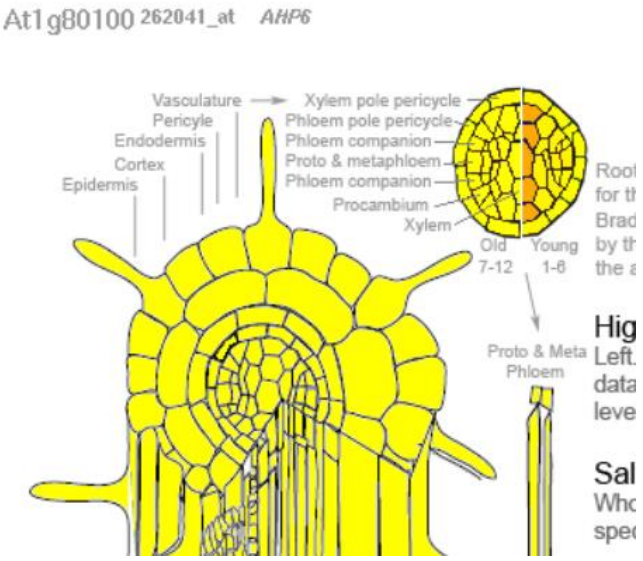




eFP browser

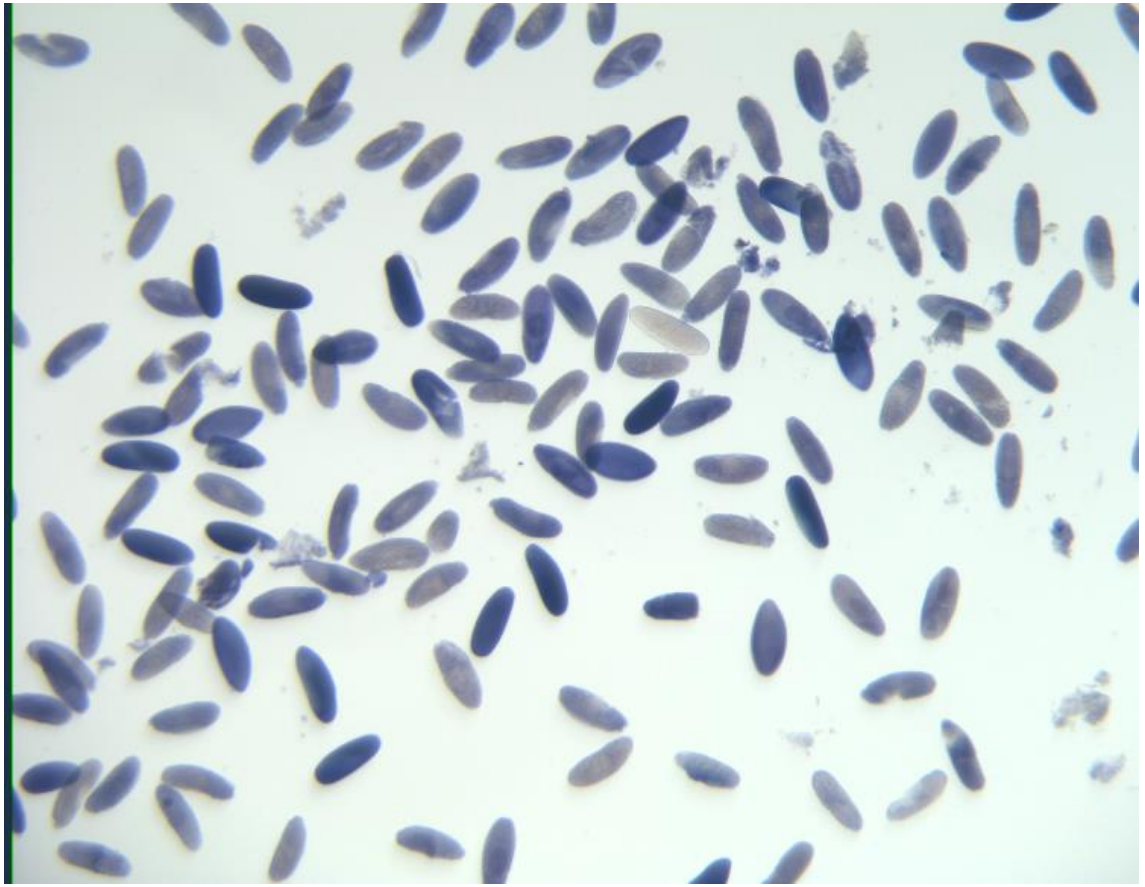






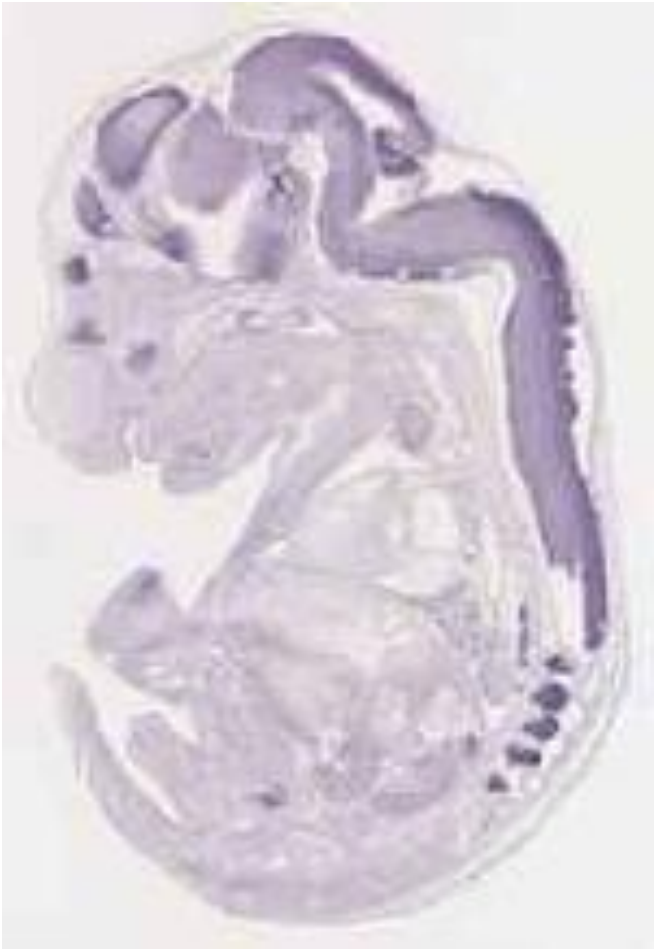
http://bar.utoronto.ca/efp/cgi-bin/efpWeb.cgi

Fl(2)D gene in Drosophila embryos

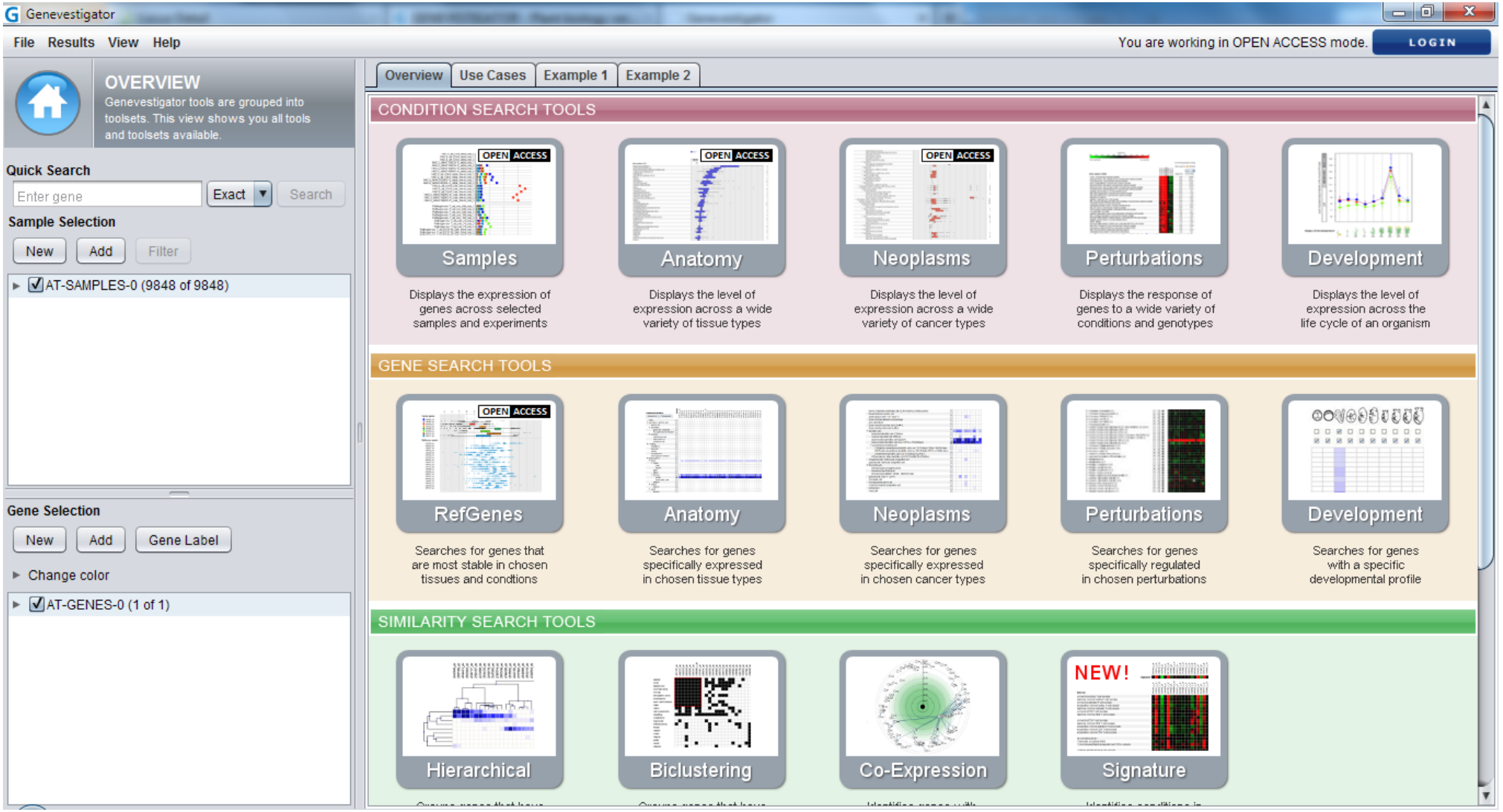


insitu.fluitfly.org

KIAA1841 in mouse expressed in neurons

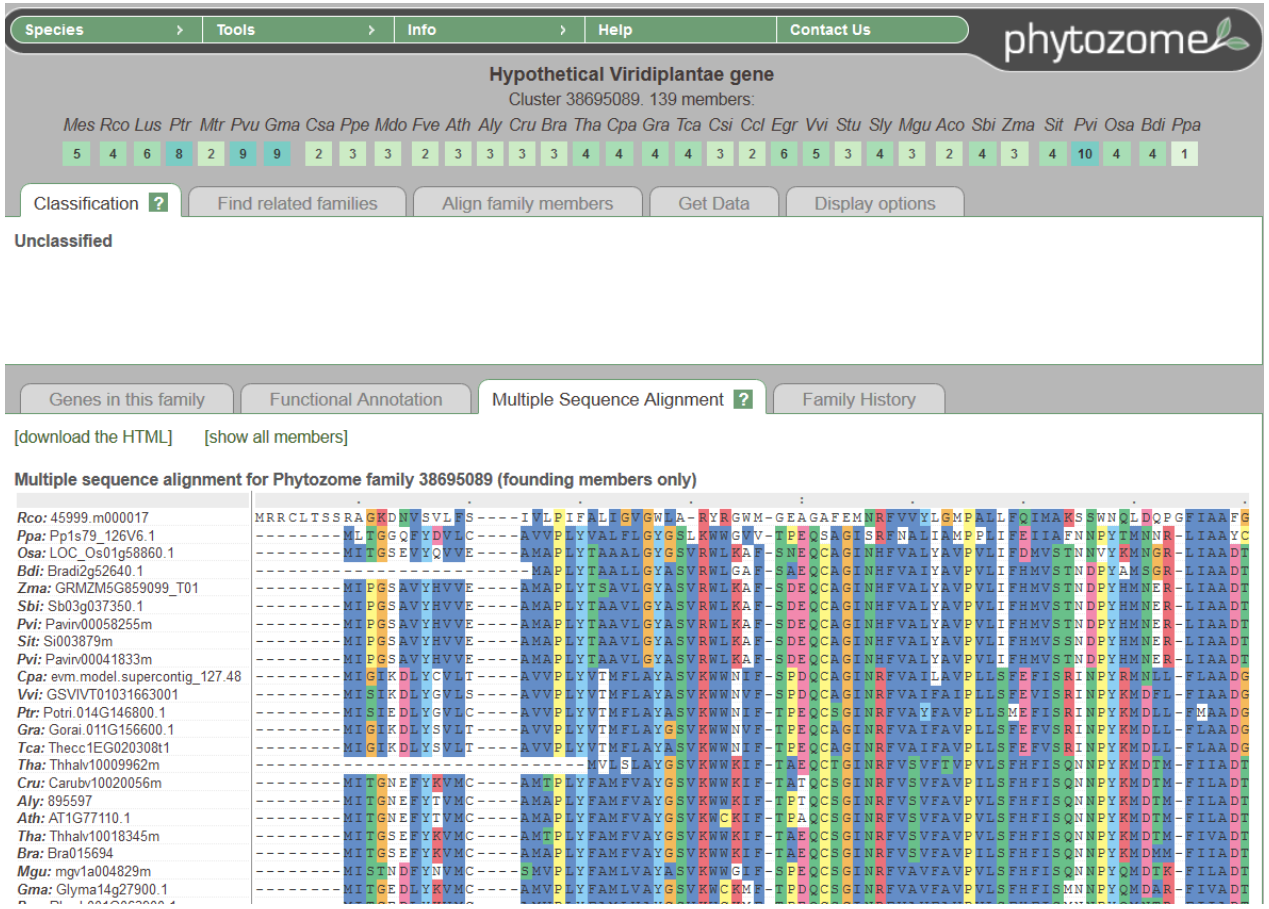


Genevestigator – check your gene's transcriptome networks



Arabidopsis and also other species for academic users free

Database of protein families in plants

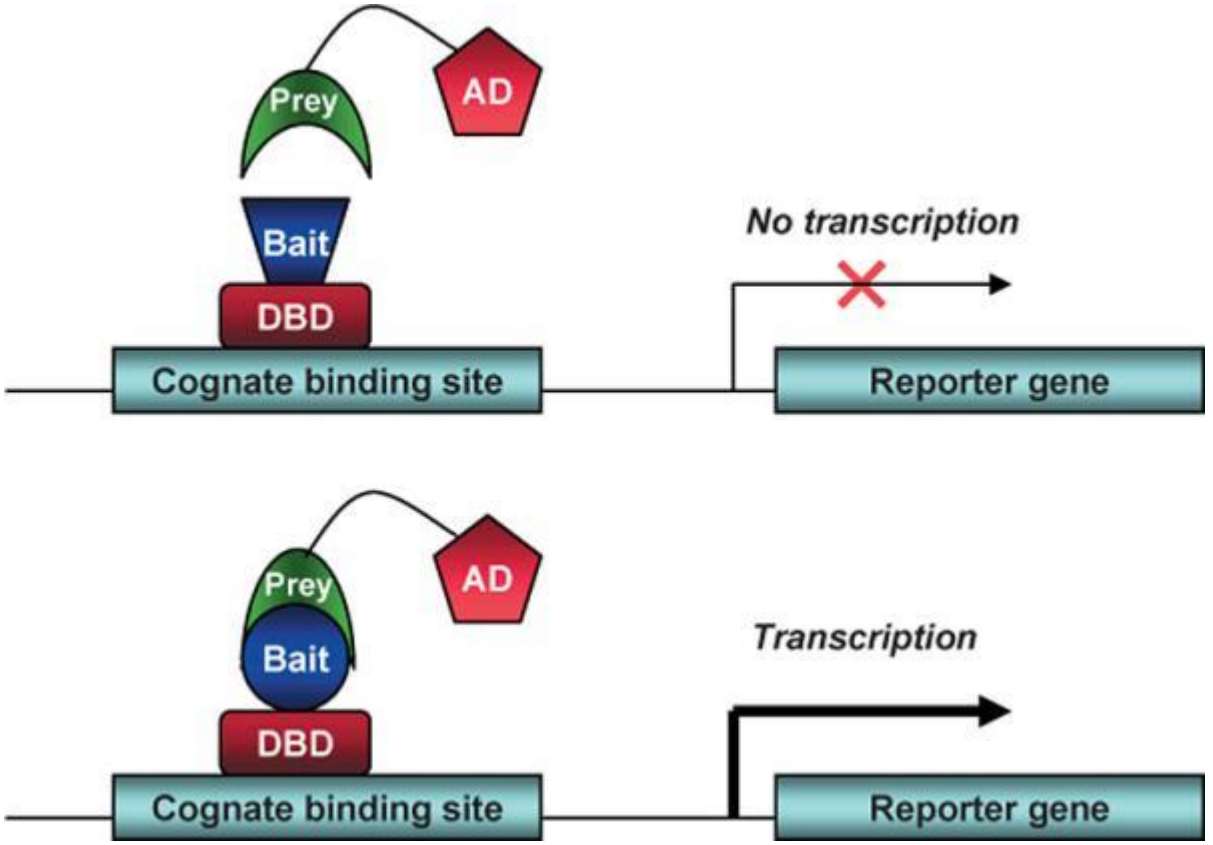


great for conservation of splicing events etc.

http://www.phytozome.net/

Yeast two-hybrid (Y2H) summary

protein-protein interaction hunt



High throughput yeast two hybrid for various organisms

articles

A comprehensive analysis of protein–protein interactions in *Saccharomyces cerevisiae*

(2000)

Peter Uetz*†, Loic Giot*‡, Gerard Cagney†, Traci A. Mansfield‡, Richard S. Judson‡, James R. Knight‡, Daniel Lockshon†, Vaibhav Narayan‡, Maithreyan Srinivasan‡, Pascale Pochart‡, Alia Qureshi-Emili†§, Ying Li‡, Brian Godwin‡, Diana Conover†§, Theodore Kalbfleisch‡, Govindan Vijayadamodar‡, Meijia Yang‡, Mark Johnston†‖, Stanley Fields†§ & Jonathan M. Rothberg‡

A Protein Interaction Map of *Drosophila melanogaster*

L. Giot,[1]* J. S. Bader,[1]*† C. Brouwer,[1]* A. Chaudhuri,[1]* B. Kuang,[1] Y. Li,[1] Y. L. Hao,[1] C. E. Ooi,[1] B. Godwin,[1] E. Vitols,[1] G. Vijayadamodar,[1] P. Pochart,[1] H. Machineni,[1] M. Welsh,[1] Y. Kong,[1] B. Zerhusen,[1] R. Malcolm,[1] Z. Varrone,[1] A. Collis,[1] M. Minto,[1] S. Burgess,[1] L. McDaniel,[1] E. Stimpson,[1] F. Spriggs,[1] J. Williams,[1] K. Neurath,[1] N. Ioime,[1] M. Agee,[1] E. Voss,[1] K. Furtak,[1] R. Renzulli,[1] N. Aanensen,[1] S. Carrolla,[1] Sickelhaupt,[1] Y. Lazovatsky,[1] A. DaSilva,[1] J. Zhong,[2] Stanyon,[2] R. L. Finley Jr.,[2] K. P. White,[3] M. Braverman,[1] rvie,[1] S. Gold,[1] M. Leach,[1] J. Knight,[1] R. A. Shimkets,[1] M. P. McKenna,[1] J. Chant,[1]‡ J. M. Rothberg[1]

(2005)

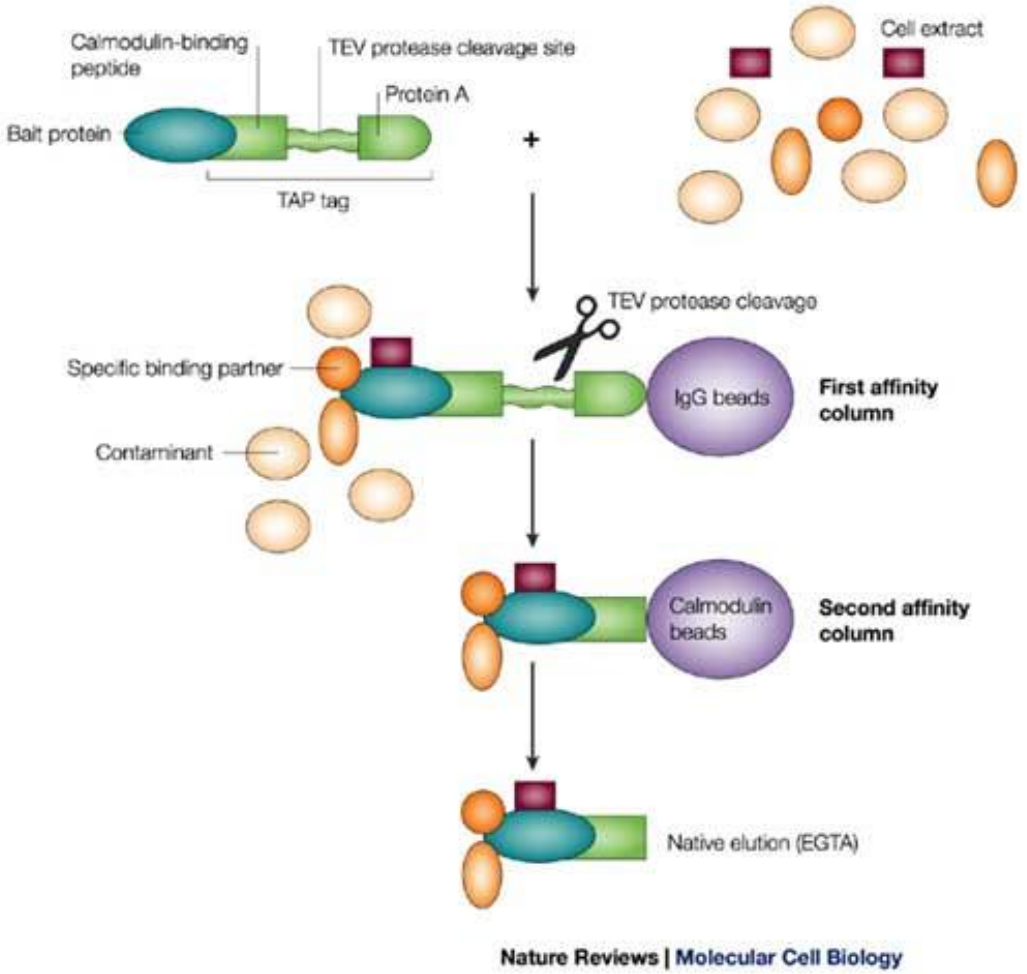
Evidence for Network Evolution in an *Arabidopsis* Interactome Map

Arabidopsis Interactome Mapping Consortium*†

(2009)

TAP purification

affinity purification interaction hunt



↓

MALDI-TOF

So, far high throughput affinity purification approach slightly less popular

Functional organization of the yeast proteome by systematic analysis of protein complexes (2002)

Anne-Claude Gavin*, Markus Bösche*, Roland Krause*, Paola Grandi*, Martina Marzioch*, Andreas Bauer*, Jörg Schultz*, Jens M. Rick*, Anne-Marie Michon*, Cristina-Maria Cruciat*, Marita Remor*, Christian Höfert*, Malgorzata Schelder*, Miro Brajenovic*, Heinz Ruffner*, Alejandro Merino*, Karin Klein*, Manuela Hudak*, David Dickson*, Tatjana Rudi*, Volker Gnau*, Angela Bauch*, Sonja Bastuck*, Bettina Huhse*, Christina Leutwein*, Marie-Anne Heurtier*, Richard R. Copley†, Angela Edelmann*, Erich Querfurth*, Vladimir Rybin*, Gerard Drewes*, Manfred Raida*, Tewis Bouwmeester*, Peer Bork†, Bertrand Seraphin†‡, Bernhard Kuster*, Gitte Neubauer* & Giulio Superti-Furga*†

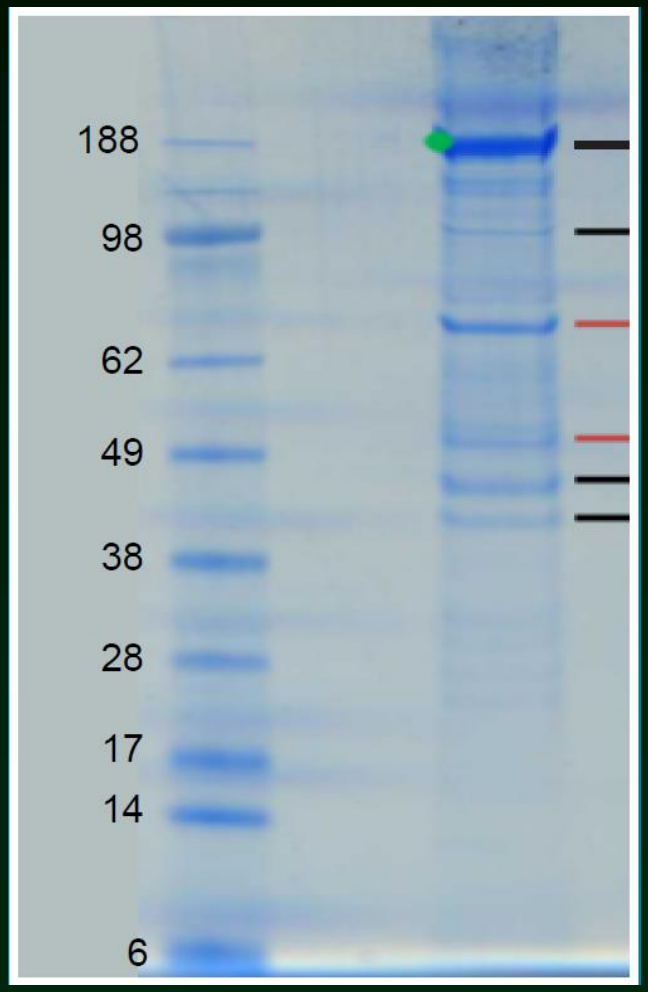
A Protein Complex Network of *Drosophila melanogaster* (2011)

K.G. Guruharsha,[1,4] Jean-François Rual,[1,4] Bo Zhai,[1,4] Julian Mintseris,[1,4] Pujita Vaidya,[1] Namita Vaidya,[1] Chapman Beekman,[1] Christina Wong,[1] David Y. Rhee,[1] Odise Cenaj,[1] Emily McKillip,[1] Saumini Shah,[1] Mark Stapleton,[2] Kenneth H. Wan,[2] Charles Yu,[2] Bayan Parsa,[2] Joseph W. Carlson,[2] Xiao Chen,[2] Bhaveen Kapadia,[2] K. VijayRaghavan,[3] Steven P. Gygi,[1] Susan E. Celniker,[2] Robert A. Obar,[1,*] and Spyros Artavanis-Tsakonas[1,*]

thebiogrid.org - highly relevant for searching for interactors, but look also elsewhere!

Interactors of EMB2016

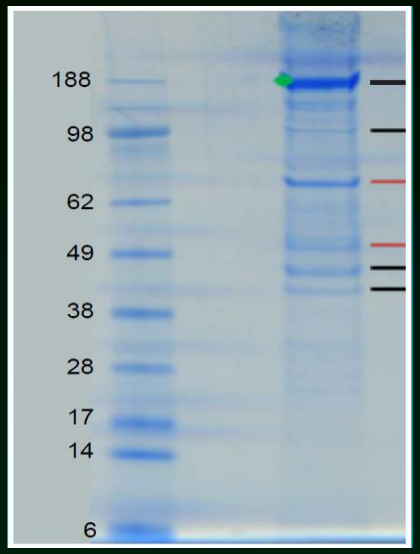
use databases if you have a conserved complex



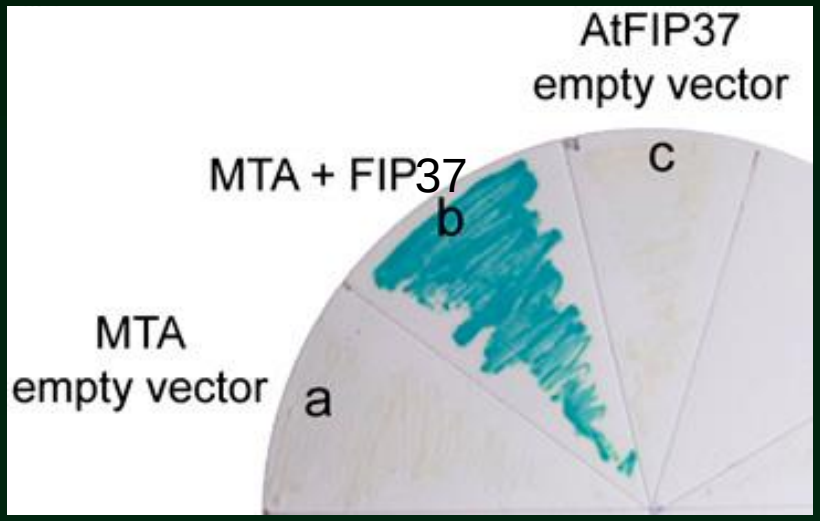
tandem affinity purification

Geert de Jaeger lab

EMB2016 interactors – RNA methylase



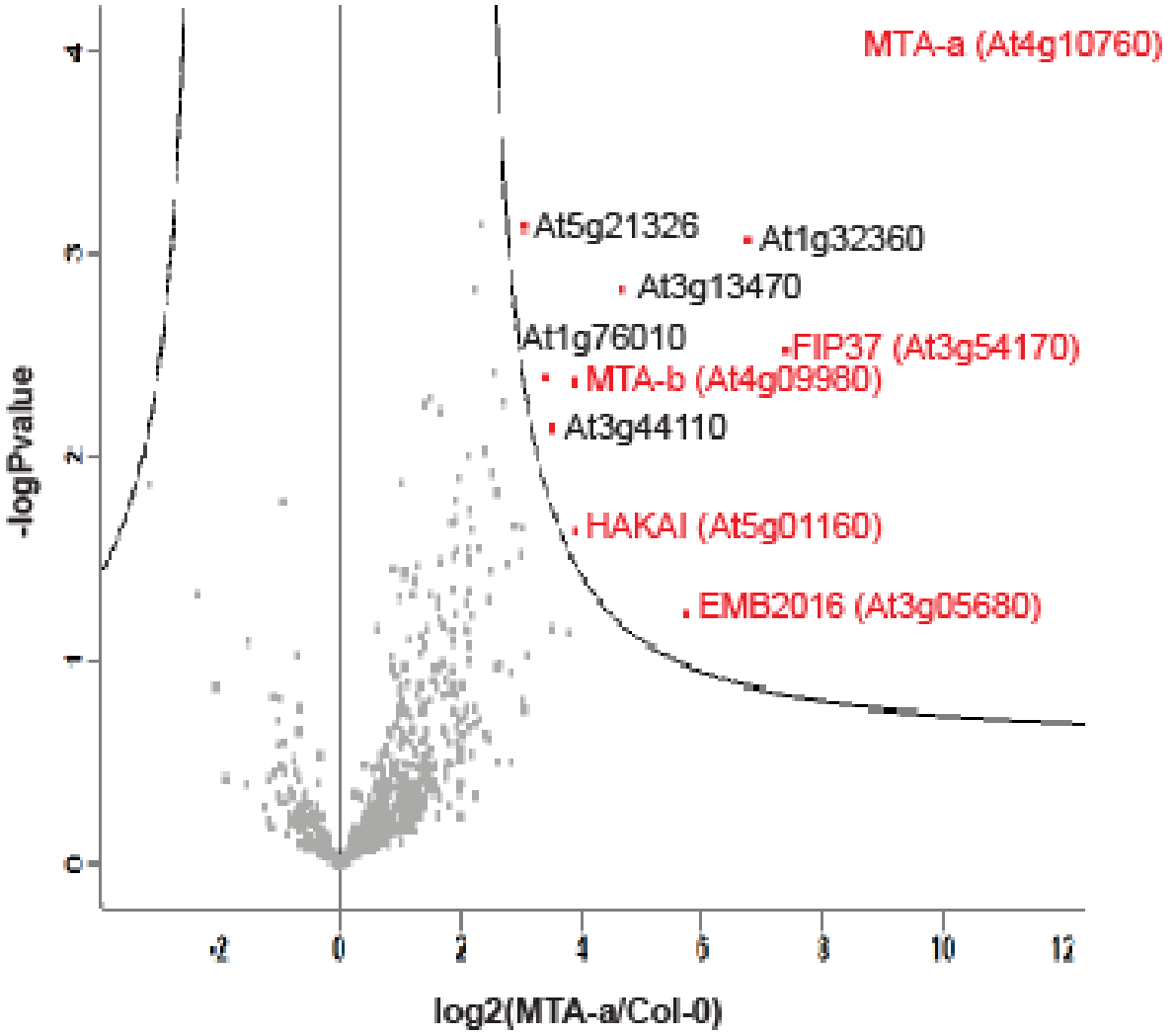
RING finger/HAKAI was also shown to associate with splicing factors (human)



MTA-A – homolog of MTA

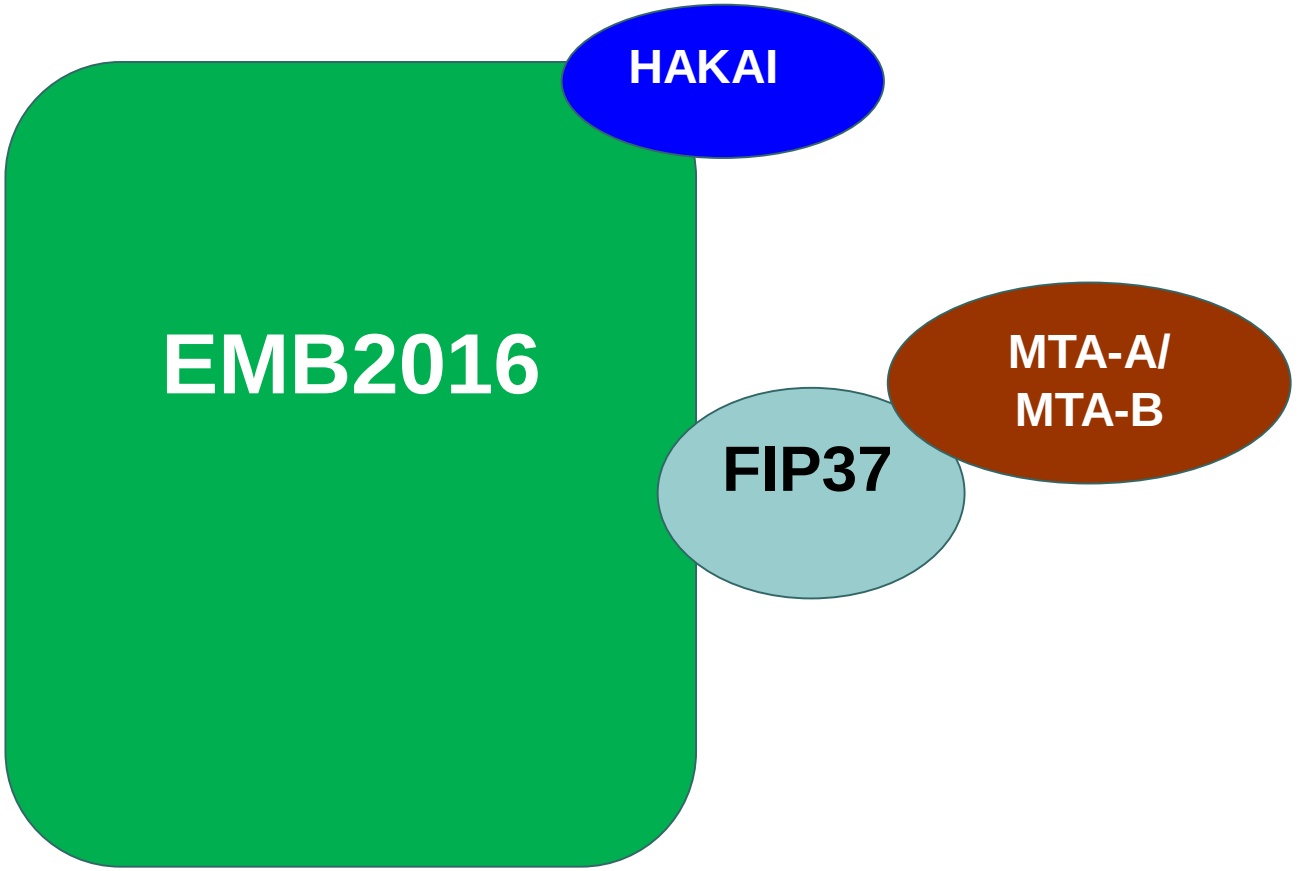
Zhong et al. 2009

All guys back here when using MTA-A as bait

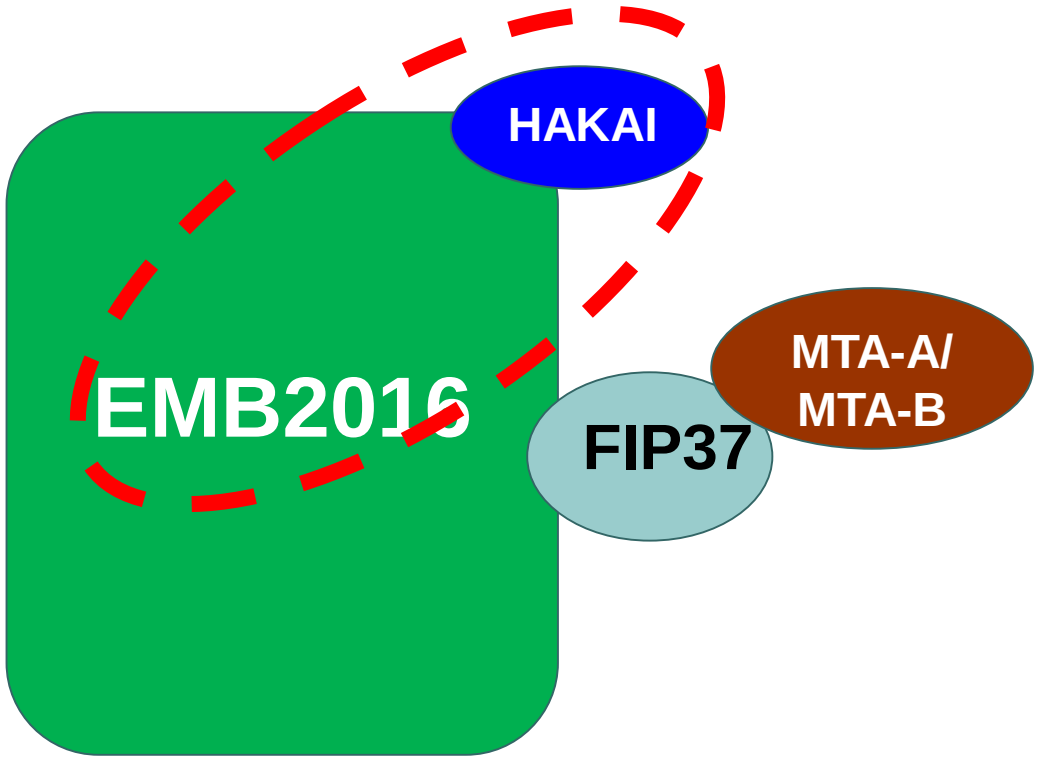


(Immunoprecipitation)

Inferred protein complex



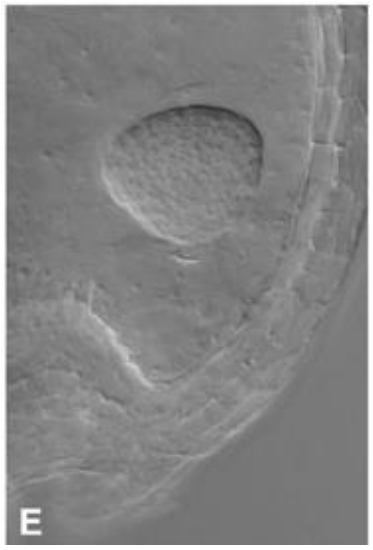
Inferred protein complex



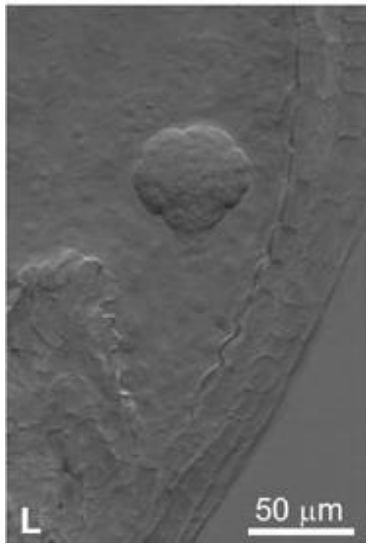
Flybase: EMB2016 interacts with HAKAI (no data on Biogrid)

Summary of Physical Interactions		
RNA-protein		
Interacting group	Assay	References
vir - stau	anti bait coimmunoprecipitation, partial dna sequence identification by hybridization	(*Laver et al., 2013*)
protein-protein		
Interacting group	Assay	References
vir - CG7358	experimental knowledge based	(*Guruharsha et al., 2011*)
vir - Hakai	experimental knowledge based	(*Guruharsha et al., 2011*)
vir - fl(2)d	experimental knowledge based	(*Guruharsha et al., 2011*)

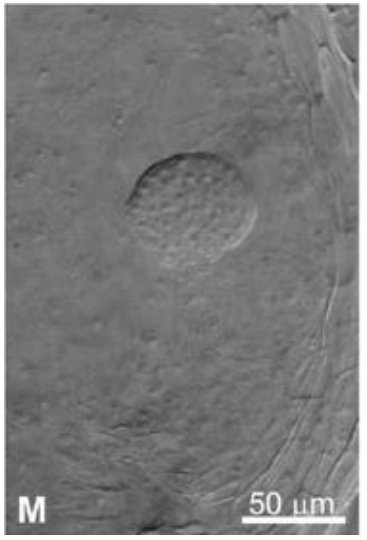
Assumption



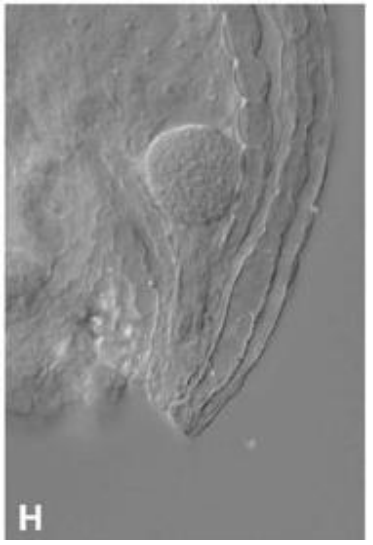
mta-a



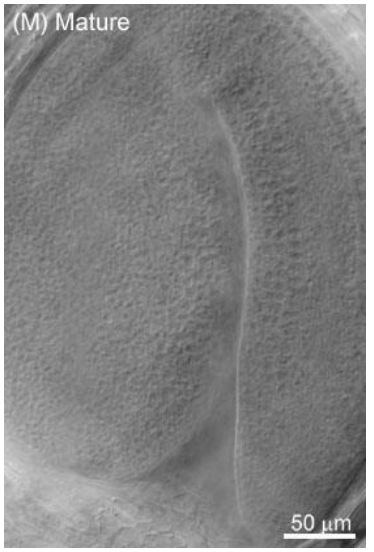
mta-b



fip37-1



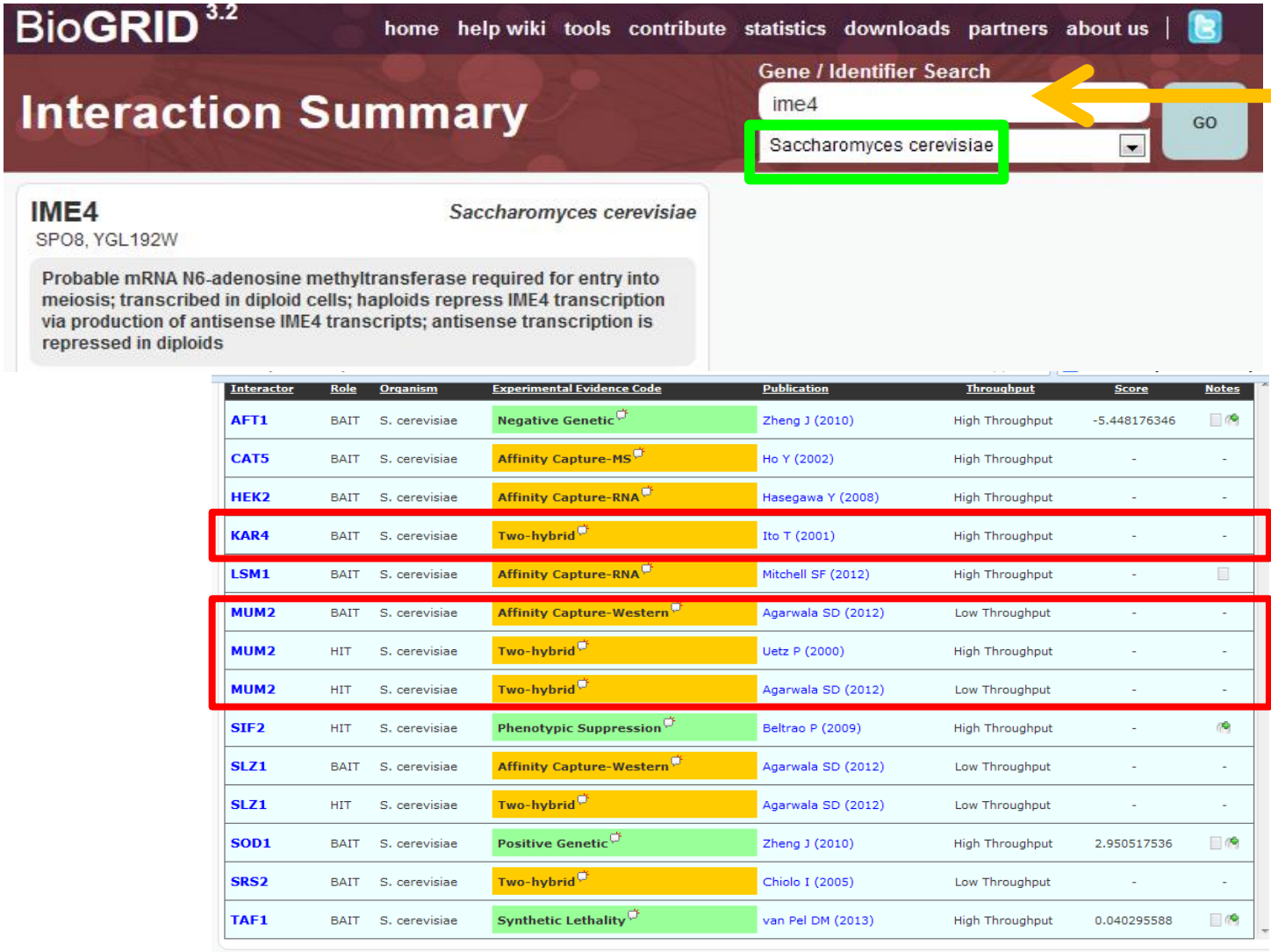
emb2016



wild type

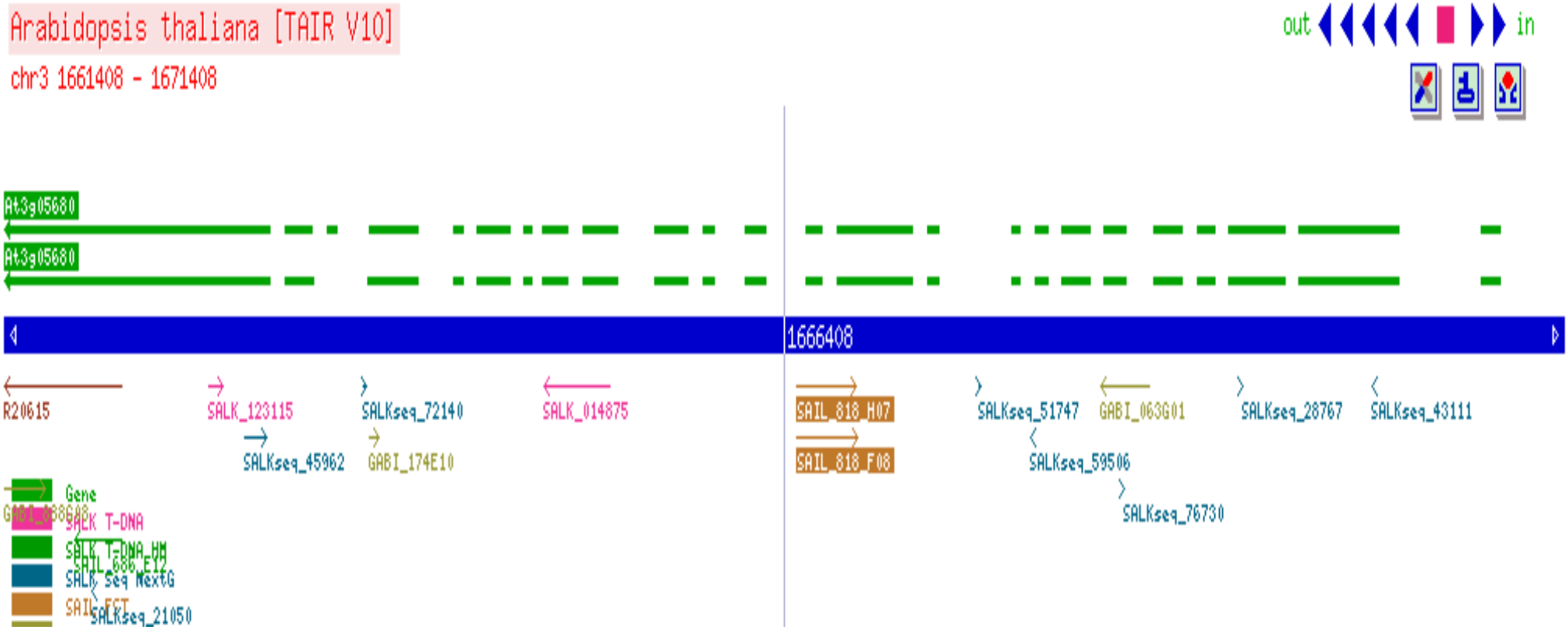
all of them: even very strong knockdowns viable
-> MTA-A and MTA-B probably necessary both ->
MTA-A and -B probably interact

MTA-A and –B yeast homologs interact, FIP37 as well



Interactor	Role	Organism	Experimental Evidence Code	Publication	Throughput	Score	Notes
AFT1	BAIT	S. cerevisiae	Negative Genetic	Zheng J (2010)	High Throughput	-5.448176346	
CAT5	BAIT	S. cerevisiae	Affinity Capture-MS	Ho Y (2002)	High Throughput	-	-
HEK2	BAIT	S. cerevisiae	Affinity Capture-RNA	Hasegawa Y (2008)	High Throughput	-	-
KAR4	BAIT	S. cerevisiae	Two-hybrid	Ito T (2001)	High Throughput	-	-
LSM1	BAIT	S. cerevisiae	Affinity Capture-RNA	Mitchell SF (2012)	High Throughput	-	
MUM2	BAIT	S. cerevisiae	Affinity Capture-Western	Agarwala SD (2012)	Low Throughput	-	-
MUM2	HIT	S. cerevisiae	Two-hybrid	Uetz P (2000)	High Throughput	-	-
MUM2	HIT	S. cerevisiae	Two-hybrid	Agarwala SD (2012)	Low Throughput	-	-
SIF2	HIT	S. cerevisiae	Phenotypic Suppression	Beltrao P (2009)	High Throughput	-	
SLZ1	BAIT	S. cerevisiae	Affinity Capture-Western	Agarwala SD (2012)	Low Throughput	-	-
SLZ1	HIT	S. cerevisiae	Two-hybrid	Agarwala SD (2012)	Low Throughput	-	-
SOD1	BAIT	S. cerevisiae	Positive Genetic	Zheng J (2010)	High Throughput	2.950517536	
SRS2	BAIT	S. cerevisiae	Two-hybrid	Chiolo I (2005)	Low Throughput	-	-
TAF1	BAIT	S. cerevisiae	Synthetic Lethality	van Pel DM (2013)	High Throughput	0.040295588	

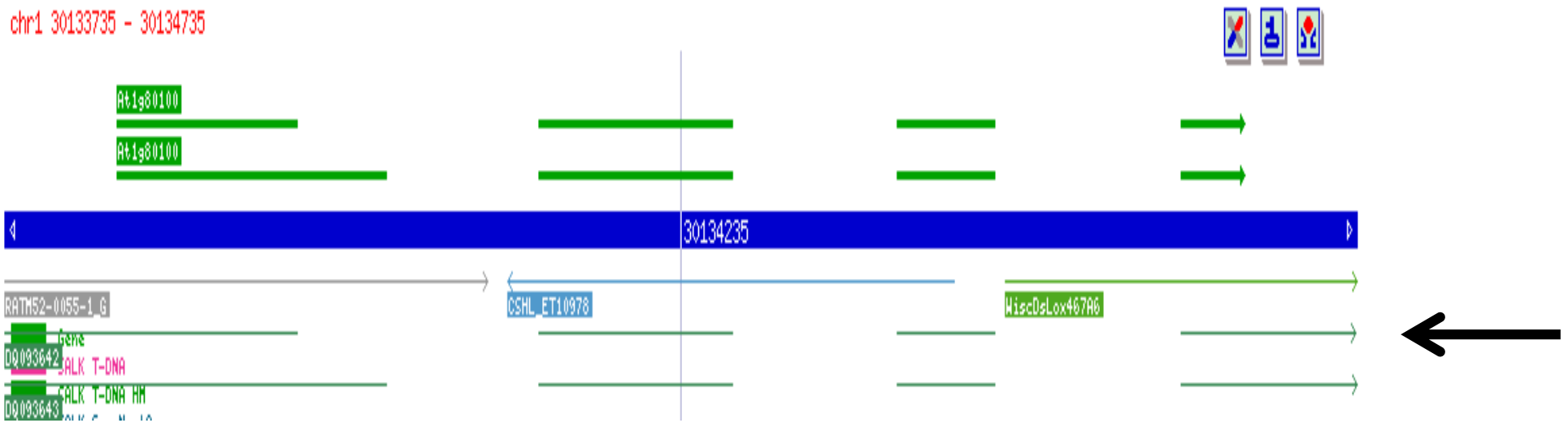
You can order your mutant from the stock center



the same for Drosophila, mouse, worm etc.

signal.salk.edu

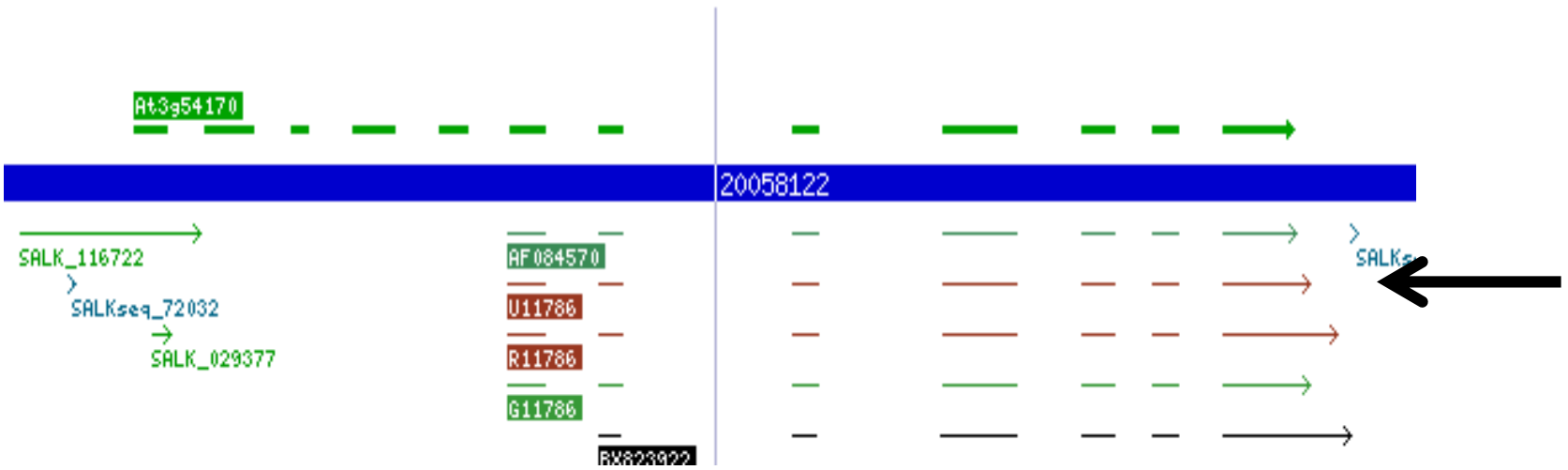
You can order your cDNA clone from the stock center



the same for yeast,
Drosophila, mouse etc.

signal.salk.edu

You can order your cDNA clone from the stock center

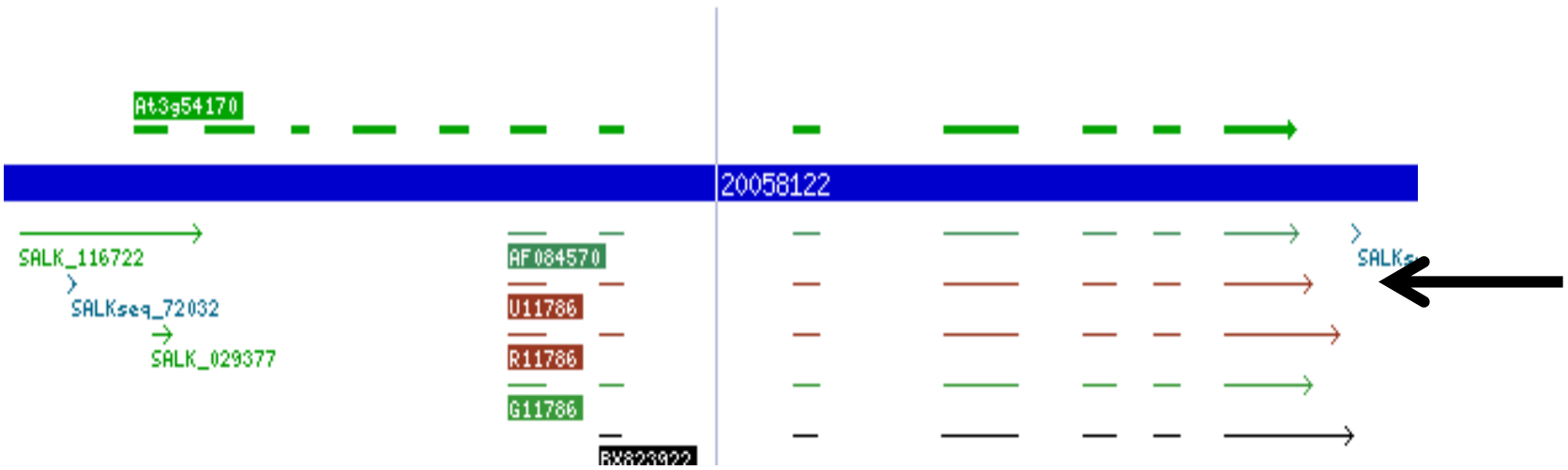


the same for Drosophila, mouse, worm etc.

signal.salk.edu

You need probably to clone this one yourself.

You can order your cDNA clone from the stock center



even basic fusions (GFP, myc, TAP etc.) often ready for you

signal.salk.edu

You can order your RNAi/amiRNA

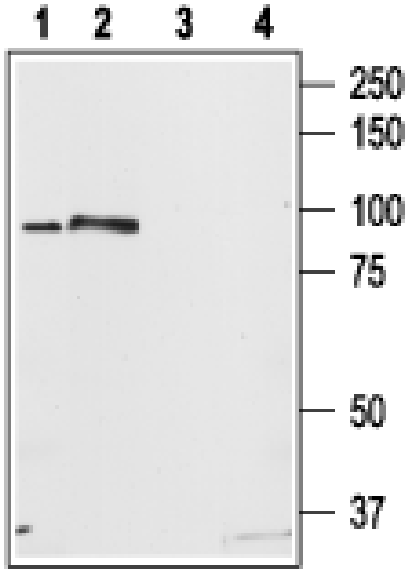
- even cloned in binary vector
- just google…

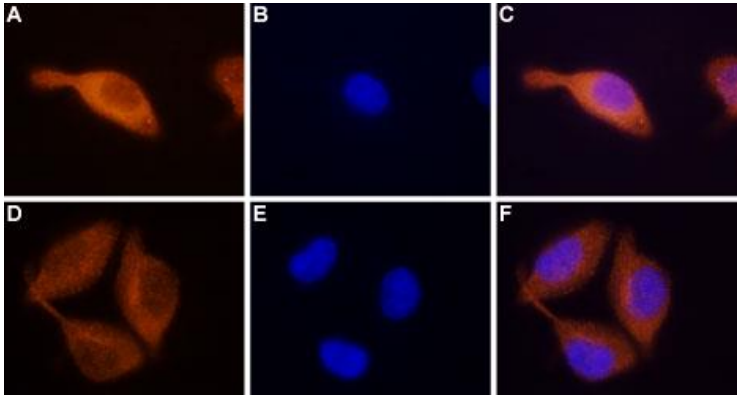
Commercial service as well.

You can order antibodies against your protein

googling human proteins:
http://www.scbt.com/
www.acris-antibodies.com/
etc.

- even get western and immunocytochemistry in advance

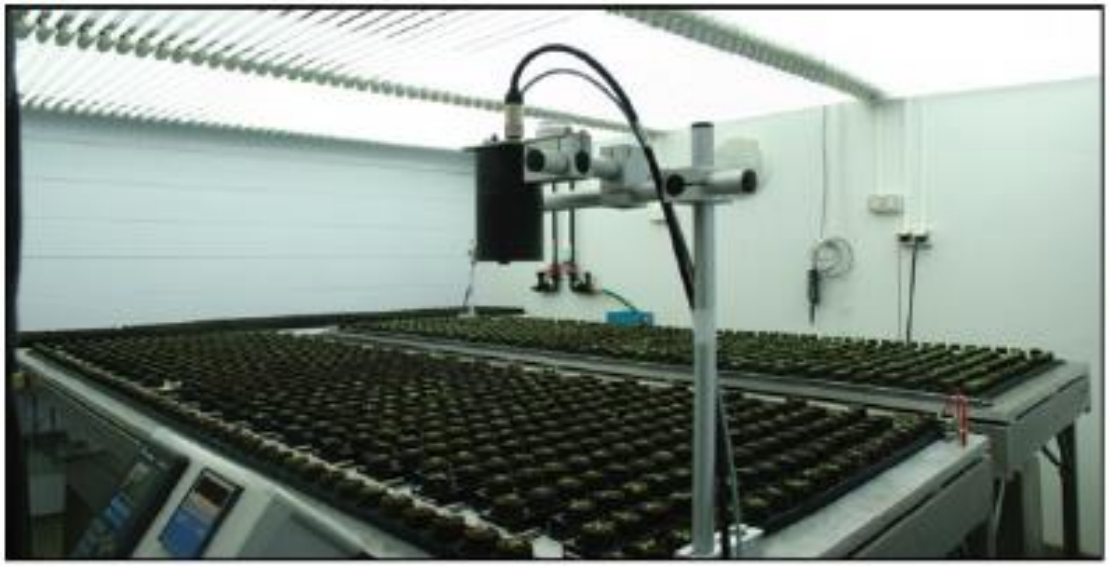


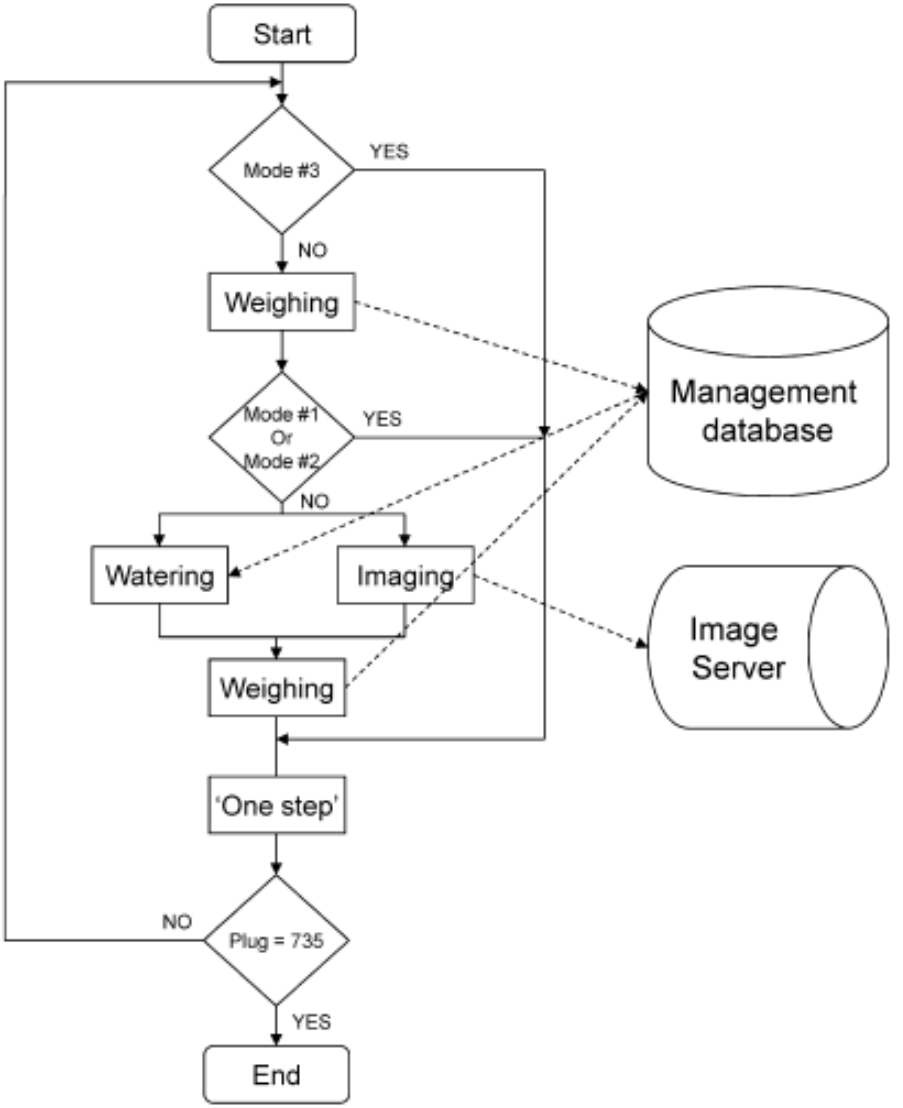


Arabidopsis so far lagging – agrisera.com perhaps little bit.
Rather commercial service.

Phenoscope

(a)

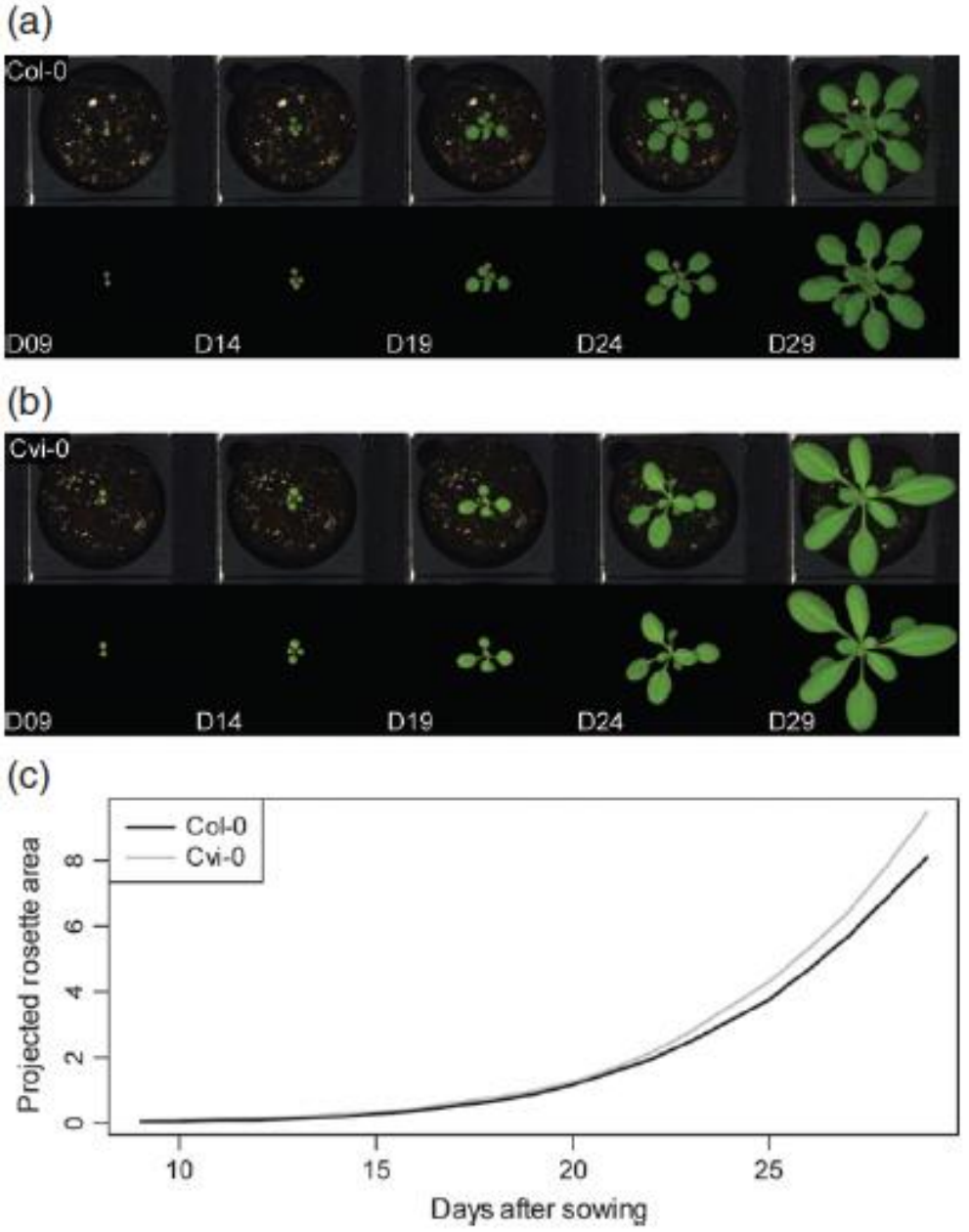




PHENOSCOPE: an automated large-scale phenotyping platform

Thisne et al. 2013

Phenoscope

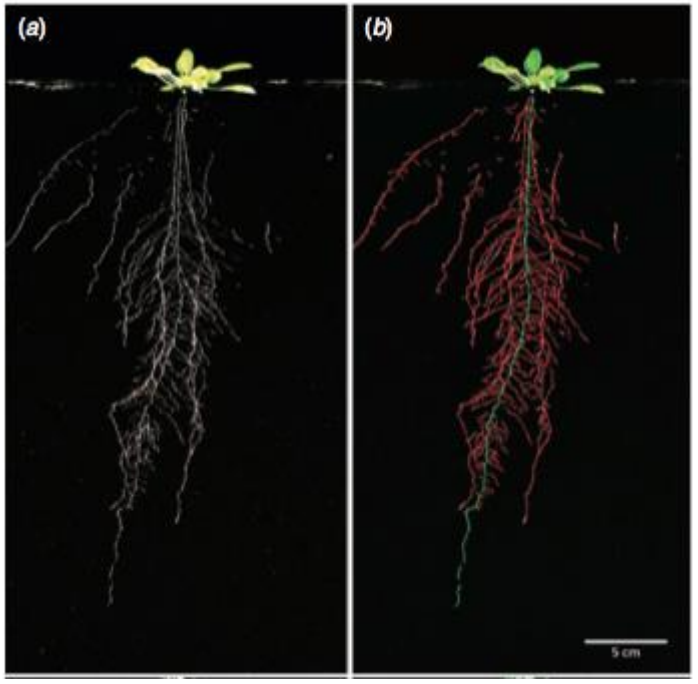

(a)
Col-0
D09
D14
D19
D24
D29
(b)
Cvi-0
D09
D14
D19
D24
D29
(c)
Col-0
Cvi-0
Projected rosette area
0
2
4
6
8
10
15
20
25
Days after sowing

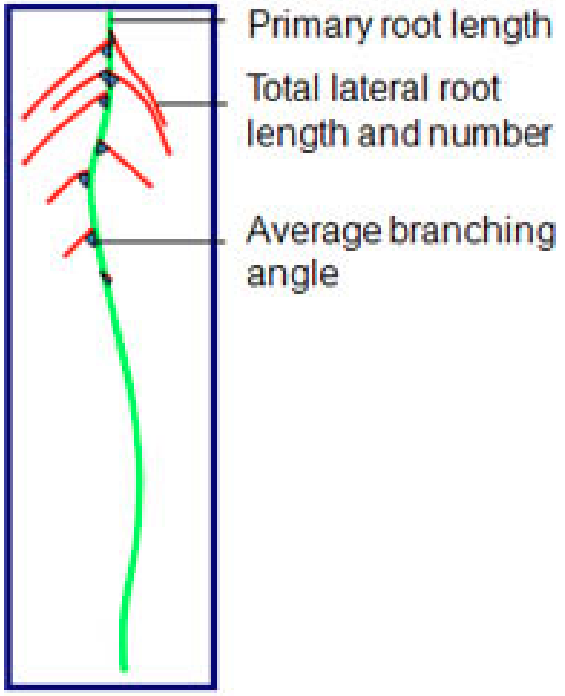
Phenoscope

- leaf area (camera)
- photosynthesis (spectra)
- weight
- temperature (thermo camera)
- in a dynamic manner
- …
- various ecotypes only, so far
- commercially promising

Phenoscope – perhaps in future

adaptation on other tissues certainly possible





GrowScreen-Root software

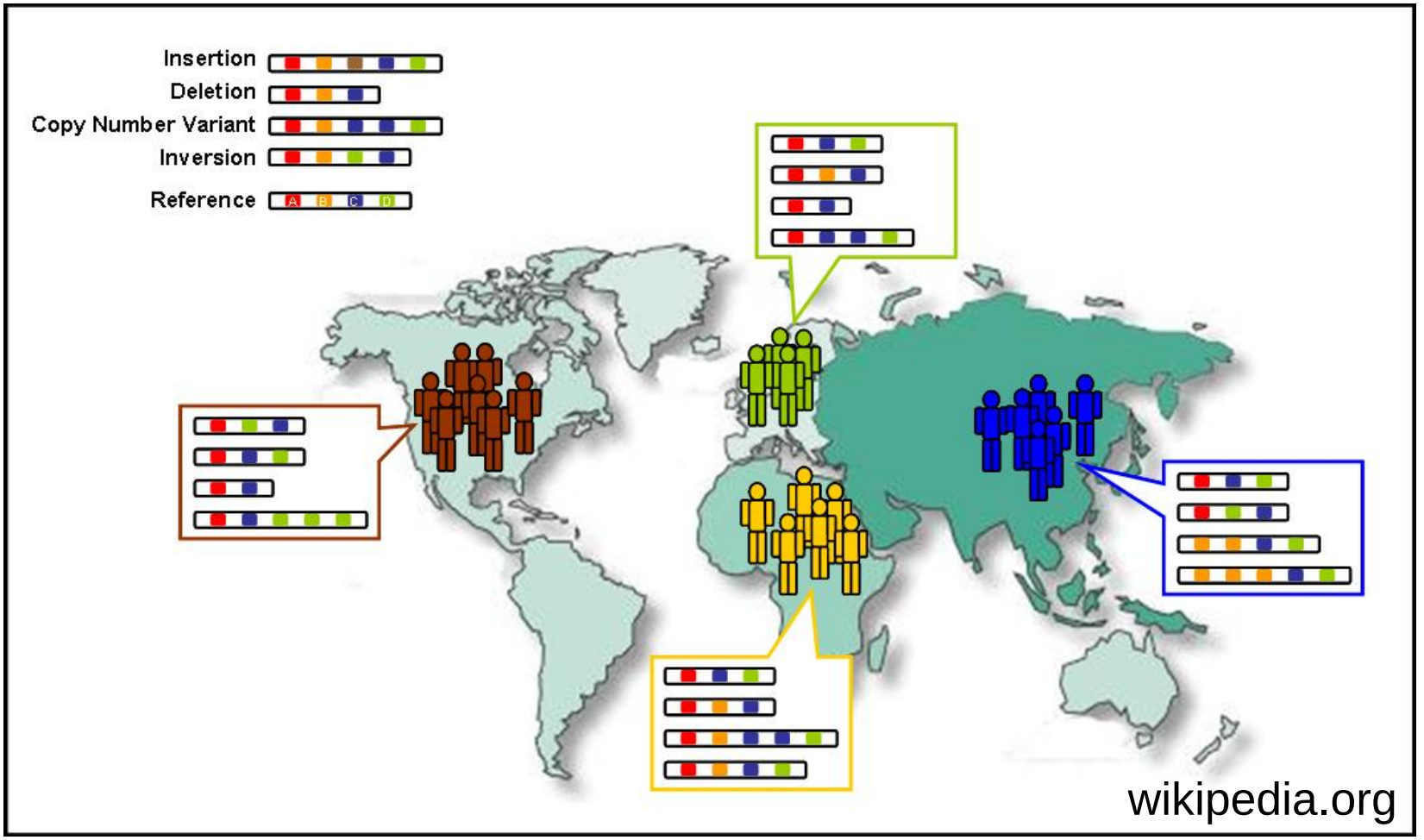
Check your phenotype online

seedgenes.org
– database of plant embryonic mutants (in-dept)

http://rarge.psc.riken.jp/phenome/
- RIKEN Arabidopsis Phenome Information Database (kind of attempt on adult plant)

1000 genomes

1000 human genomes over the world

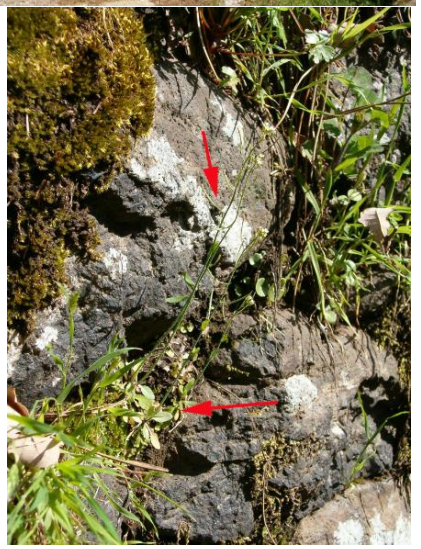


1001 genomes - Arabidopsis

http://1001genomes.org/

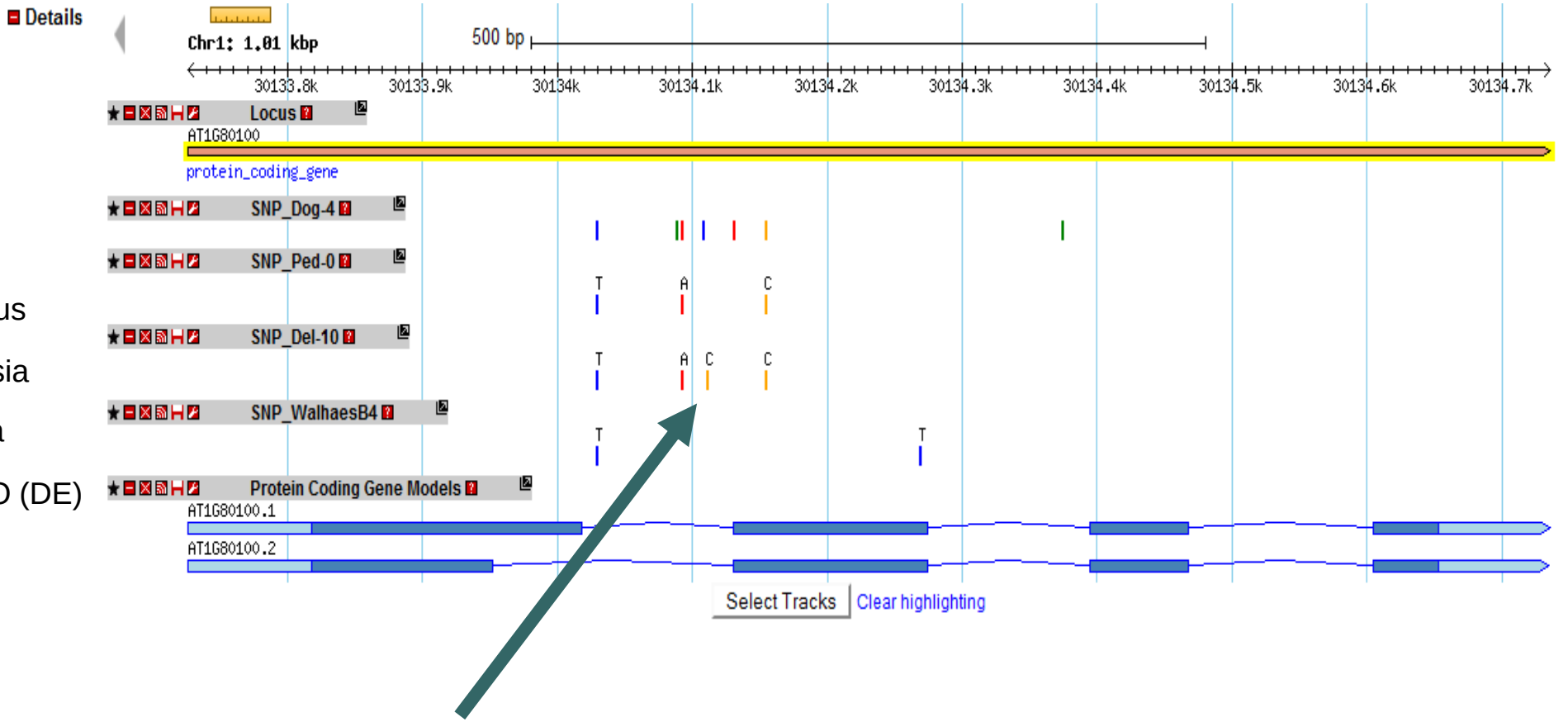
in both cases, much more lines already sequenced

How the ecotypes are collected



Olivier Loudet web page

1001 genomes user interface



Caucasus

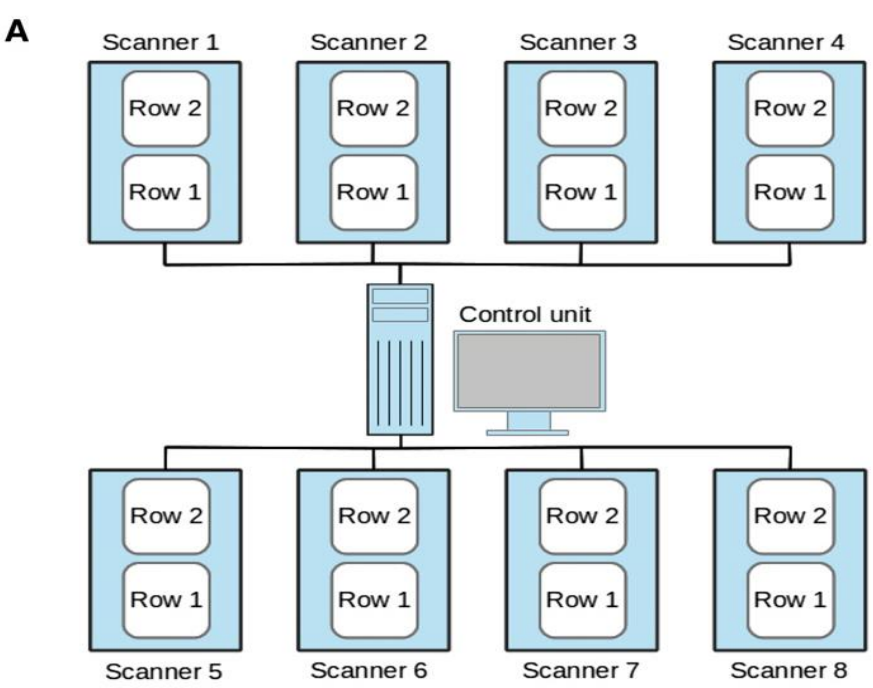
Cent. Asia

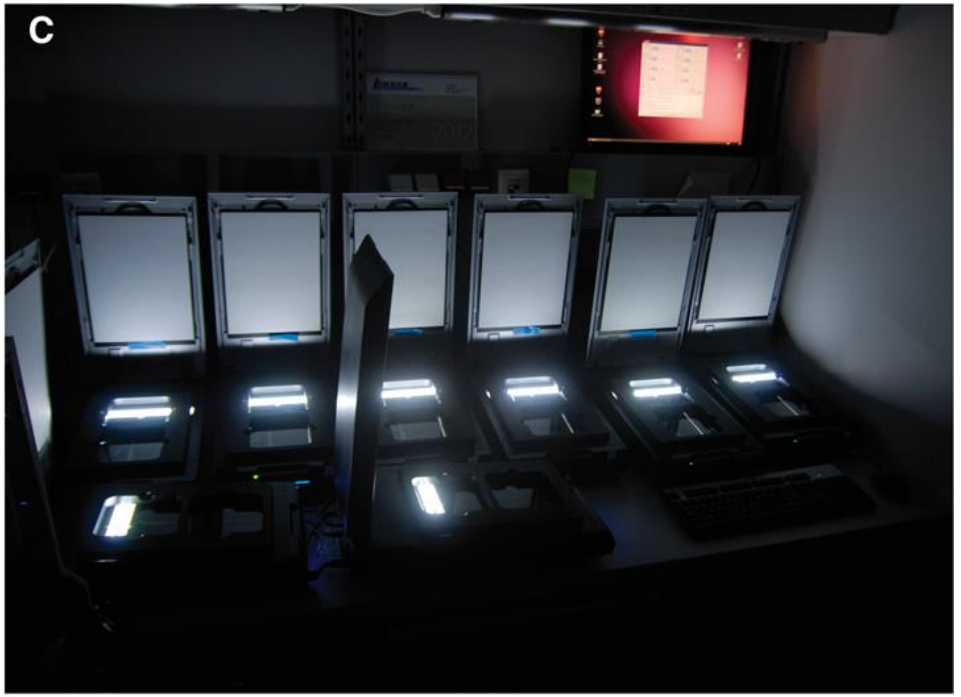
S. Africa

Tü-WHO (DE)

several single nucleotide polymorphisms (**SNP**) in the selected gene

Genome wide association studies (GWAS)





Slovak et al. 2014, Busch lab, Vienna

Genome wide association studies (GWAS)

Trait No.	Trait
1	Total length
2	Euclidian length
3	Root tortuosity
4	Root growth rate
5	Relative root growth rate
6	Root angle
7	Root direction index
8	Root horizontal index
9	Root vertical index
10	Root linearity
11	Average root width
12	Root width 20
13	Root width 40
14	Root width 60
15	Root width 80
16	Root width 100

163 accessions (ecotypes),
several replicates (8 x 3)

searching for those different
(say how different they might be!)

Slovak et al. 2014

Genome wide association studies (GWAS)

Trait No.	Trait
1	Total length
2	Euclidian length
3	Root tortuosity
4	Root growth rate
5	Relative root growth rate
6	Root angle
7	Root direction index
8	Root horizontal index
9	Root vertical index
10	Root linearity
11	Average root width
12	Root width 20
13	Root width 40
14	Root width 60
15	Root width 80
16	Root width 100

163 accessions (ecotypes),
several replicates (8 x 3)

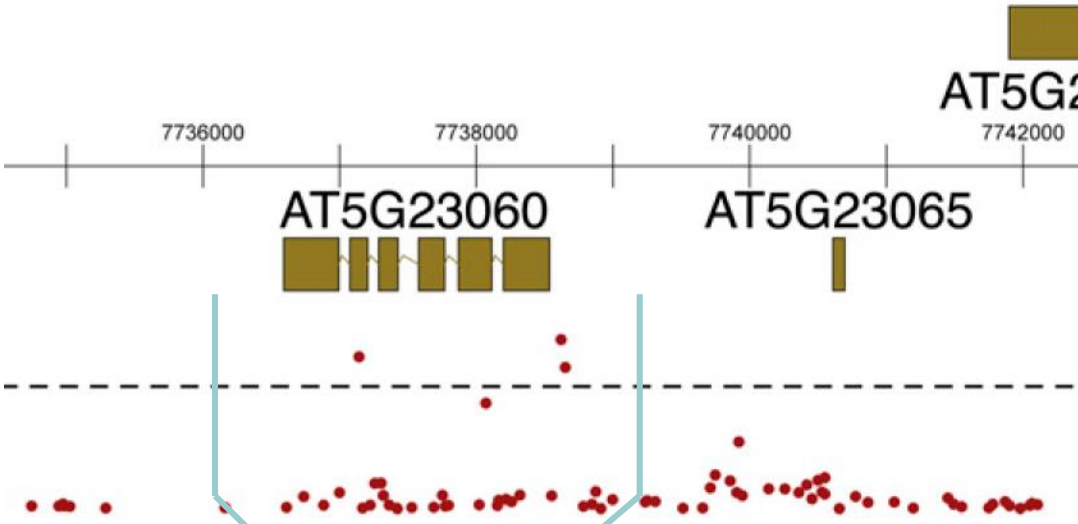
searching for those different
(e. g. root growth, slim root,
resistant to exogenous treatment)

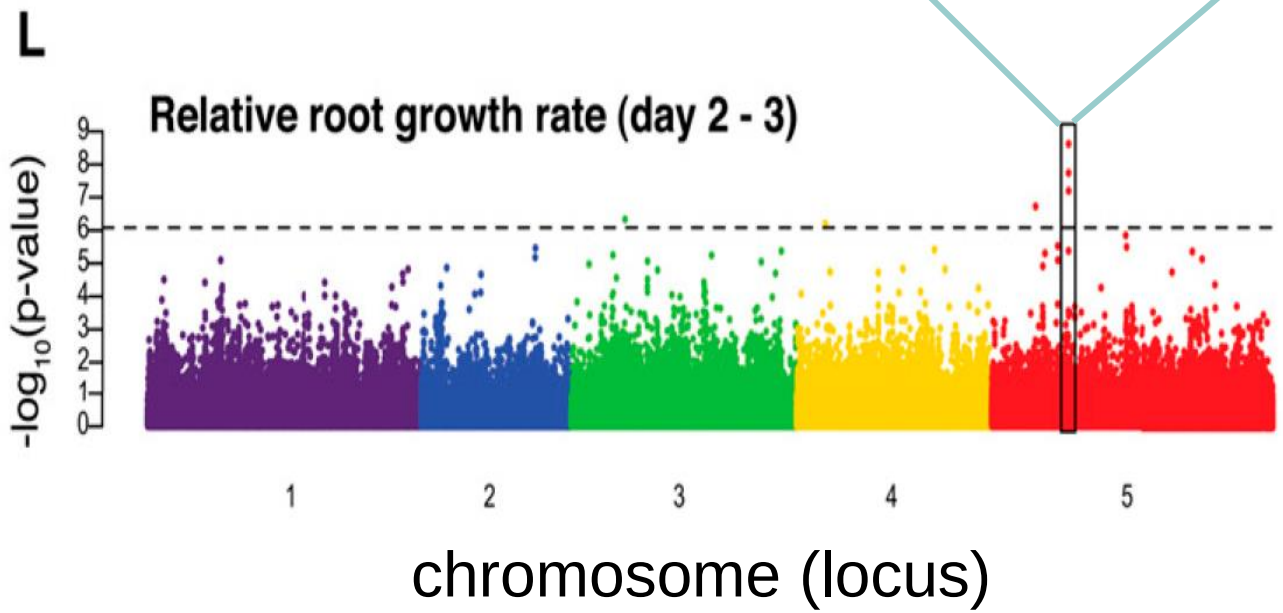
Slovak et al. 2014

Genome wide association studies (GWAS)

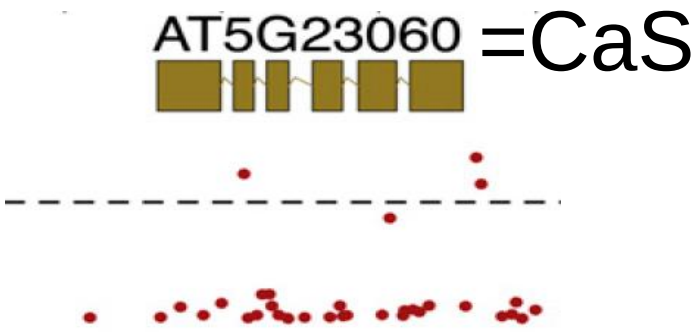
high p-value => SNP specifically
in the “resistant” line
(*N*-way ANOVA etc.)

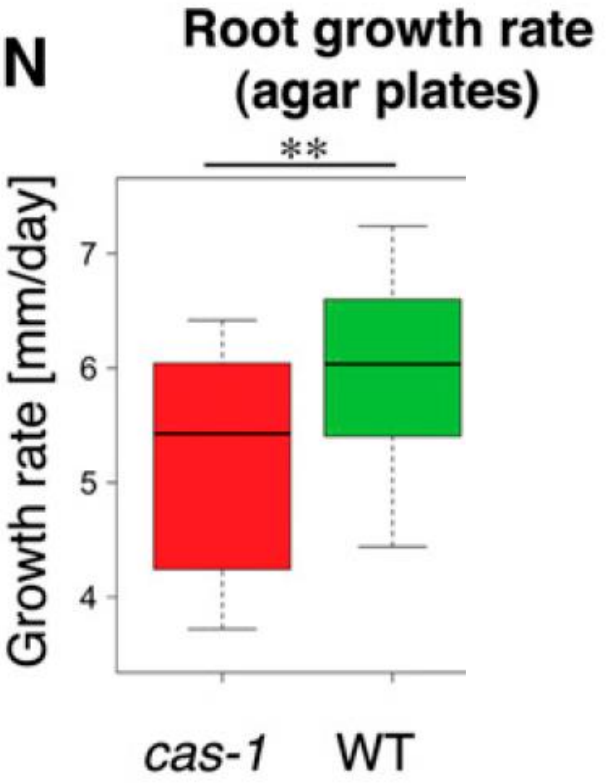
In contrast to human:
- how to test it?





Genome wide association studies (GWAS)



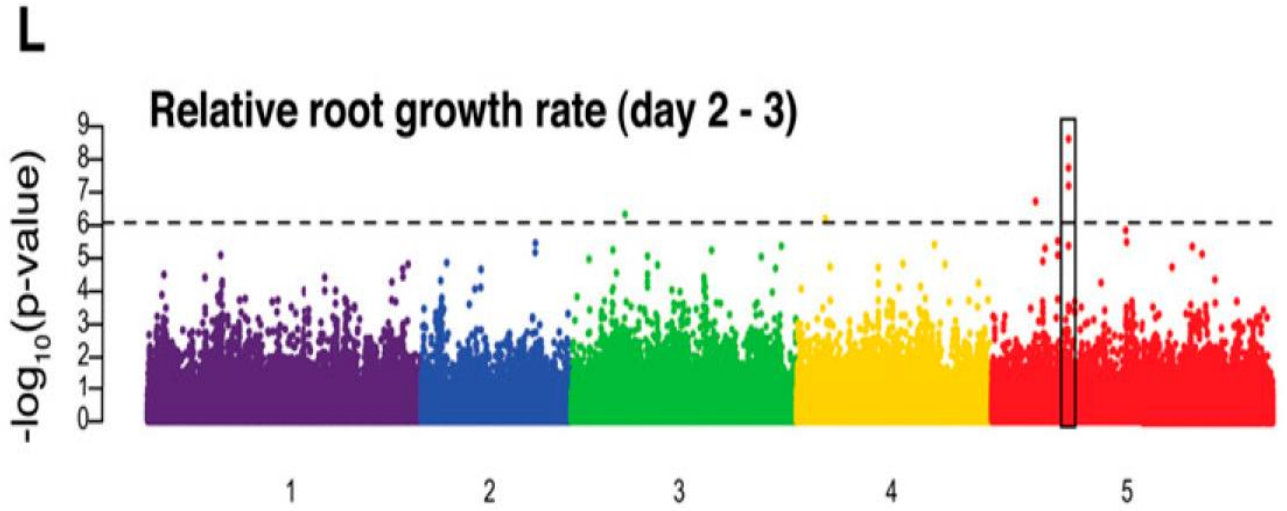


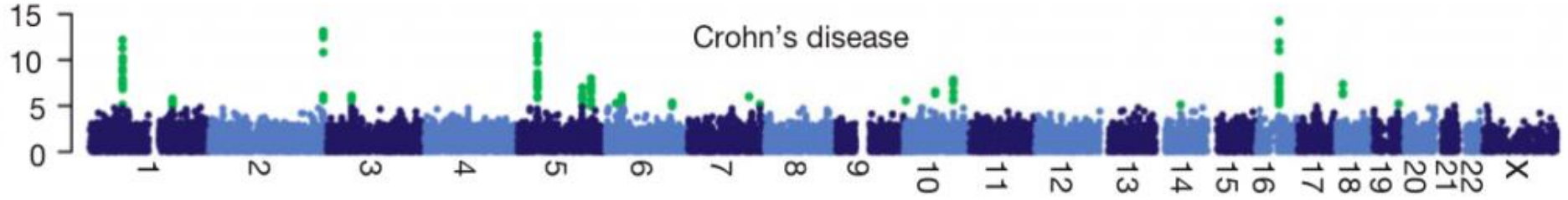
cas-1 mutant has
indeed shorter root

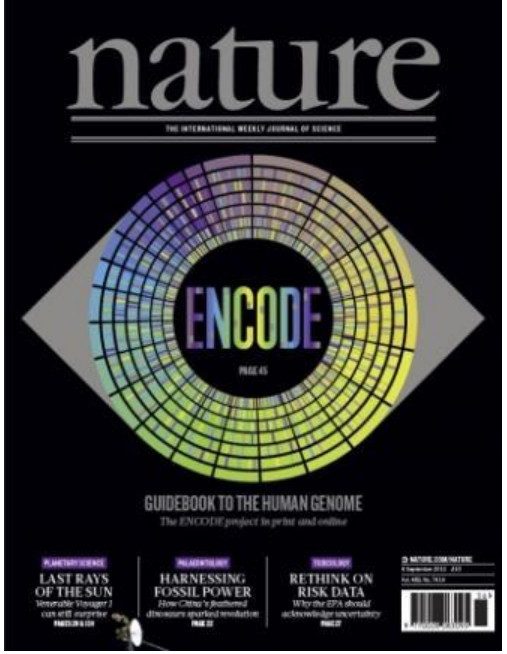
Slovak et al. 2014

Genome wide association studies (GWAS)

Manhattan plot by human







The ENCODE project

The Encyclopedia of DNA Elements

Is really only ~1 % human genome functional?

1 % = gene coding regions

September 2012

ENCODE – think big

- 80 million dollars (1/2 yearly GAČR budget)
- 1,640 data sets
- 147 cell types
- Nature (6), Genome Biology (18), Genome Research (6 papers)

The ENCODE project

Mainly cancer cells, lymphocytes etc.

RNA transcribed regions:
RNA-seq, CAGE, RNA-PET and manual annotation

Protein-coding regions:
mass spectrometry

Transcription-factor-binding sites:
ChIP-seq, DNase-seq

Chromatin structure:
DNase-seq, FAIRE-seq, histone ChIP-seq and MNase-seq

DNA methylation sites:
RRBS assay

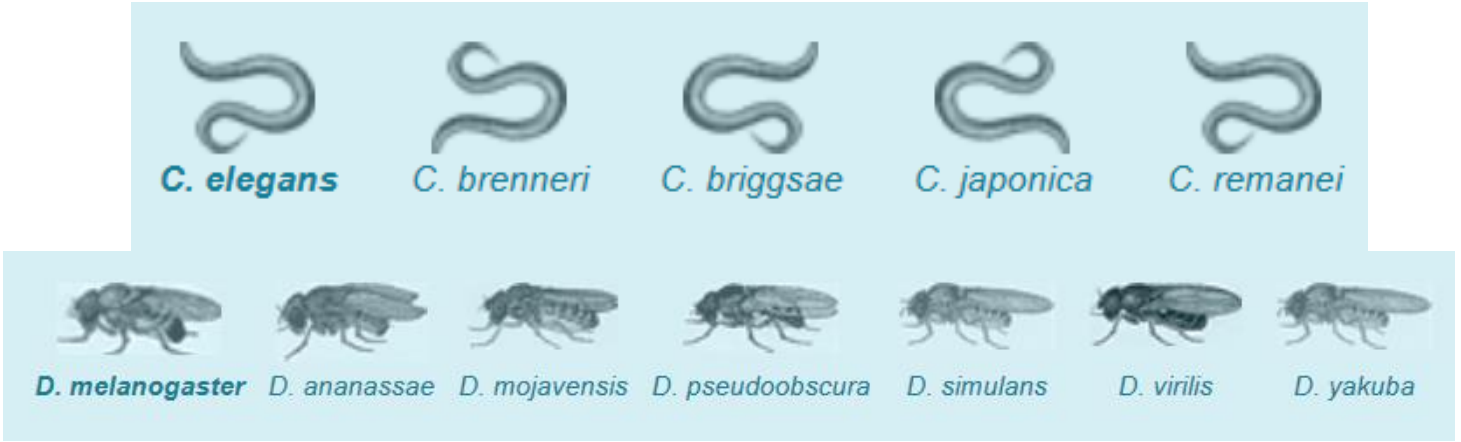
ENCODE - summary

~80 % genome associated with biochemical function:

- enhancers, promoters
- transcribed to non-coding RNA
- 75 % genome transcribed, at least little bit
- number of recognition sequences of DNA binding proteins doubled

E. g. 75 % meaningful number?

ModENCODE on the way



Drosophila tissue sources:

Adult eclosion + several days
Adult female
Adult male
Embryos 0-1, 0-2, 0-12, 10-12 hr etc
Larvae in various instars
Pupae in various stages
Mated males or females
etc.

http://www.modencode.org/

Question: where do you see the limits of high throughput biology?

Cons

- sometimes low quality data or artifacts
- occasionally data missing
- biological material is quite complex
- what to do with so many data?
- where is the idea?

What is systems biology

- next name for something between biology and chemistry?
  biochemistry -> proteomics
  molecular biology -> (functional) genomics
- a real new concept?

“Multidimensional biology”

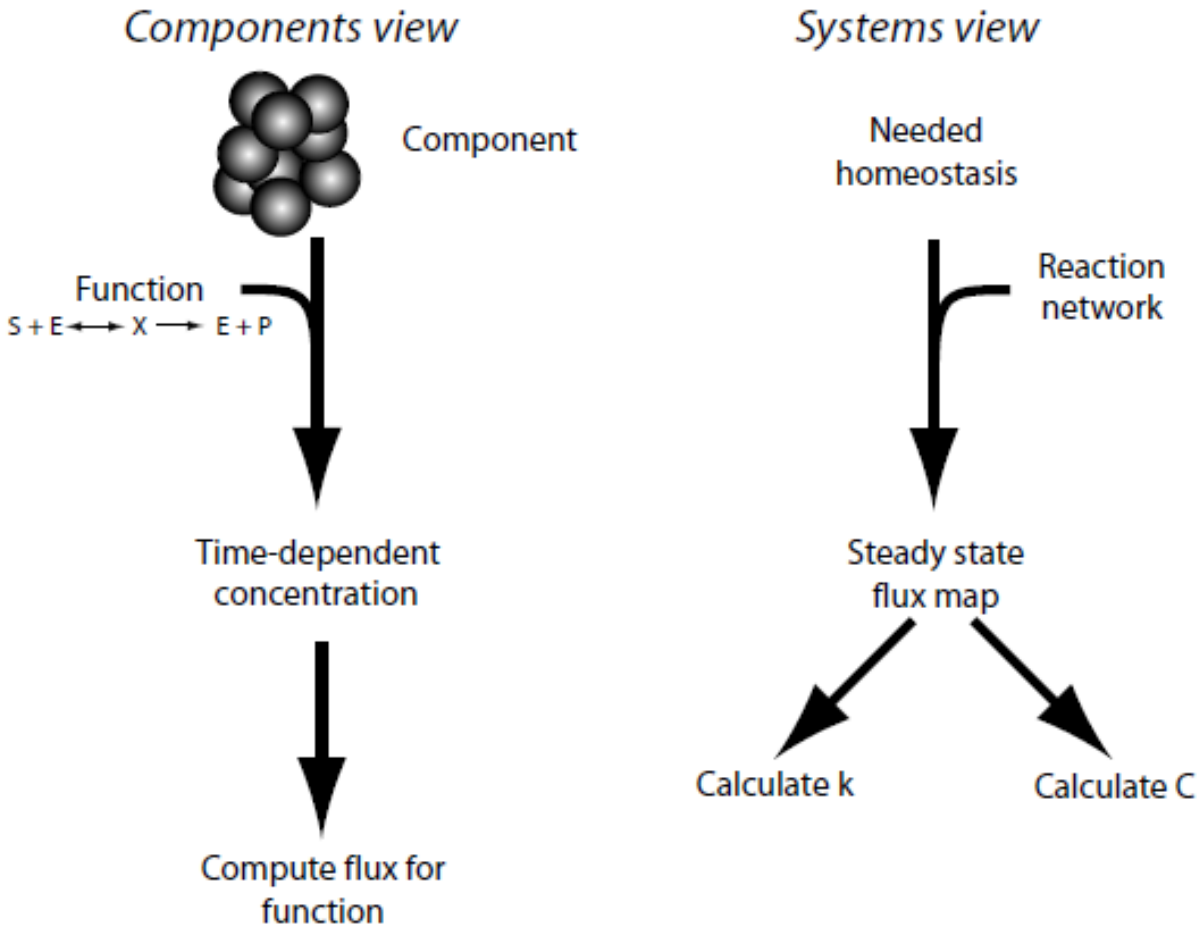
- Genomics
- Epigenomics
- Transcriptomics
- Epitranscriptomics
- Translatomics / Proteomics
- Metabolomics
- Interactomics
- Fluxomics
- NeuroElectroDynamics
- Phenomics
- Biomics

Systems theory

Forget about **reductionism**, think **holistically**.

ὅλος [hol'-os] – greek. all, the whole, entire, complete

Reductionism vs. holism



Ludwig von Bertalanffy
(1901-1972)

$15.95

GENERAL SYSTEM THEORY

Gathered here are Ludwig von Bertalanffy's writings on general system theory, selected and edited to show the evolution of systems theory and to present its applications to problem solving. An attempt to formulate common laws that apply to virtually every scientific field, this conceptual approach has had a profound impact on such widely diverse disciplines as biology, economics, psychology, and demography.

A German-Canadian biologist and philosopher, Ludwig von Bertalanffy (1901–1972) was the creator and chief exponent of general system theory. He is the author of ten books including *Robots, Men, and Minds* and *Modern Theories of Development,* both which have been published in several languages.

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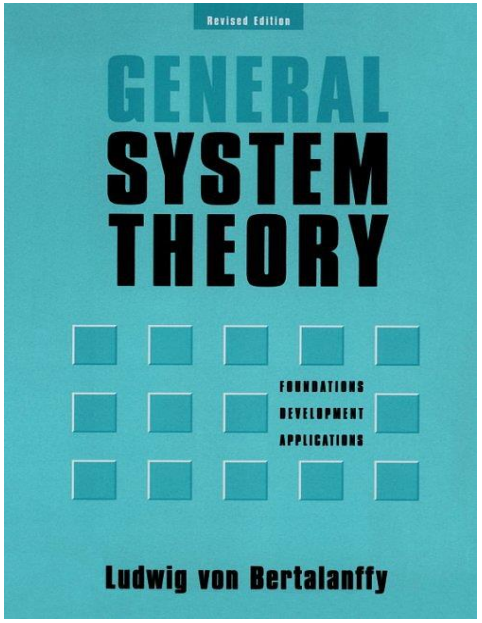

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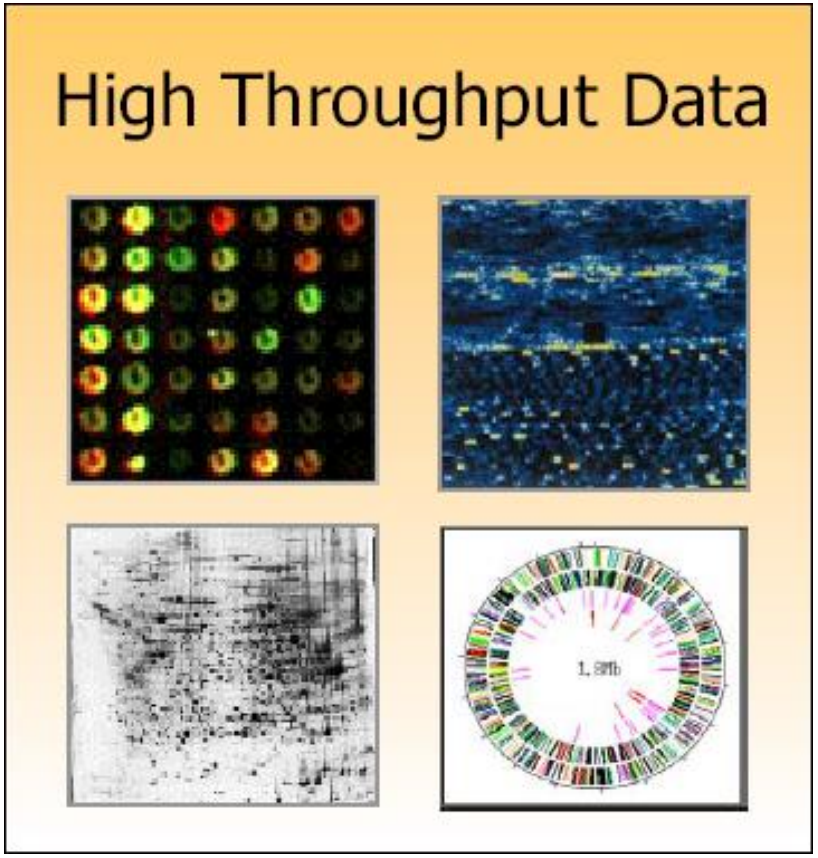
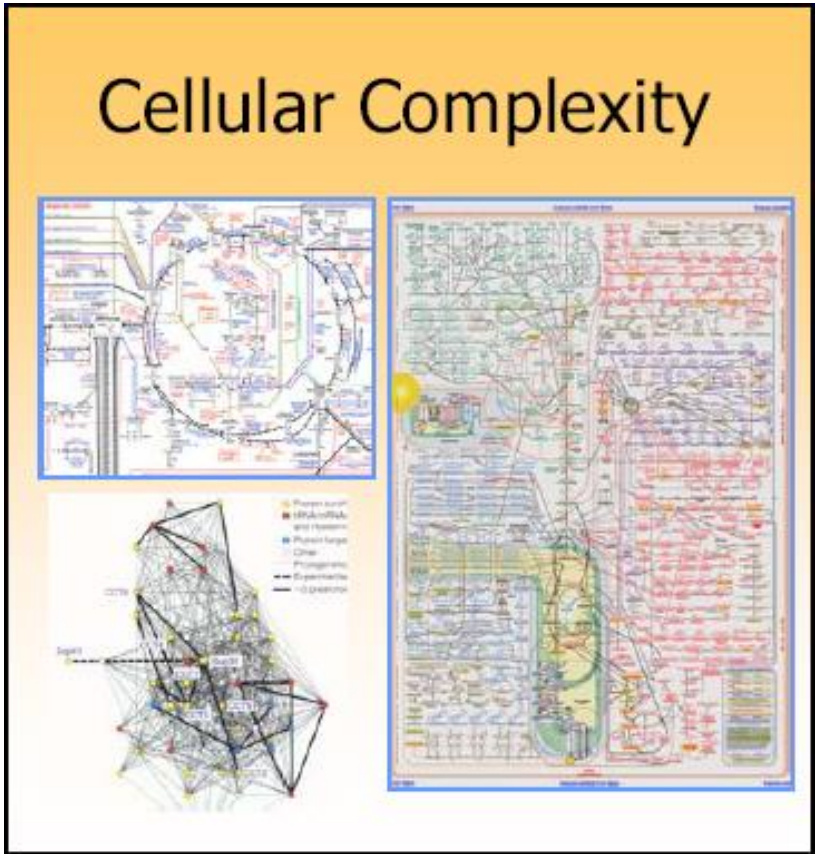
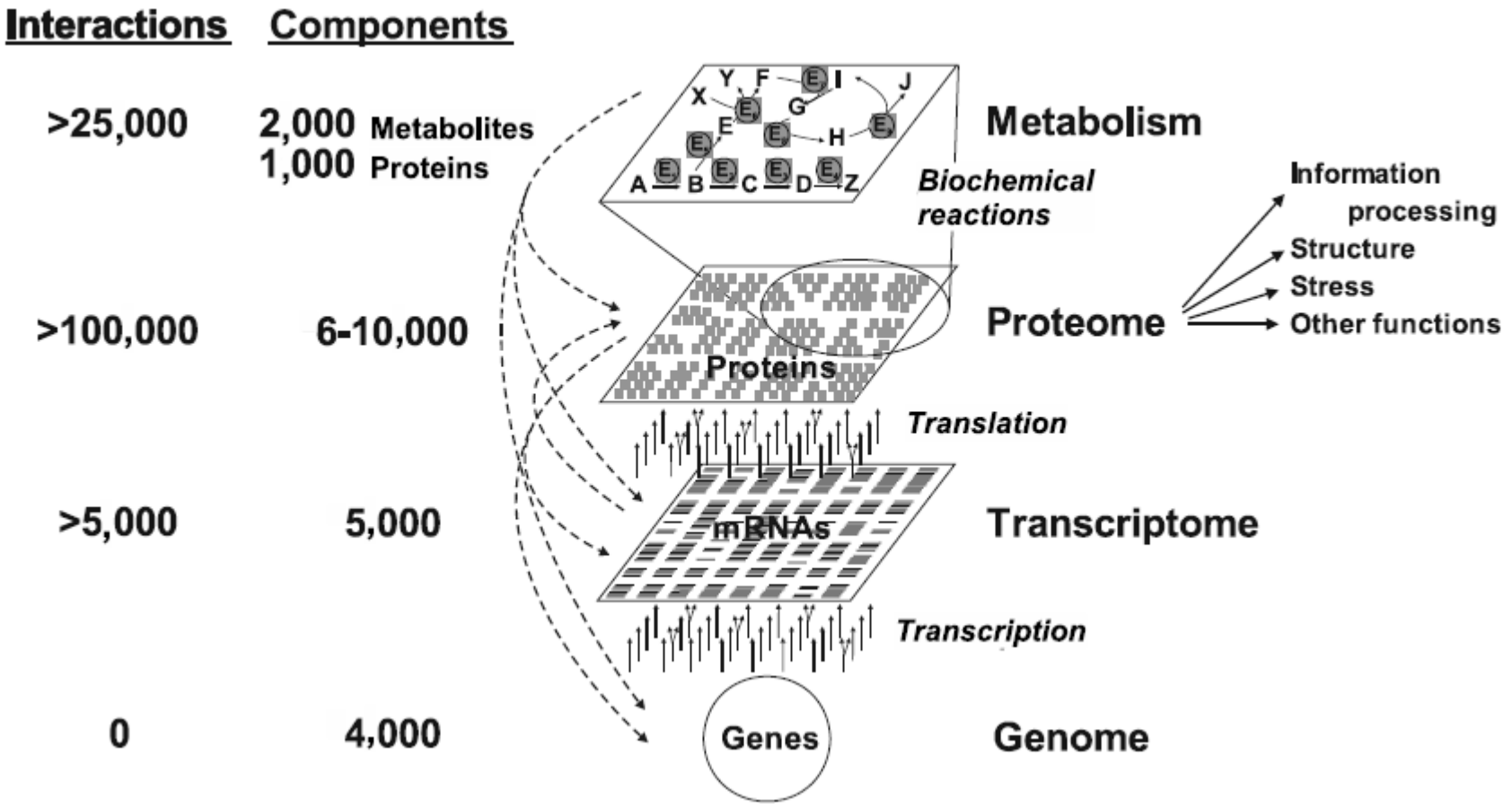
Omics-revolution shifts paradigm to large systems



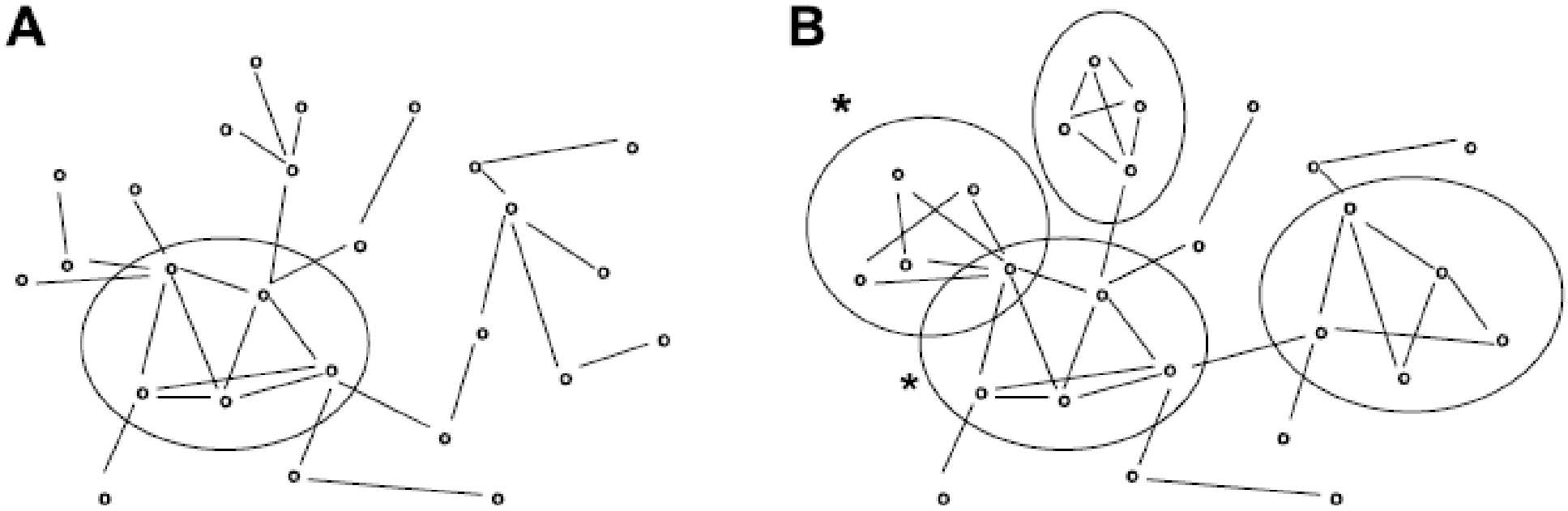


- Integrative bioinformatics
- (Network) modeling

E. coli genome and proteome is small



Reductionism within holism



Lets e.g. assume that transcription and translation is one module.

E. coli

Binding of a small molecule (a signal) to a transcription factor, causing a change in transcription factor activity	~1 msec
Binding of active transcription factor to its DNA site	~1 sec
Transcription + translation of the gene	~5 min
Timescale for 50% change in concentration of the translated protein (stable proteins)	~1 h (one cell generation)
Generation time	20 min

Description of gene regulation

Transcription factor X regulates gene Y:

$$X \rightarrow Y$$

$$(X \rightarrow transcription \rightarrow translation \rightarrow Y)$$

Description of gene regulation

$$X \rightarrow Y$$

Rate of production: $ß$ [units .time^{-1}]

Rate of degradation: α [time^{-1}]

Description of gene regulation

$$X \rightarrow Y$$

Rate of production: $ß$ [units .time^{-1}]

Rate of degradation: α [time^{-1}]

$$\alpha = \alpha_{dil} + \alpha_{deg}$$

Description of gene regulation

$$X \rightarrow Y$$

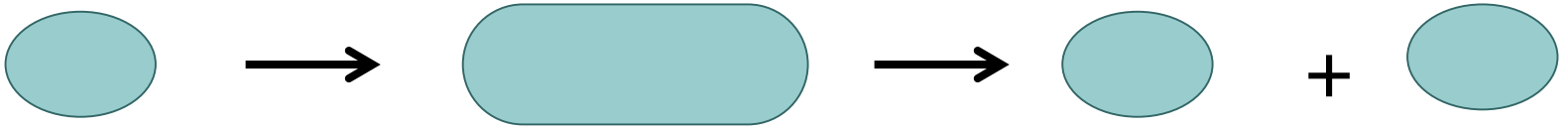
Rate of production: β [units .time^{-1}]

Rate of degradation: α [time^{-1}]

$$\alpha = \alpha_{dil} + \alpha_{deg}$$

cells grow

protein is degraded



Description of gene regulation

$$X \rightarrow Y$$

Rate of production: ß [units.time^{-1}]

Rate of degradation: α [time^{-1}]

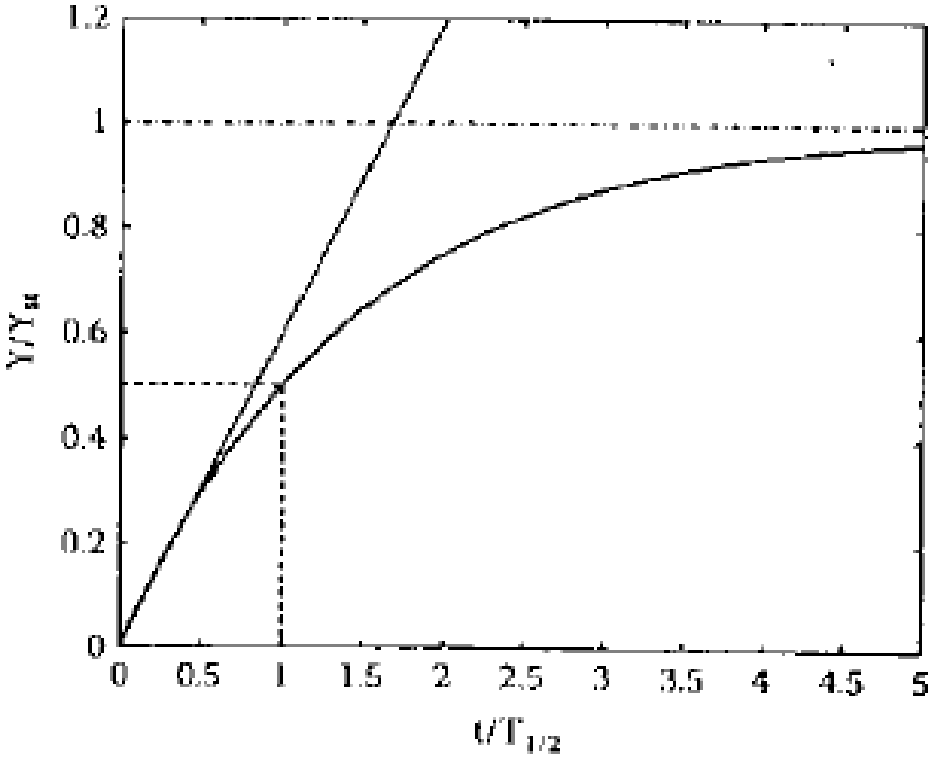
Change of concentration:

$$\frac{dY}{dt} = \beta - \alpha Y$$

Production of Y starts from zero

$$\frac{dY}{dt} = \beta - \alpha Y$$

$$Y_t = \frac{ß}{\alpha}(1 - e^{-\alpha t})$$



(imagine Baťa and cvičky)

Solve the separable equation $\frac{d\,y(x)}{d\,x} = b - a\,y(x)$:

Divide both sides by $b - a\,y(x)$:

$$\frac{\frac{d\,y(x)}{d\,x}}{b - a\,y(x)} = 1$$

Integrate both sides with respect to x:

$$\int \frac{\frac{d\,y(x)}{d\,x}}{b - a\,y(x)}\,d\,x = \int 1\,d\,x$$

Evaluate the integrals:

$-\frac{\log(b - a\,y(x))}{a} = x + c_1$, where c_1 is an arbitrary constant.

Solve for $y(x)$:

Answer:

$$y(x) = \frac{b - e^{-(a\,(x + c_1))}}{a}$$

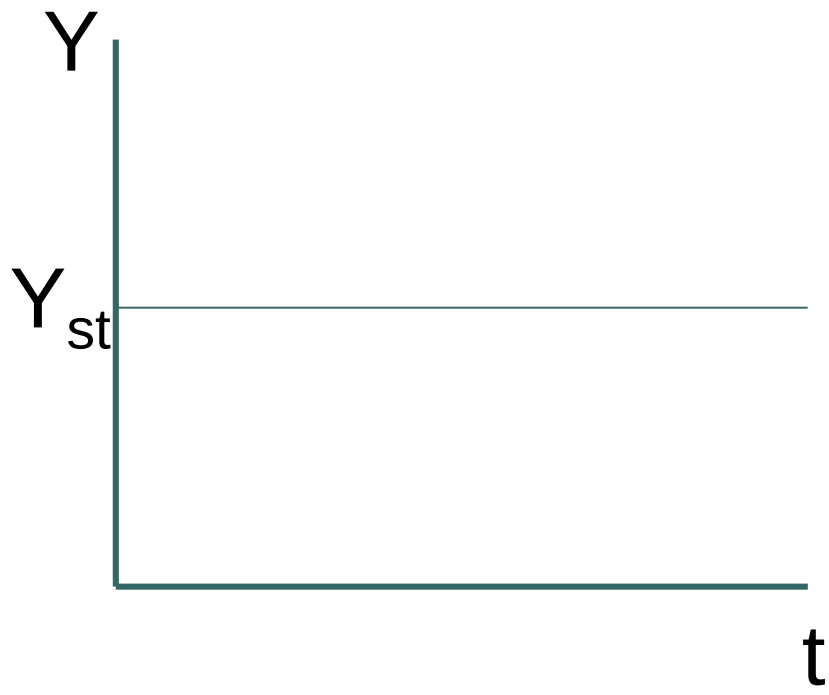
1. Steady state – ustálený stav

$$\frac{dY}{dt} = \beta - \alpha Y$$

$$\frac{dY}{dt} = 0$$

$$\downarrow$$

$$Y_{st} = \frac{\beta}{\alpha}$$



2. Production of Y stops

$$\frac{dY}{dt} = \beta - \alpha Y$$

$$\beta = 0$$

$$Y_t = Y_{st} e^{-\alpha t}$$

The decay is exponential.

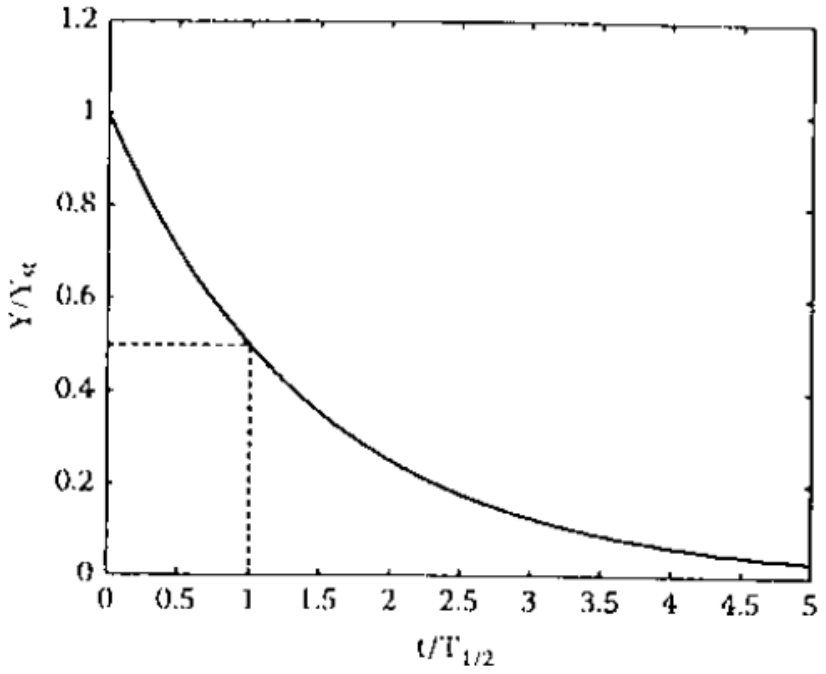
2. Production of Y stops:

Measure of Y decay – response time ($T_{1/2}$).

$$Y_t = Y_{st} e^{-\alpha t}$$

$$Y_t = \frac{1}{2} Y_{st}$$

$$T_{1/2} = \frac{\log 2}{\alpha}$$



(log => ln [.CZ])

2. Production of Y stops:

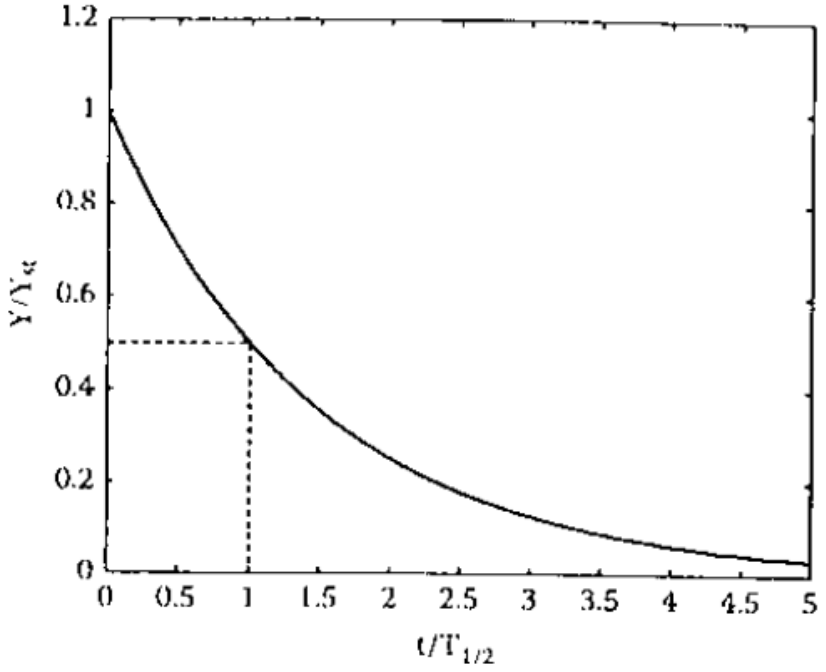
Measure of Y decay – response time ($T_{1/2}$).

$$Y_t = Y_{st} e^{-\alpha t}$$

$$Y_t = \frac{1}{2} Y_{st}$$

$$\downarrow$$

$$T_{1/2} = \frac{\log 2}{\alpha}$$



Large $\alpha \rightarrow$ rapid degradation

(log => ln [.CZ])

$$\gamma_t = \gamma_{st}\, e^{-\alpha t}$$

$$\gamma_t = \frac{1}{2}\,\gamma_{st}$$

$$\frac{1}{2}\,\gamma_{st} = \gamma_{st}\, e^{-\alpha t}$$

$\left|\cdot\right.$ ln

$$1 = 2\, e^{-\alpha t}$$

$$0 = \ln 2 - \alpha t$$

$$t = \frac{\ln 2}{\alpha}$$

$\therefore = T_{1/2}$

Stable proteins

(most of E. coli proteins)

$$T_{1/2} = \frac{\log 2}{\alpha}$$

$$\alpha = \alpha_{dil} + \alpha_{deg}$$

$$\alpha \approx \alpha_{dil}$$

τ – cell generation

$$T_{1/2} = \frac{\log 2}{\alpha_{dil}} = \tau$$

Stable proteins

$$T_{1/2} = \frac{\log 2}{\alpha}$$

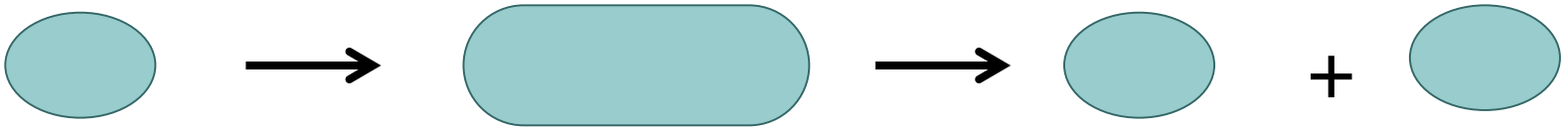
$$\alpha = \alpha_{dil} + \alpha_{deg}$$

$$\alpha \approx \alpha_{dil}$$

τ – cell generation

$$T_{1/2} = \frac{\log 2}{\alpha_{dil}} = \tau$$

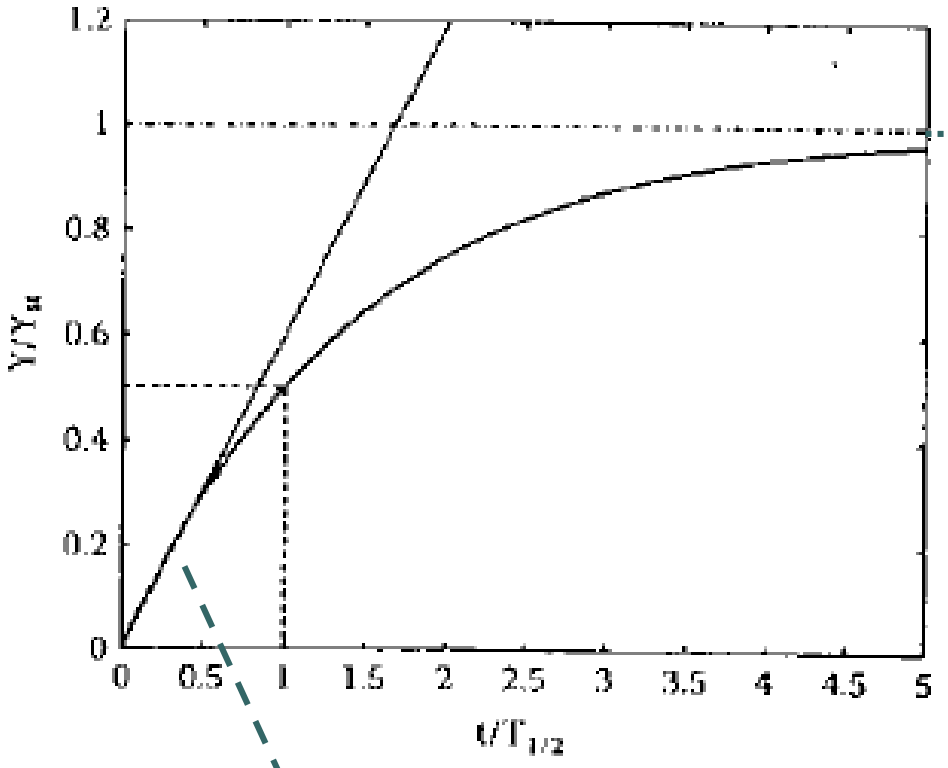
Response time is one generation.



3. Production of Y starts from zero

$$\frac{dY}{dt} = \beta - \alpha Y$$

$$Y_t = \frac{ß}{\alpha}(1 - e^{-\alpha t})$$



$$Y_{st} = \frac{ß}{\alpha}$$

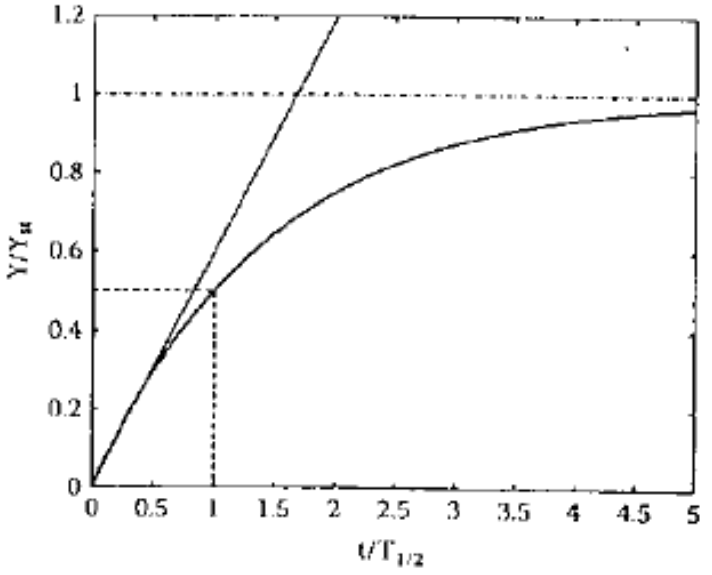
Y grows almost linearly initially

3. Production of Y starts from zero

Response time:

$$Y_t = Y_{st}(1 - e^{-\alpha t})$$

$$Y_t = \frac{1}{2} Y_{st}$$



$$T_{1/2} = \frac{\log 2}{\alpha}$$

The same response time as in case 2.

Response time does not depend on production rate!

$$y_t = y_{st}\left(1 - e^{\alpha t}\right)$$

$$y_t = \frac{1}{2} y_{st} \quad \Rightarrow \quad \frac{1}{2} y_{st} = y_{st}\left(1 - e^{\alpha t}\right)$$

$$1 = 2 - 2e^{\alpha t}$$

$$1 = 2e^{\alpha t} \quad | \ln$$

$$0 = \ln 2 + \alpha t$$

$$t = \frac{\ln 2}{\alpha}$$

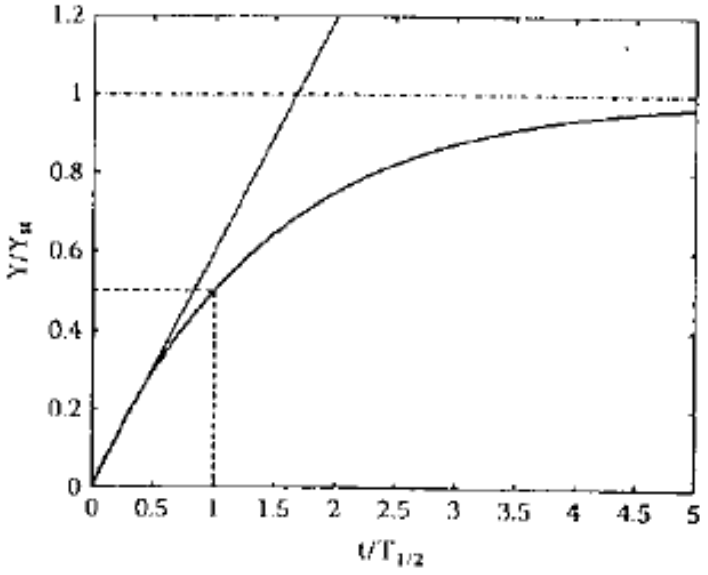
i.e. $T_{1/2}$

3. Production of Y starts from zero

Response time:

$$Y_t = Y_{st}(1 - e^{-\alpha t})$$

$$Y_t = \frac{1}{2} Y_{st}$$



$$T_{1/2} = \frac{\log 2}{\alpha}$$

Degradation – faster response time. However, energetically demanding.

F-box regulatory ubiquitin genes in organism

Arabidopsis: 700

Saccharomyces: 14

Drosophila: 24

Human: 38

Arabidopsis does not have problems with energy

Great web sites

http://www.yeastgenome.org/	*S. cerevisiae*
http://www.pombase.org/	*S. pombe*
http://flybase.org/	*Drosophila*
http://www.wormbase.org/	*C. elegans*
http://www.arabidopsis.org/	*A. thaliana*

Also nice web sites

http://encodeproject.org/
http://www.thebiogrid.org/
http://www.genemania.org/
http://string-db.org/
…and many others
…pay attention, if they are kept alive and curated

Literature

- Source literature (systems biology)
  - http://sybila.fi.muni.cz/cz/index - obor na fakultě informatiky.
  - http://www.youtube.com/watch?v=Z__BHVFP0Lk and further – excellent talks about systems biology from Uri Alon (Weizman Institute) – absolutely best
  - Alon U. Network motifs: theory and experimental approaches. Nat Rev Genet. 2007 Jun;8(6):450-61. Review about the same.
  - Alon, U. (2006). An Introduction to Systems Biology: Design Principles of Biological Circuits (Chapman and Hall/CRC).

- For enthusiasts
  - Venter, J.C. (2008). A life decoded: my genome, my life (London: Penguin).
  - Albert-László Barabási (2005) V pavučině sítí. (Paseka) (znamenitá kniha o matematice sítí, dynamicky se rozvíjejícím oboru od předního světového vědce)
  - PA052 Úvod do systémové biologie, Přednášky. Fakulta Informatiky MU
  - http://www.pnas.org/content/110/29/11952 (paper which challenges something conclusions in ENCODE)