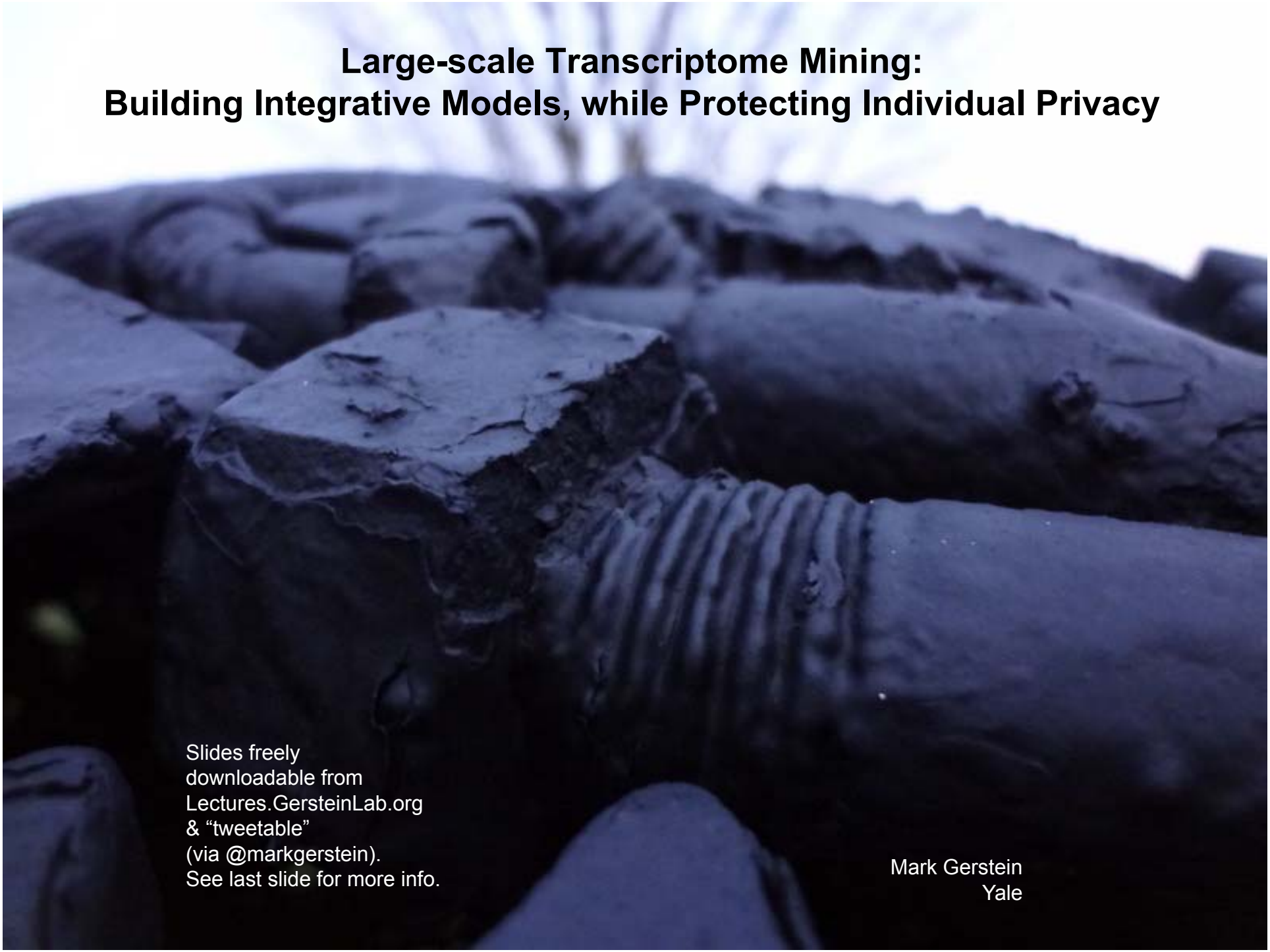
Large-scale Transcriptome Mining: Building Integrative Models, while Protecting Individual Privacy

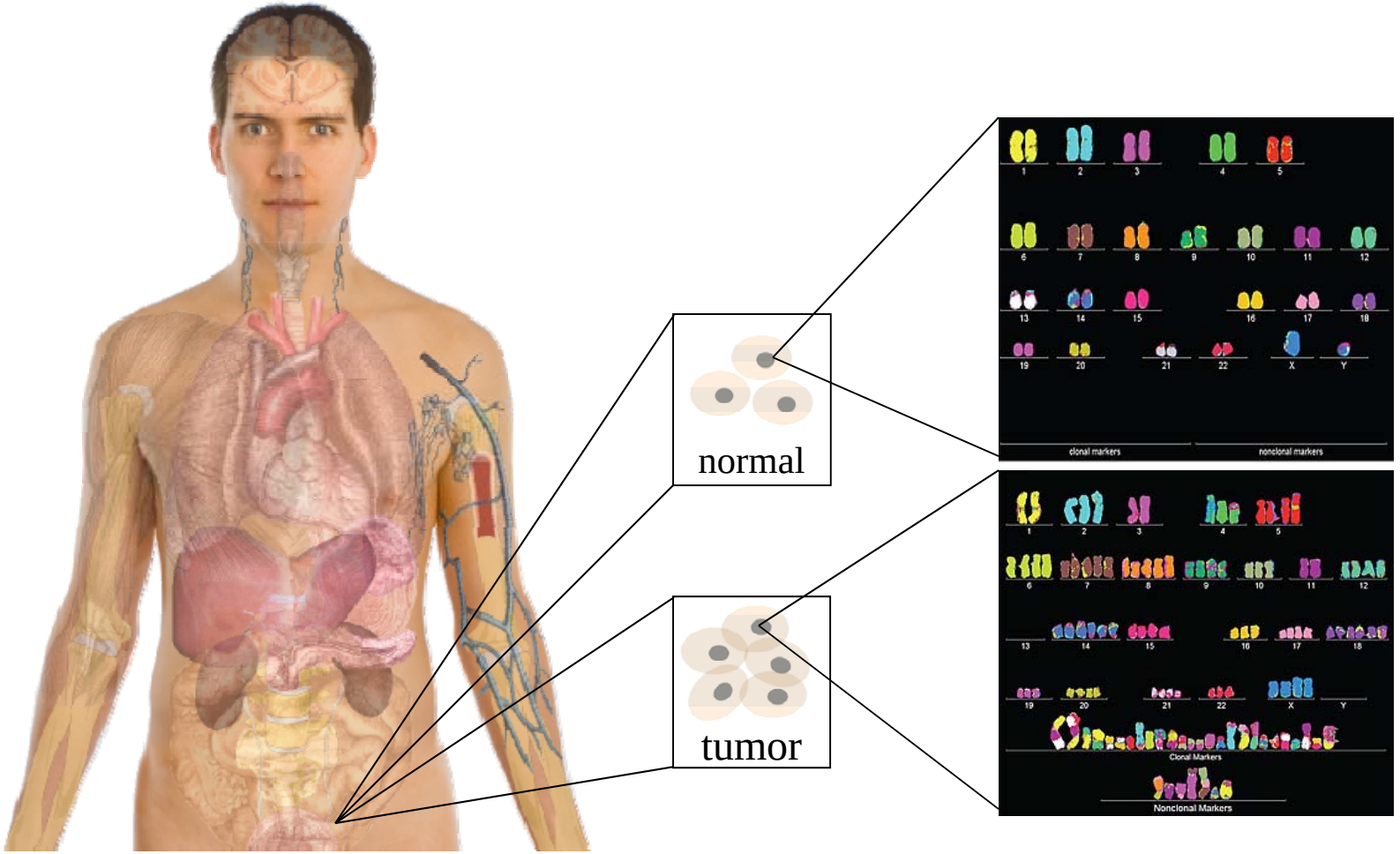


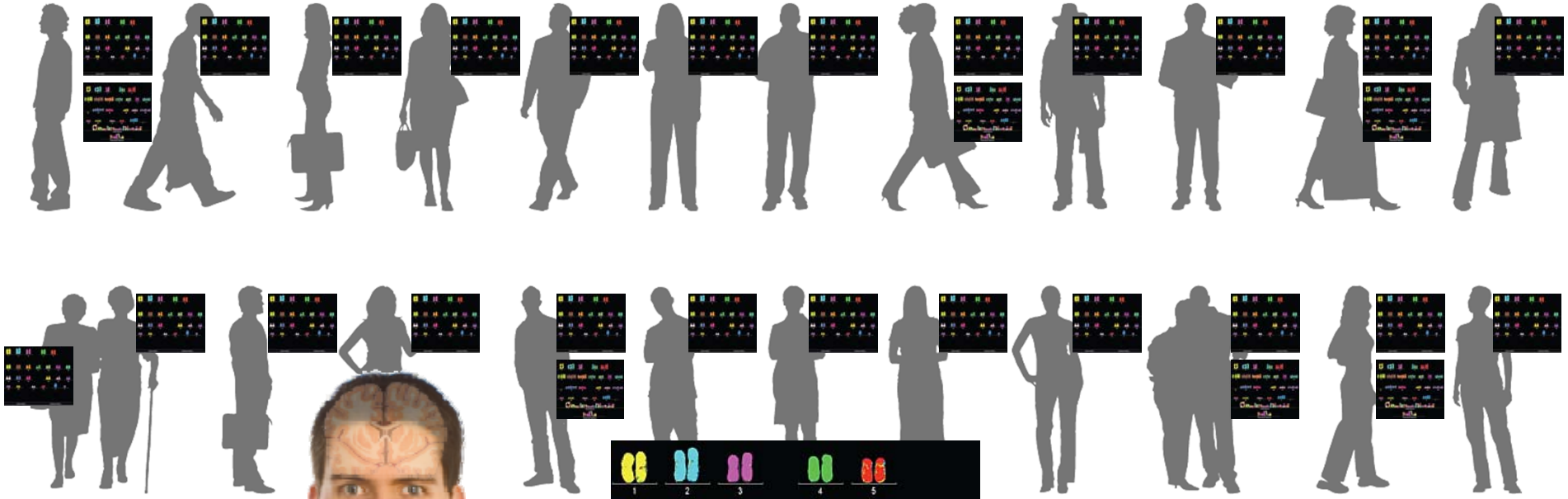
Slides freely
downloadable from
Lectures.GersteinLab.org
& “tweetable”
(via @markgerstein).
See last slide for more info.

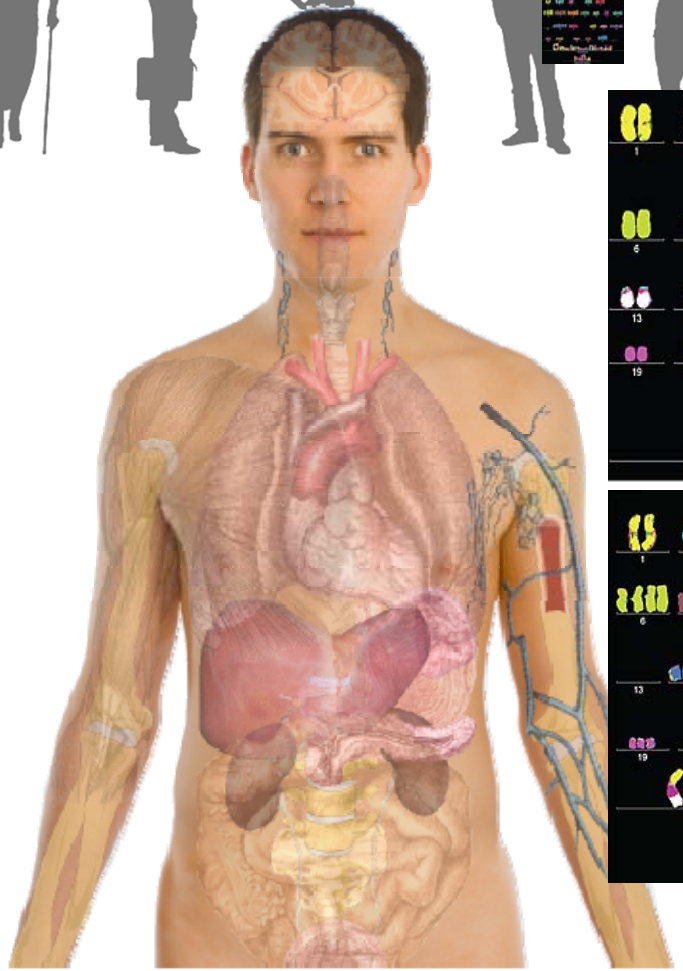
Mark Gerstein
Yale

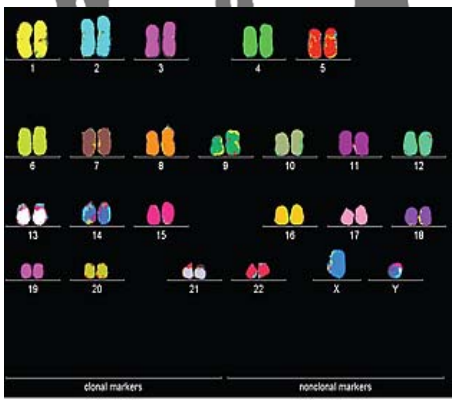
Personal Genomics & Transcriptomics as a Gateway into Biology

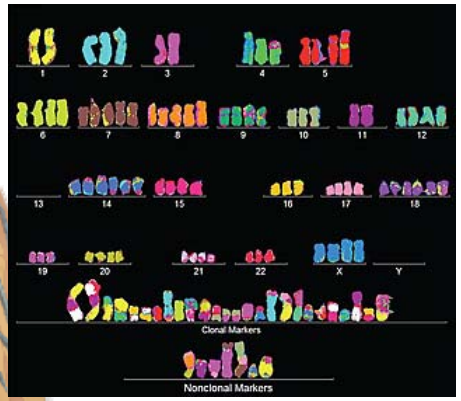
Personal genomes soon will become a commonplace part of medical research & eventually treatment (esp. for cancer). They will provide a primary connection for biological science to the general public.









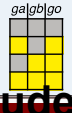


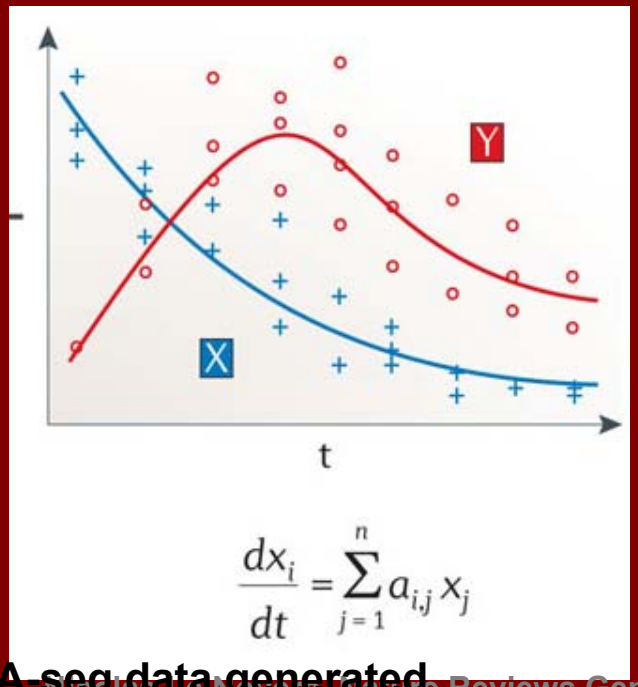
Placing the individual into the context of the population & using the population to build a model

Building Regulatory Models from Large-scale RNA-seq Data v Privacy Aspects of Large-scale RNA-seq Analysis

- Boolean logical model
- Continuous model

Key *gi,ga,gb,gc:* input genes; *go:* output gene; off; on

	Logic		Example	
	Operator	Definition	Vector Function	Model
Boolean	**NOT**	the output is off if the input is on	*go*: if **NOT** *gi*=1 then=1 else=0	
	OR	the output is on if at the least one of the inputs is on	*go*: if *ga*=1 **OR** *gb*=1 then=1 else=0	
	AND	the output is on only if both inputs are on	*go*: if *ga*=1 **AND** *gb*=1 then=1 else=0	
	AND NOT	the output is on if the first input is on and the second is off	*go*: if *ga*=1 **AND NOT** *gb*=1 then=1 else=0	
	[ ]	brackets for subsidiary functions	*go*: if *ga*=1 AND **[** *gb*=1 OR *gc*=1 **]** then=1 else=0	
	the vector equation can incorporate different module or functions		*go*: if **Mod1** OR **Mod2** then=1 else=0 **Mod1** : if *ga*=1 then=1 else=0 **Mod2** : if *gb*=1 then=1 else=0	



Istrail & Davidson, PNAS, ‘04

Nicolas Le Novère, Nature Reviews Genetics, ‘15

Large magnitude of RNA-seq data generated
ENCODE, modENCODE, TCGA, GTEx, Roadmap, psychENCODE, etc.
Mostly the data is about the phenotype (e.g.

Large-scale Transcriptome Mining: Building Interpretative Models while Protecting Individual Privacy

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  - Current Social & Tech Approaches
    - Issues: burdensome security, inconsistencies + ways the solutions have been partially "hacked"
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The Conundrum of Genomic Privacy: Is it a Problem?

Yes

Genetic Exceptionalism :
genome is potentially very revealing about one's identity & characteristics

- Most discussion of Identification Risk but what about Characterization Risk?
  - Finding you were in study X vs identifying that you have trait Y from studying your identified genome

No

Shifting societal foci

No one really cares about *your* genes

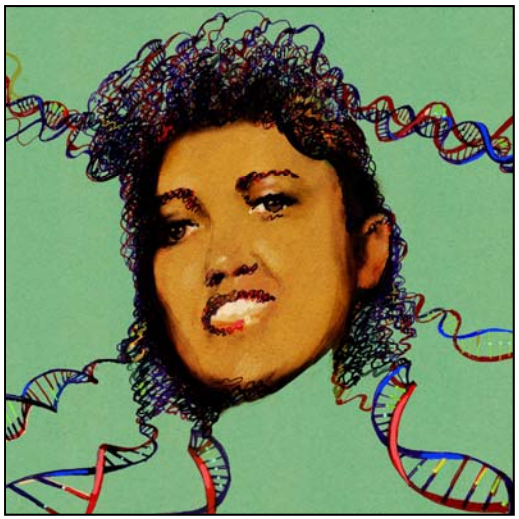
You might not care

[Klitzman & Sweeney ('11), J Genet Couns 20:98l; Greenbaum & Gerstein ('09), New Sci. (Sep 23)]

Tricky Privacy Considerations in Personal Genomics

- Personal Genomic info. essentially meaningless currently but will it be in 20 yrs? 50 yrs?
  - Genomic sequence very revealing about one's children. Is true consent possible?
  - Once put on the web it can't be taken back
- Culture Clash: Genomics historically has been a proponent of "open data" but not clear personal genomics fits this
- Ethically challenged history of genetics

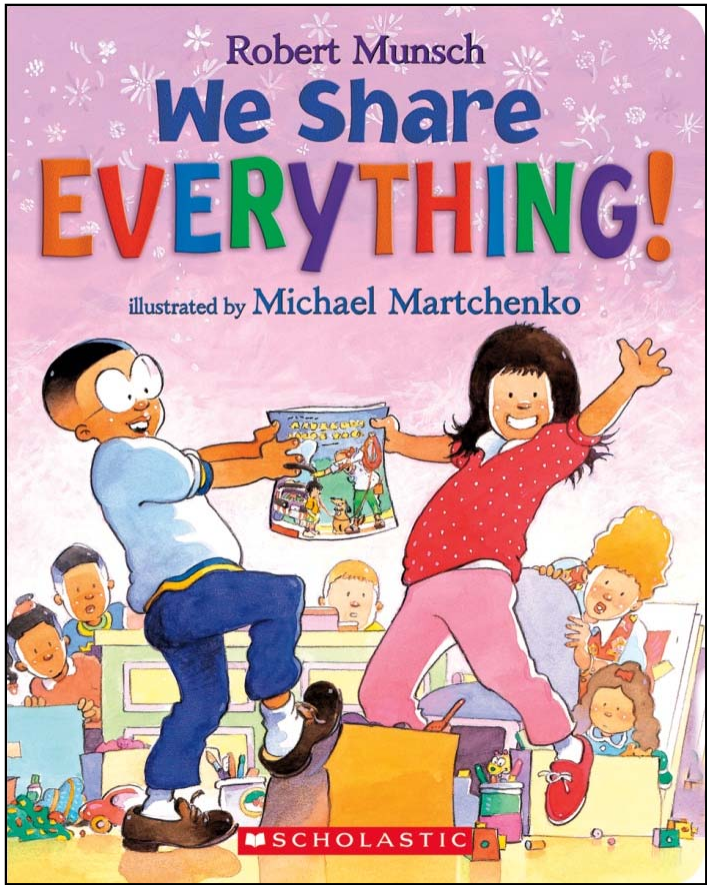
- Ownership of the data & what consent means (Hela)
  - Could your genetic data give rise to a product line?



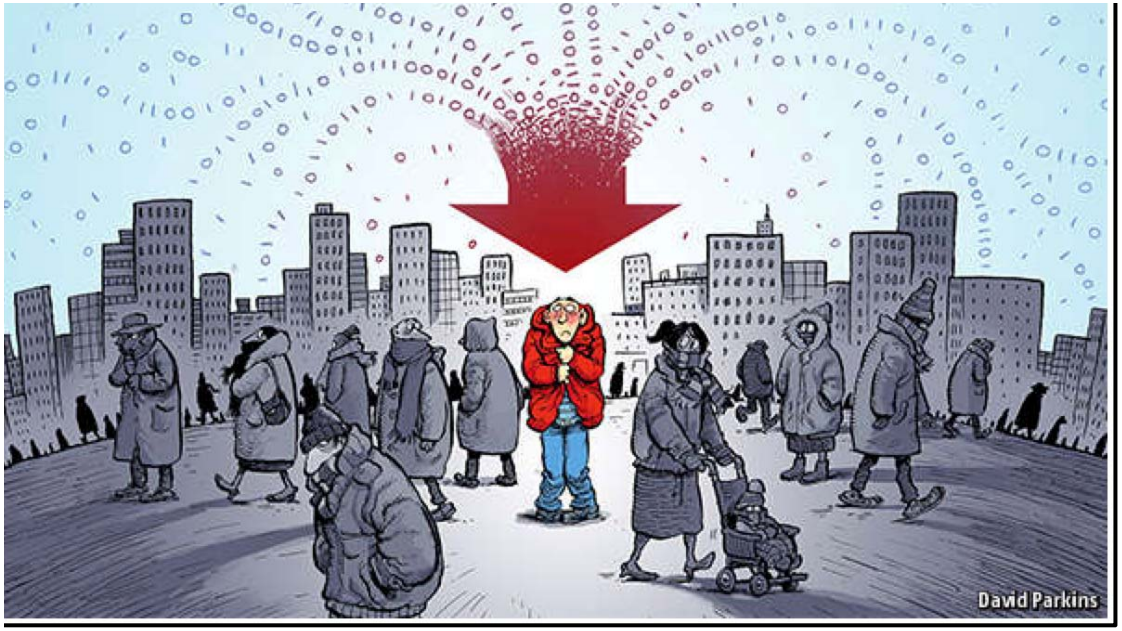
[D Greenbaum & M Gerstein ('08). Am J. Bioethics; D Greenbaum & M Gerstein, Hartford Courant, 10 Jul. '08 ; SF Chronicle, 2 Nov. '08; Greenbaum et al. *PLOS CB* ('11) ; Greenbaum & Gerstein ('13), The Scientist; Photo from NY Times]

The Other Side of the Coin: Why we should share

- Sharing helps speed research
  - Large-scale mining of this information is important for medical research
  - Privacy is cumbersome, particularly for big data
  - Sharing is important for reproducible research
- Sharing is useful for education



[Yale Law Roundtable ('10). Comp. in Sci. & Eng. 12:8; D Greenbaum & M Gerstein ('09). Am. J. Bioethics; D Greenbaum & M Gerstein ('10). SF Chronicle, May 2, Page E-4; Greenbaum et al. *PLOS CB* ('11)]



[Economist, 15 Aug '15]

The Dilemma

- What is acceptable risk? What is acceptable data leakage? Can we quantify leakage?
- Cost Benefit Analysis: how helpful is identifiable data in genomic research v. potential harm from a breach?
- The individual (harmed?) v the collective (benefits)
  - But do sick patients care about their privacy?
- Maybe a we need a few "test pilots" (ala PGP)?
  - Sports stars & celebrities?

Genomics has similar "Big Data" Dilemma in the Rest of Society

- Sharing & "peer-production" is central to success of many new ventures, with the same risks as in genomics
- We confront privacy risks every day we access the internet
- (...or is the genome more exceptional & fundamental?)

[Seringhaus & Gerstein ('09), *Hart. Courant* (Jun 5); Greenbaum & Gerstein ('11), *NY Times* (6 Oct)]

Current Social & Technical Solutions

- Consents
- “Protected” distribution of data (dbGAP)
- Local computes on secure computer

- Issues
  - Non-uniformity of consents & paperwork
    - Different international norms, leading to confusion
  - Encryption & computer security creates burdensome requirements on data sharing & large scale analysis
  - Many schemes get “hacked”

[Greenbuam et al ('04), Nat. Biotech; Greenbaum & Gerstein ('13), The Scientist]

Privacy Hacks

- Personalized genomic data generation is booming
- Main focus is on protecting variants

- "Detection of genome in a mixture"
  - Individuals give consent to participate but request anonymity
    - HAPMAP, Personal genome project, 1000 Genomes…
- Larger and more datasets leads to more realistic risks of linking attacks, that may be much more damaging than detection of genome in a mixture attacks

Identifying Personal Genomes by Surname Inference

Melissa Gymrek,[1,2,3,4] Amy L. McGuire,[5] David Golan,[6] Eran Halperin,[7,8,9] Yaniv Erlich[1*]

Resolving Individuals Contributing Trace Amounts of DNA to Highly Complex Mixtures Using High-Density SNP Genotyping Microarrays

Nils Homer[1,2], Szabolcs Szelinger[1], Margot Redman[1], David Duggan[1], Waibhav Tembe[1], Jill Muehling[1], John V. Pearson[1], Dietrich A. Stephan[1], Stanley F. Nelson[2], David W. Craig[1*]

On Sharing Quantitative Trait GWAS Results in an Era of Multiple-omics Data and the Limits of Genomic Privacy

Hae Kyung Im,[1,*] Eric R. Gamazon,[2] Dan L. Nicolae,[2,3,4] and Nancy J. Cox[2,3,*]

Identifying Participants in the Personal Genome Project by Name

Latanya Sweeney, Akua Abu, Julia Winn

Harvard College
Cambridge, Massachusetts
latanya@fas.harvard.edu, aabu@college.harvard.edu, jwinn@post.harvard.edu

Privacy Hacks

- Early genomic studies were based on small cohorts
  - The focus was on hiding the participation of individuals
  - Individuals give consent to participate but request anonymity
    - HAPMAP, Personal Genome Project, 1000 Genomes…
  - Attacks aimed at detecting whether an individual with known genotypes participated a study
    - "Detection of genomes in a mixture"
    - Homer et al 2008, Im et al 2012
- As more people are genotyped, more individuals are in large private genomic databases
  - Detection of an individual is irrelevant, as their participation is already known
    - Example: "An individual's genomic/phenotypic data is most certainly stored in their hospital"
    - Future: Everyone's is genotype is recorded in a centralized dataset
- The attacks will now focus on pinpointing individuals by cross-referencing large seemingly independent datasets
  - A leaked/hacker/stolen dataset, even when anonymized, can leak information
  - Sweeney et al 2013, Gymrek et al 2013

Gymrek et al, "Identifying Personal Genomes by Surname Inference" (2013)
Homer et al, "Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays." (2008)
Im et al, "On Sharing Quantitative Trait GWAS Results in an Era of Multiple-omics Data and the Limits of Genomic Privacy" (2012)
Sweeney et al, "Identifying Participants in the Personal Genome Project by Name" (2013)

Identif

Robust De-anonymization of Large Datasets (How to Break Anonymity of the Netflix Prize Dataset)

Arvind Narayanan and Vitaly Shmatikov

The University of Texas at Austin

February 5, 2008

Abstract

We present a new class of statistical de-anonymization attacks against high-dimensional micro-data, such as individual preferences, recommendations, transaction records and so on. Our techniques are robust to perturbation in the data and tolerate some mistakes in the adversary's background knowledge.

We apply our de-anonymization methodology to the Netflix Prize dataset, which contains anonymous movie ratings of 500,000 subscribers of Netflix, the world's largest online movie rental service. We demonstrate that an adversary who knows only a little bit about an individual subscriber can easily identify this subscriber's record in the dataset. Using the Internet Movie Database as the source of background knowledge, we successfully identified the Netflix records of known users, uncovering their apparent political preferences and other potentially sensitive information.

Cross correlated small set of identifiable IMDB movie database rating records with large set of "anonymized" Netflix customer ratings

Strawman Hybrid Social & Tech Proposed Solution?

- Fundamentally, researchers have to keep genetic secrets
  - Genetic Licensure & training for individuals (similar to medical license, drivers license)
- Technology to make things easier
  - Cloud computing & enclaves (eg solution of Genomics England)
- Technological barriers shouldn't create a social incentive for “hacking”

- **Quantifying Leakage & allowing a small amounts of it (eg photos of eye color)**
- **Careful separation & coupling of private & public data**
  - **Lightweight, freely accessible secondary datasets coupled to underlying variants**
  - Selection of stub & "test pilot" datasets for benchmarking
  - Develop programs on public stubs on your laptop, then move the program to the cloud for private production run

[D Greenbaum, M Gerstein (‘11). Am J Bioeth 11:39. Greenbaum & Gerstein, The Scientist ('13)]

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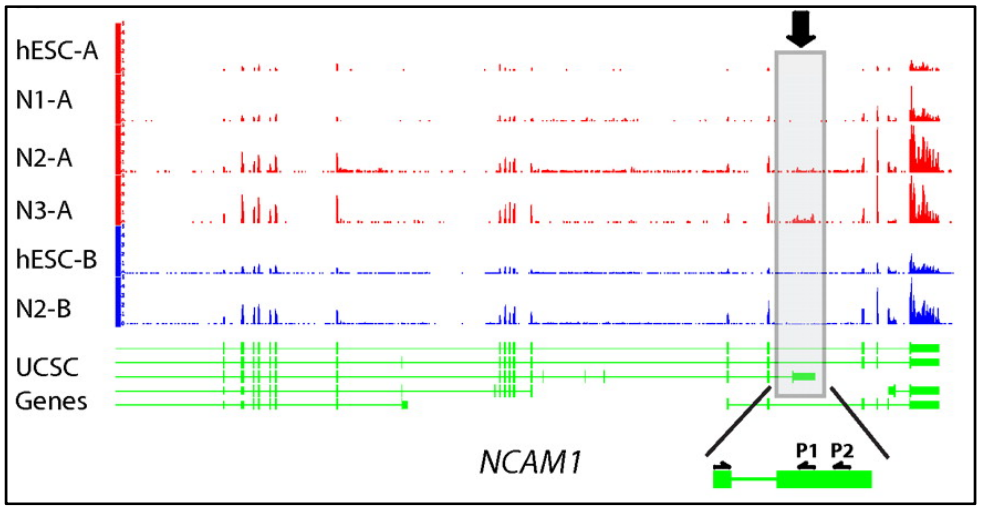
RNA-seq

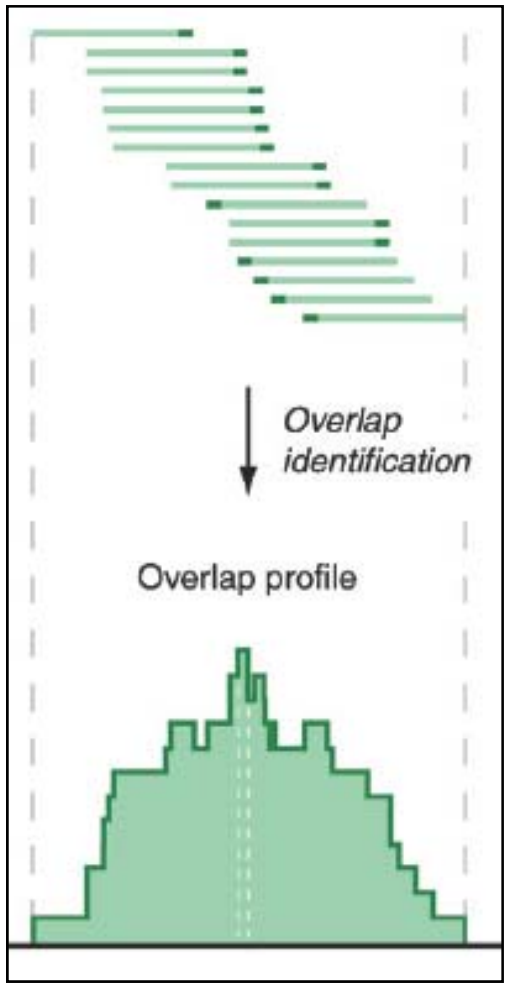
RNA-seq uses next-generation sequencing technologies to reveal RNA presence and quantity within a biological sample.

```
ATACAAGCAAGTATAAGTTCGTATGCCGTCTT
GGAGGCTGGAGTTGGGGACGTATGCGGCATAG
TACCGATCGAGTCGACTGTAAACGTAGGCATA
ATTCTGACTGGTGTCATGCTGATGTACTTAAA
```

Reads (fasta)
- Quality scores (fastq)
- Mapping (BAM)
- Contain variant information in transcribed regions



Quantitative information from RNA-seq signal: average signals at exon level (RPKMs)

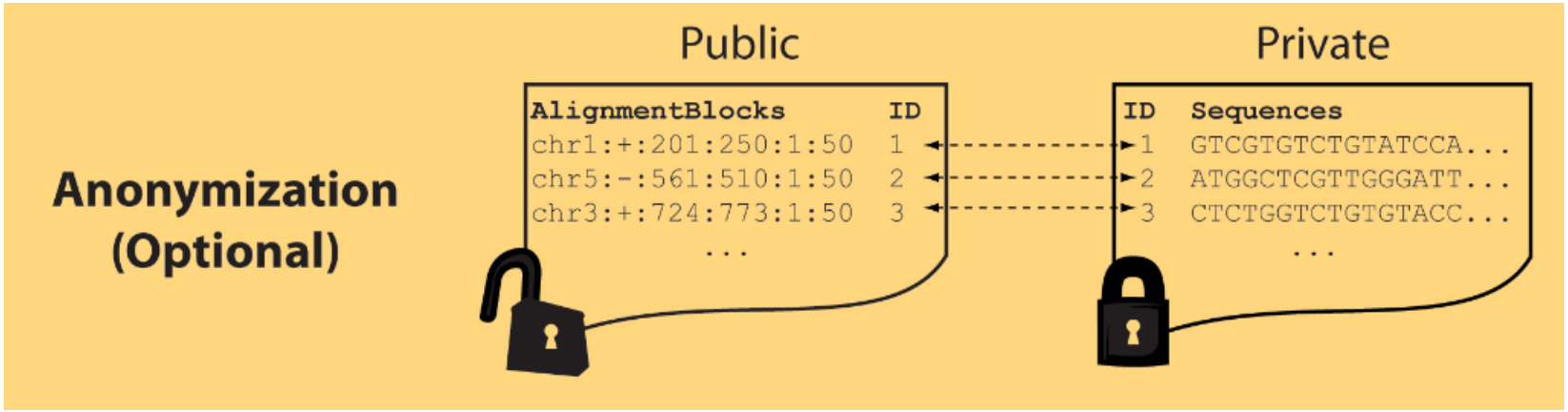


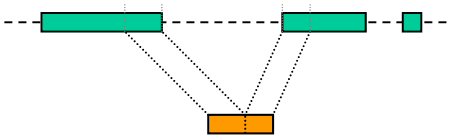
Reads => Signal

[*PLOS CB* 4:e1000158; *PNAS* 4:107: 5254 ; *IJC* 123:569]

Light-weight formats

- Some lightweight format clearly separate public & private info., aiding exchange
- Files become much smaller
- Distinction between formats to compute on and those to archive with – become sharper with big data





Mapping coordinates without variants (MRF)

Reads (linked via ID, 10X larger than mapping coord.)

[*Bioinformatics* 27: 281]

MRF Examples

10X Compression Ex.

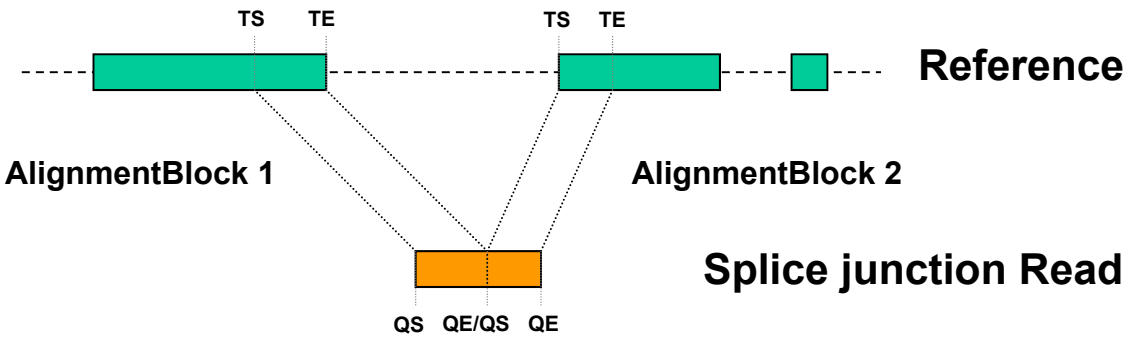
Raw ELAND export file has uncompressed file size: ~4 GB; total number of reads: ~20 million; number of mapped reads: ~12 million .

MRF file is significantly smaller (~400 MB uncompressed, ~130 MB compressed with gzip).

BAM file
has a size of ~1.2 GB.

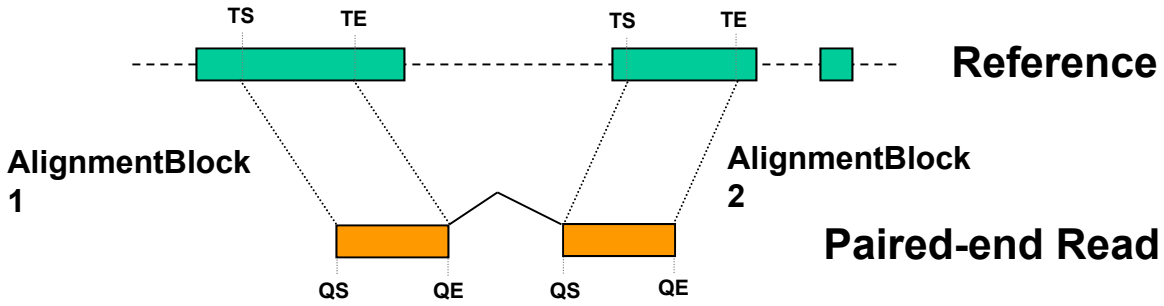
Reference based compression (ie CRAM) is similar but it stores actual variant beyond just position of alignment block

```
chr2:+:601:630:1:30,chr2:+:921:940:31:50
```



Legend: TS = TargetStart, TE = TargetEnd, QS = QueryStart, QE = QueryEnd

```
chr9:+:431:480:1:50|chr9:+:945:994:1:50
```



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[Habegger et al., Bioinformatics ('11)]

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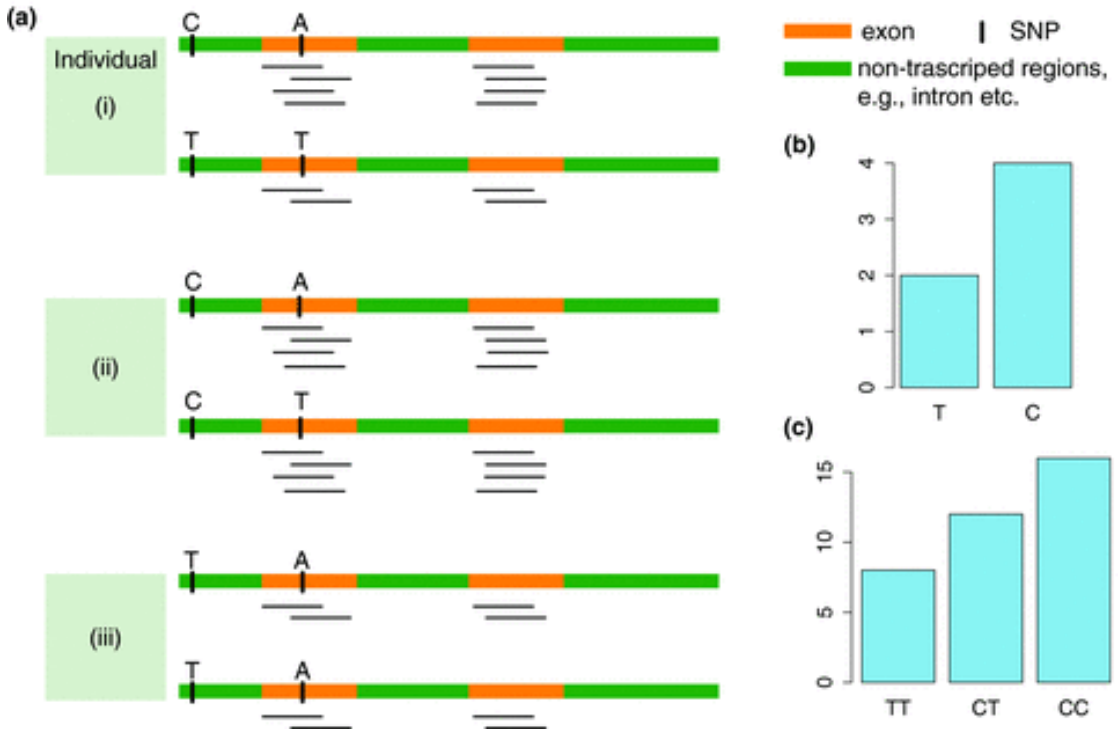
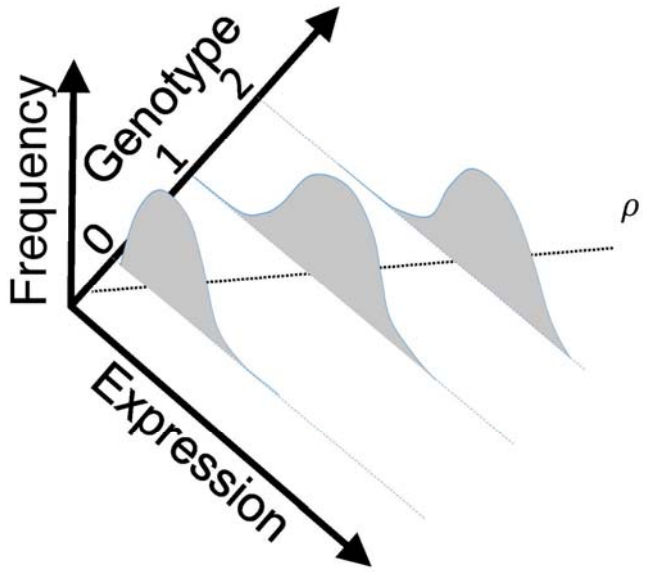
eQTL Mapping Using RNA-Seq Data

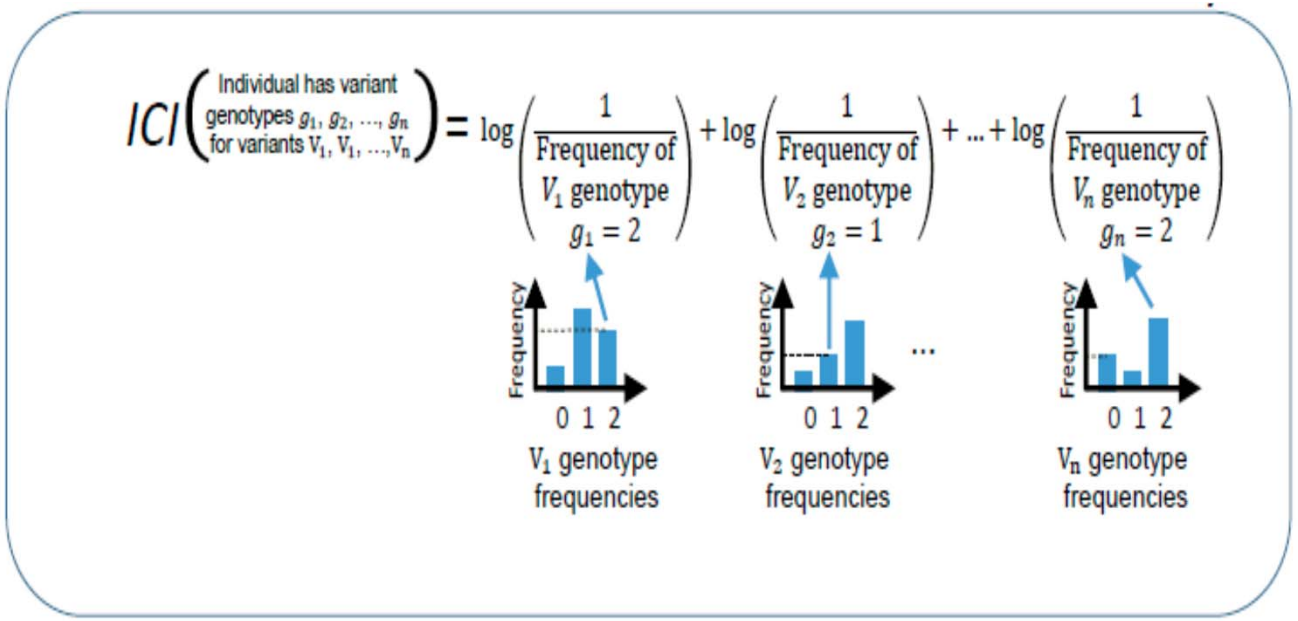


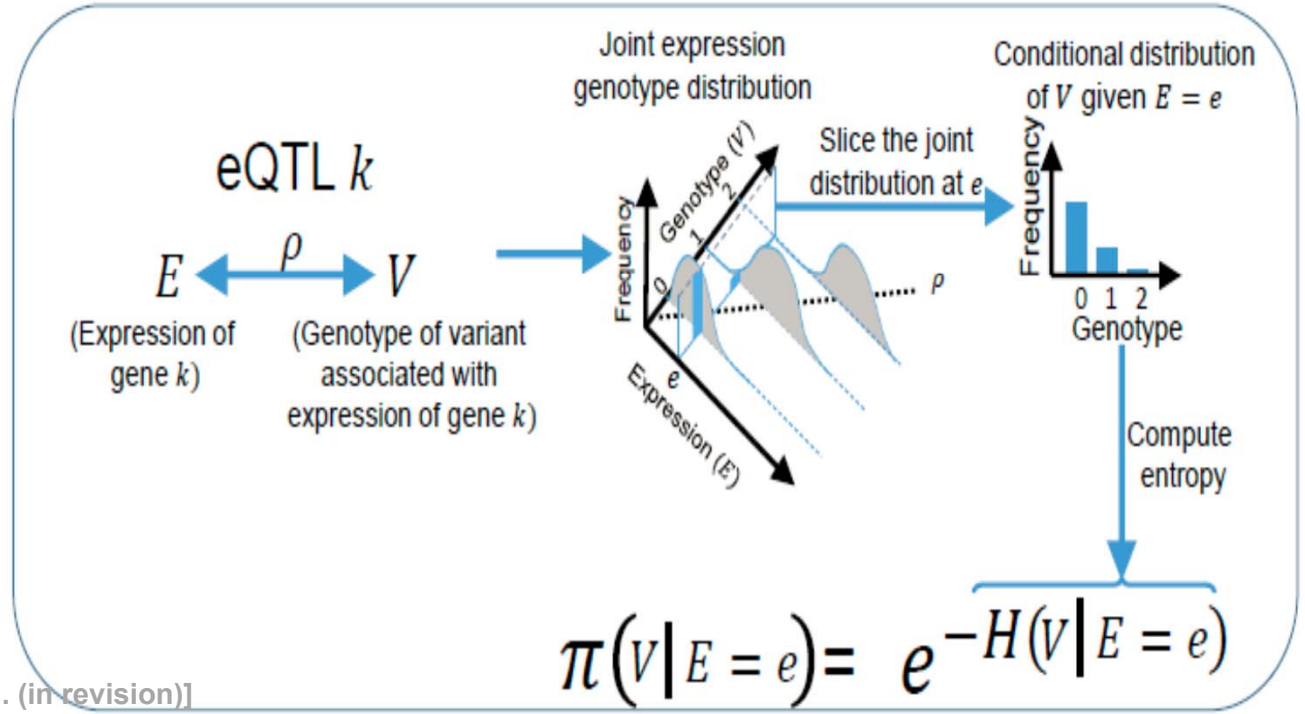
[*Biometrics 68(1) 1–11*]



- eQTLs are genomic loci that contribute to variation in mRNA expression levels
- eQTLs provide insights on transcription regulation, and the molecular basis of phenotypic outcomes
- eQTL mapping can be done with RNA-Seq data

Information Content and Predictability





[Harmanciet al. Nat. Meth. (in revision)]

Representative Expression, Genotype, eQTL Datasets

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- mRNA sequencing for 462 individuals
  - Publicly availableQuantification for protein coding genes
- Approximately 3,000 cis-eQTL (FDR<0.05)

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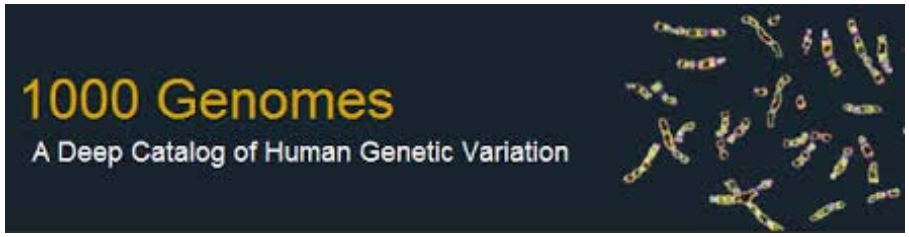
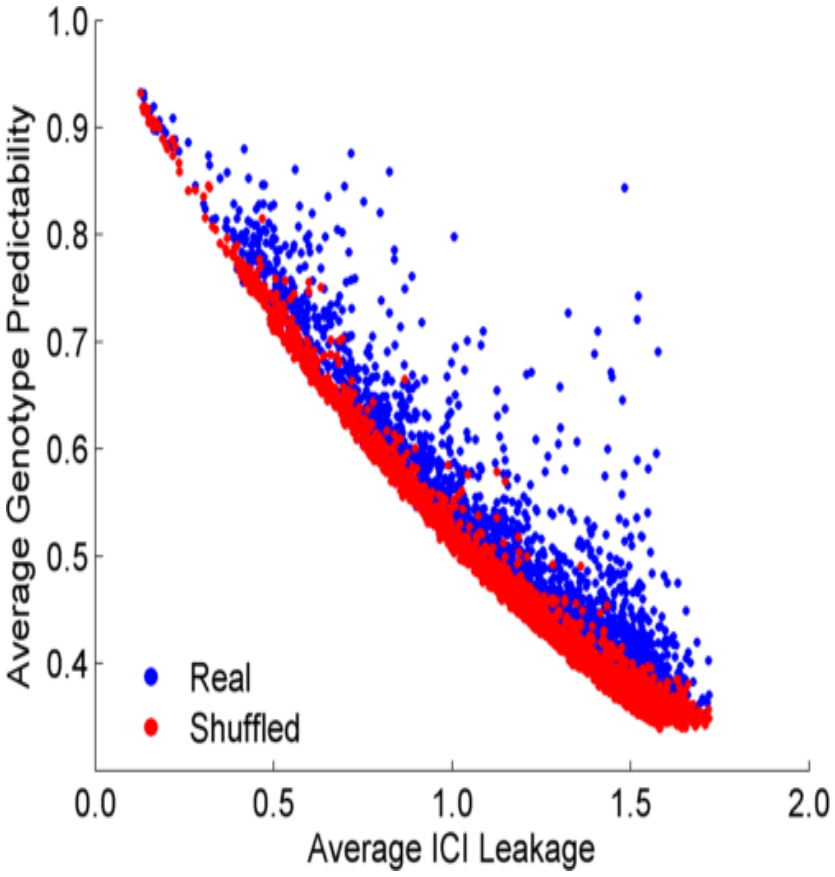
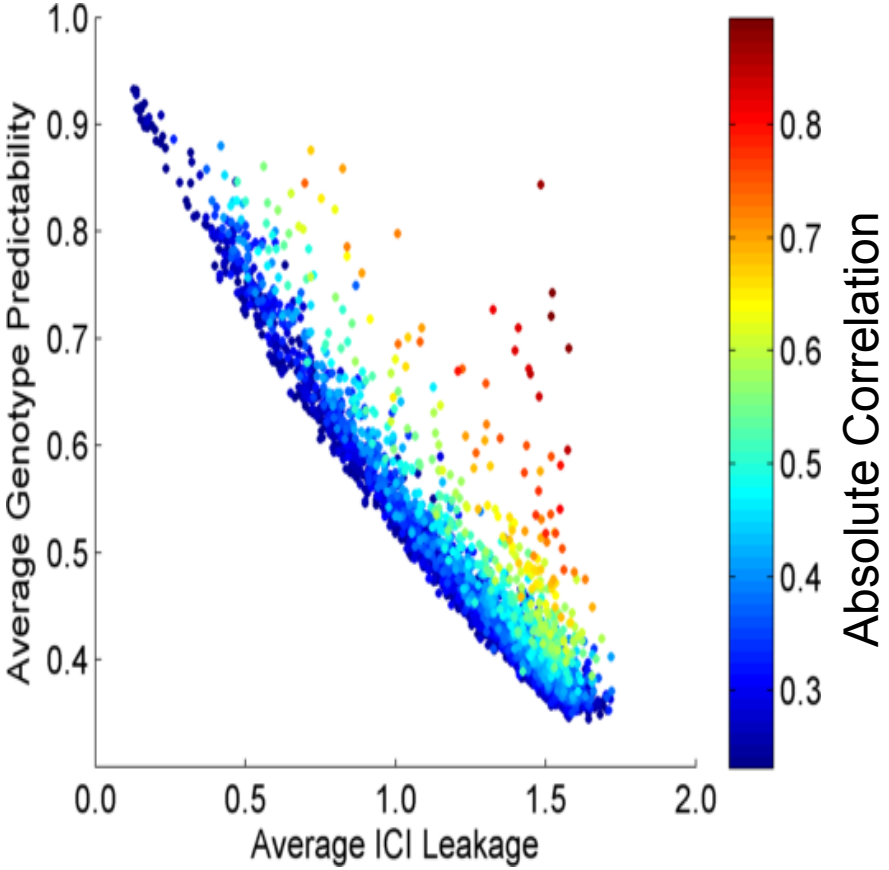


Per eQTL and ICI Cumulative Leakage versus Genotype Predictability

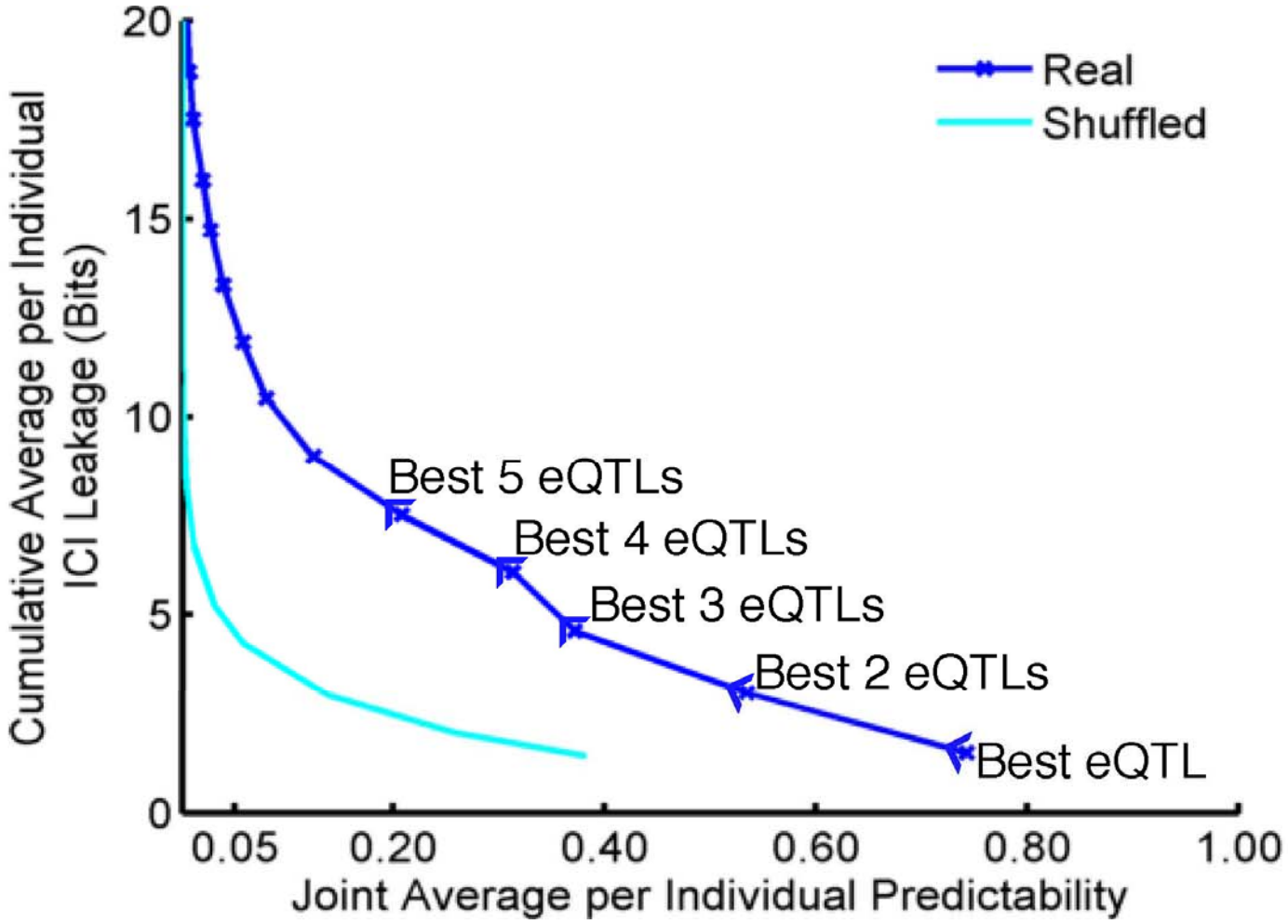


Colors by absolute correlation



[Harmanciet al. Nat. Meth. (in revision)]

Cumulative Leakage versus Joint Predictability



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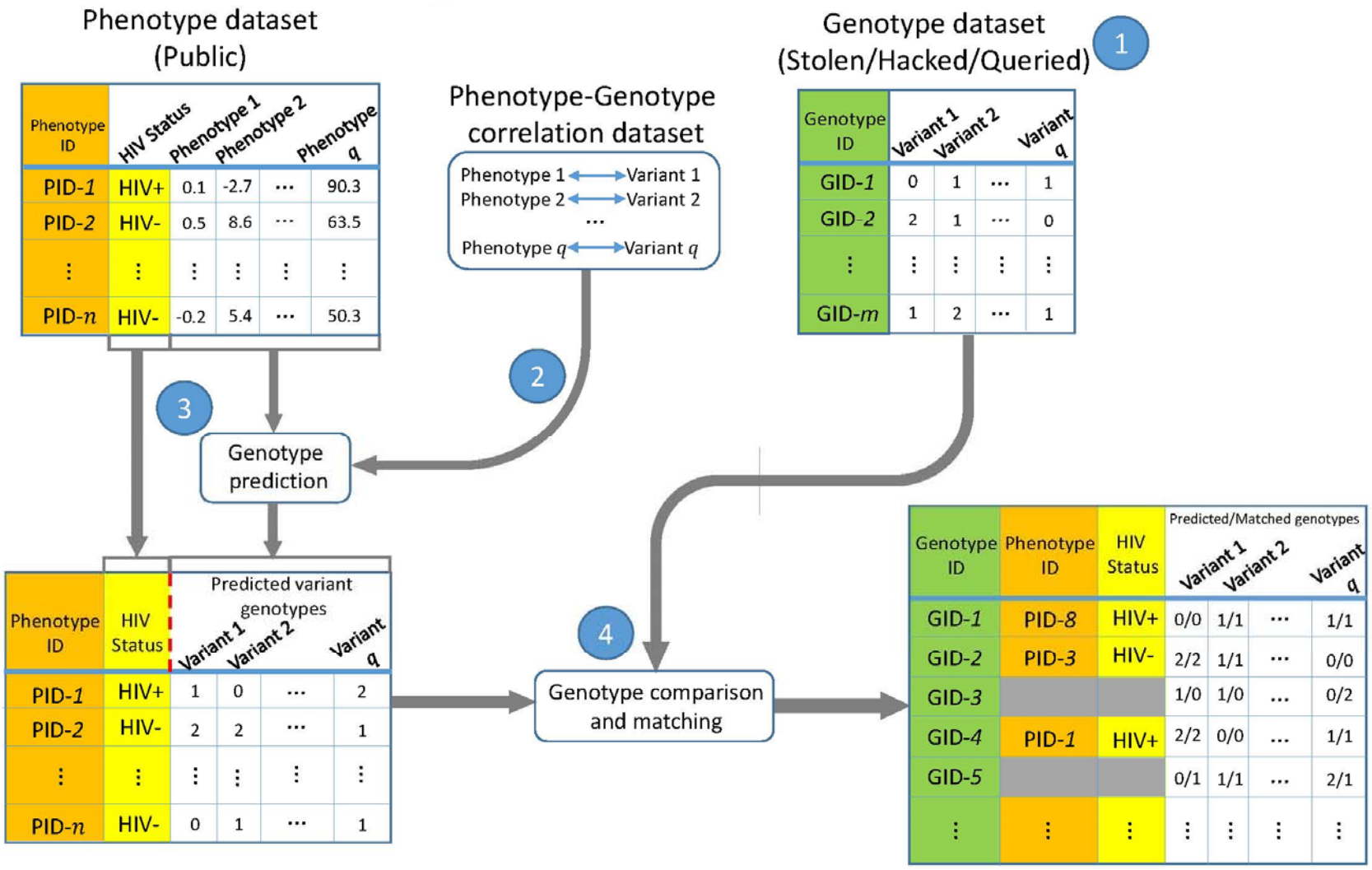
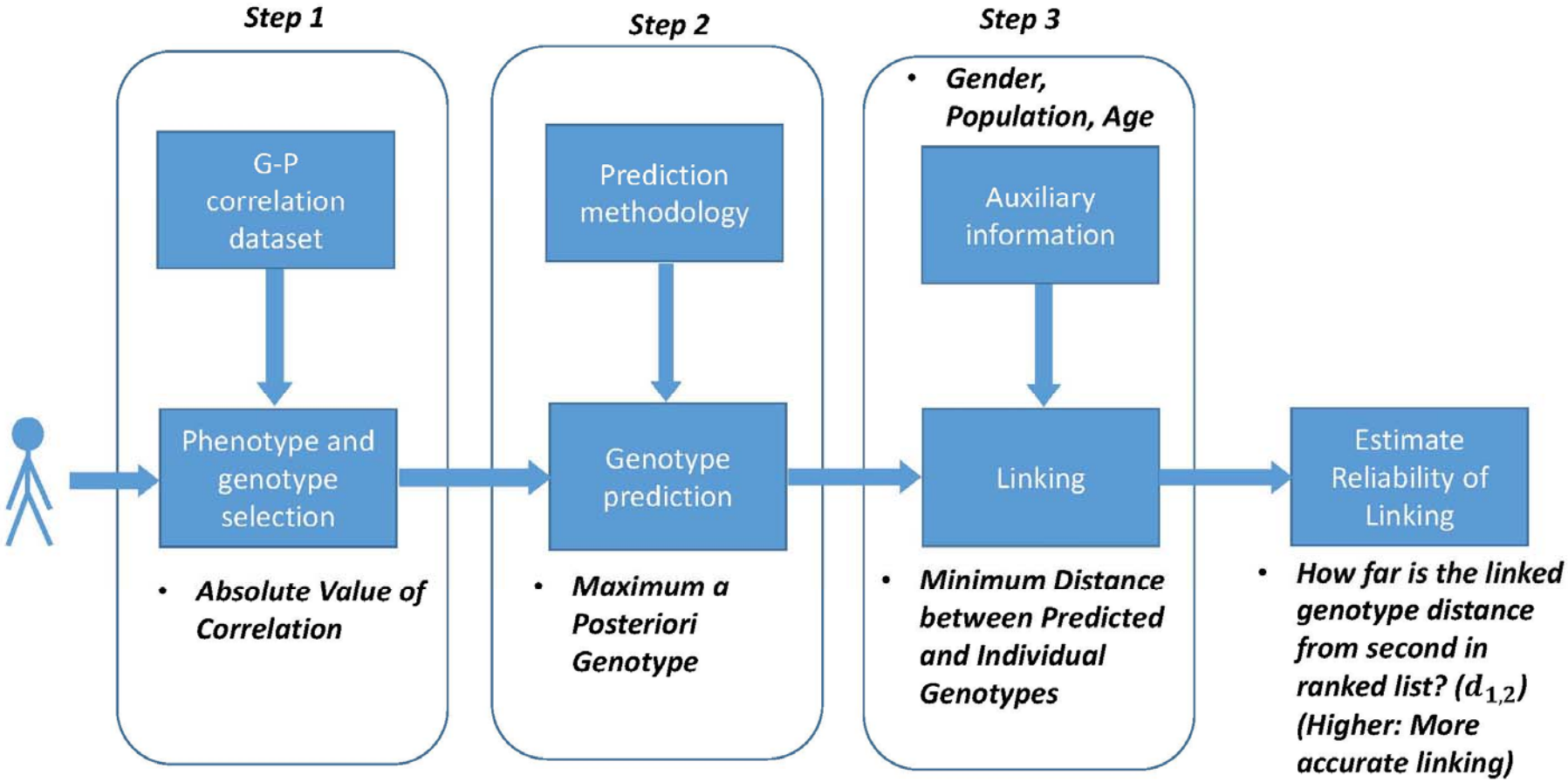
Linking Attack Scenario



[Harmanciet al. Nat. Meth. (in revision)]

Steps in Instantiation of a (Mock) Linking Attack



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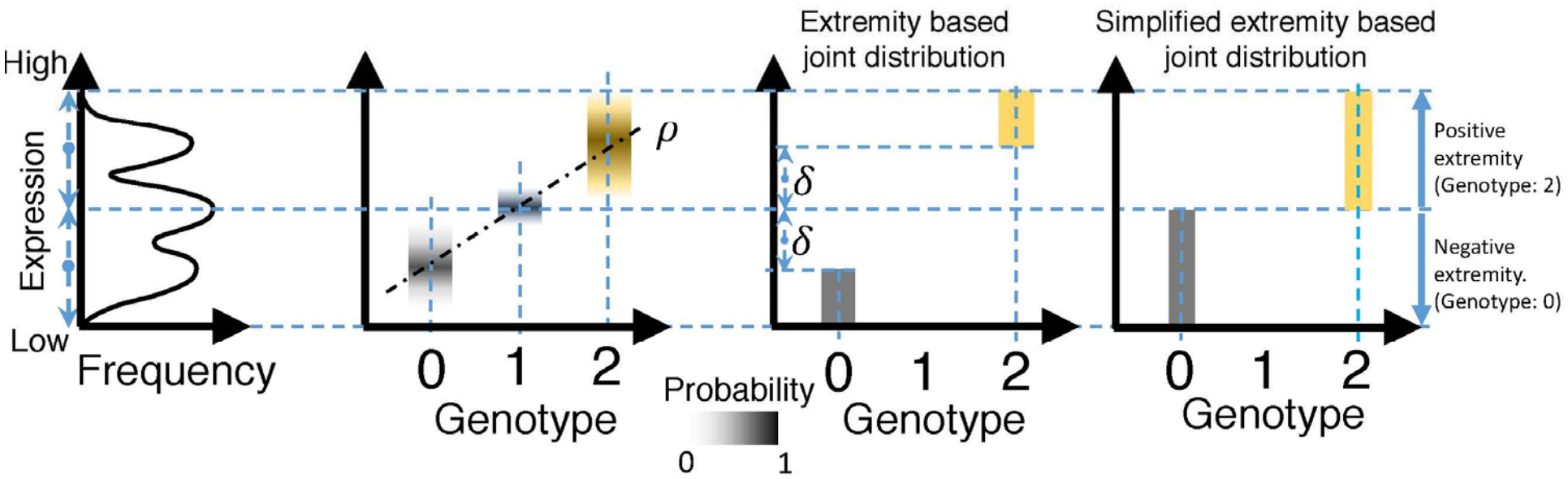
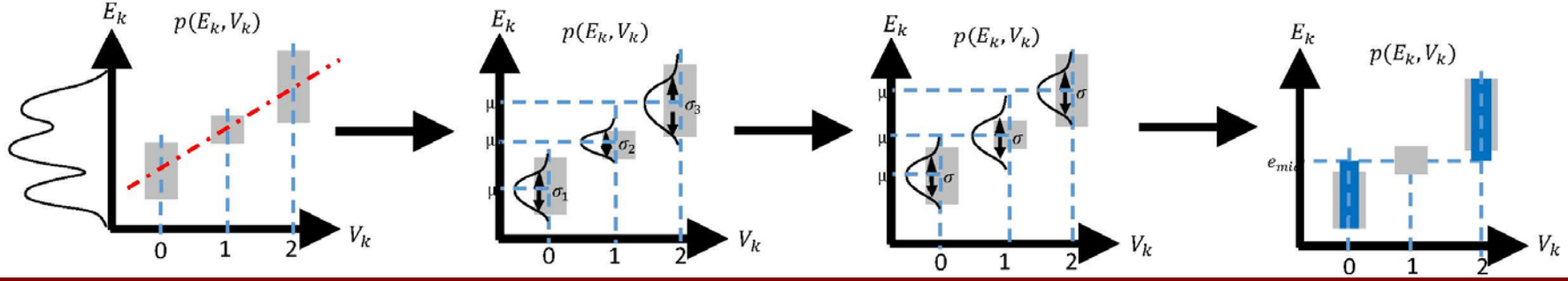
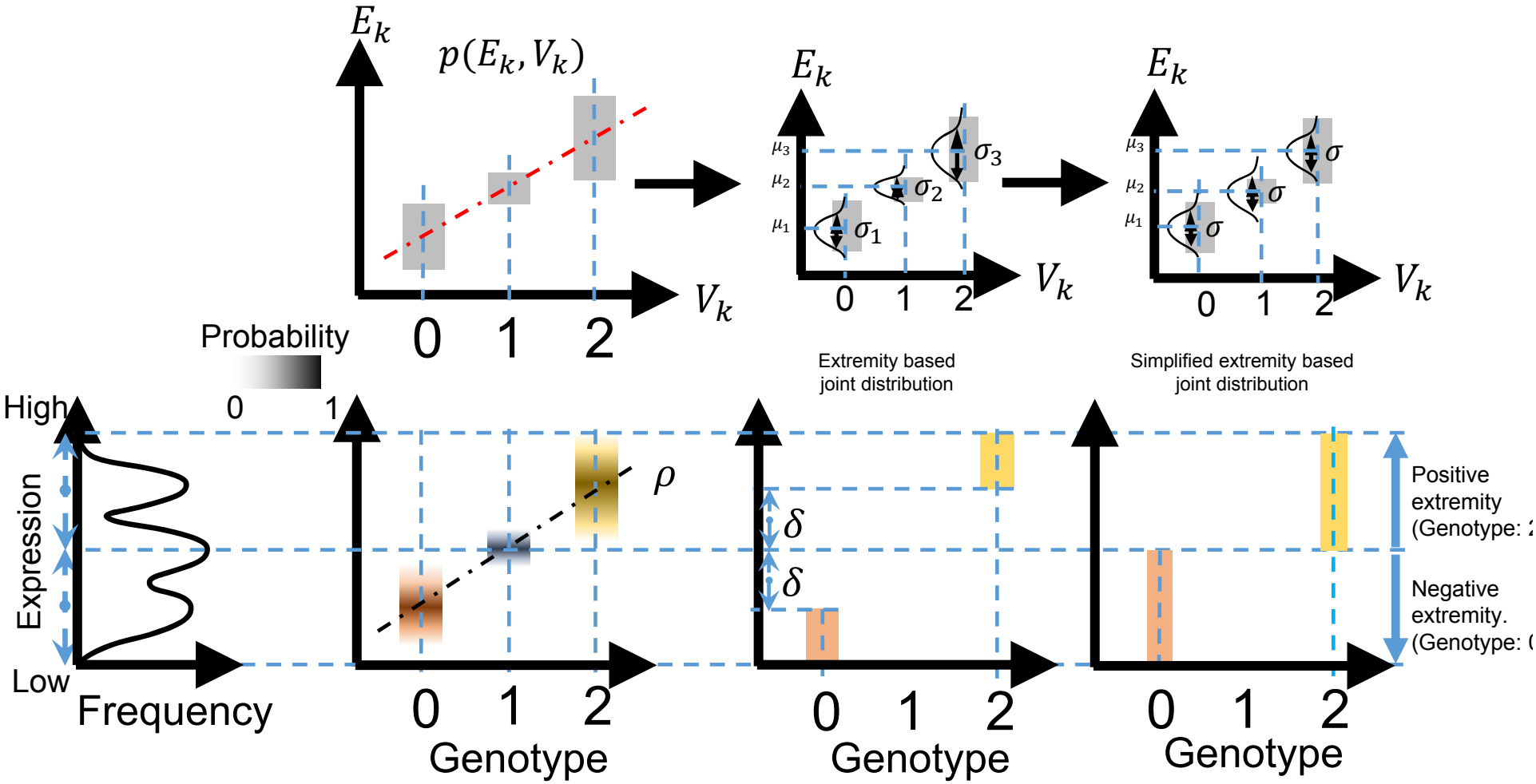


Levels of Expression-Genotype Model Simplifications:

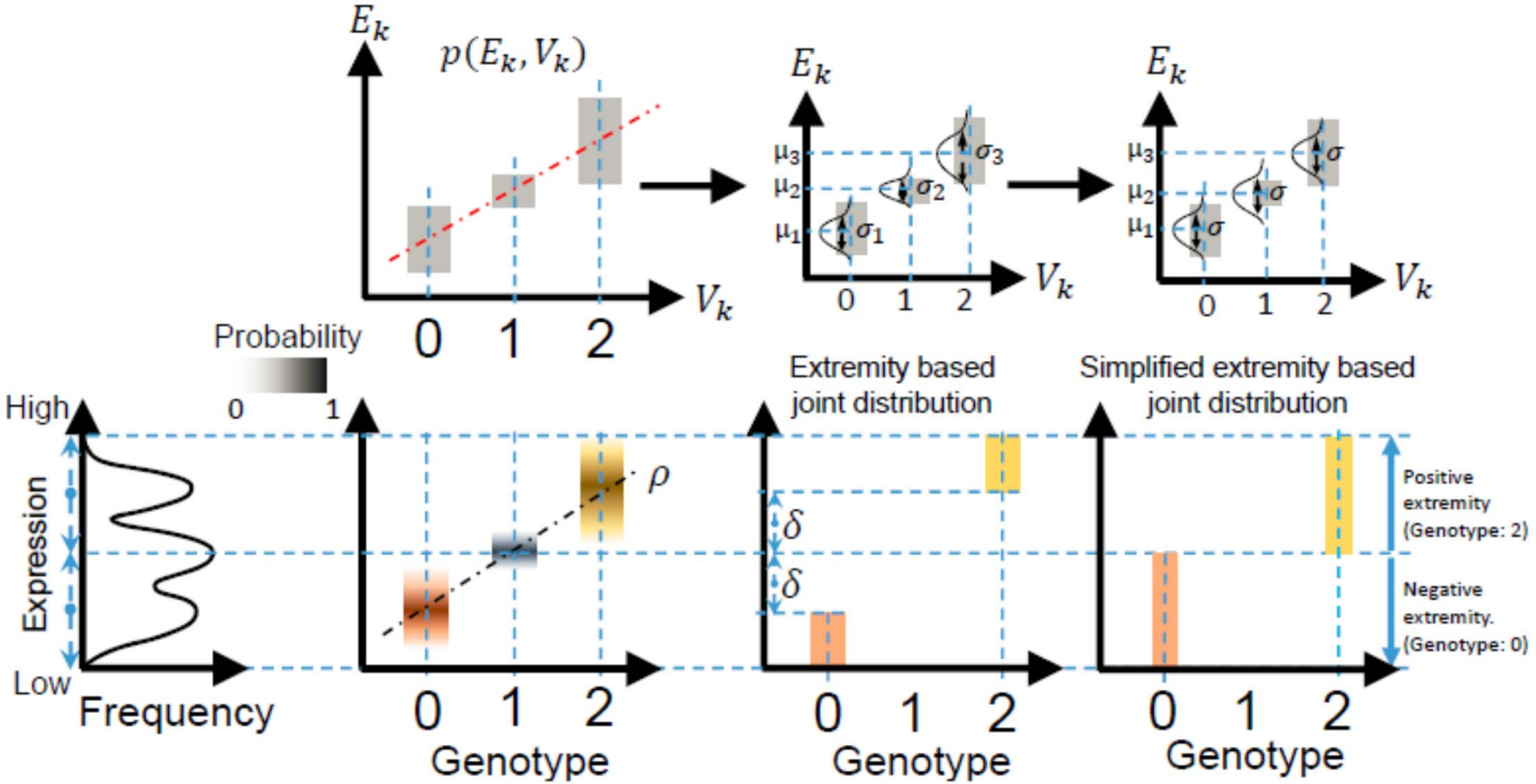


[Harmanciet al. Nat. Meth. (in revision)]

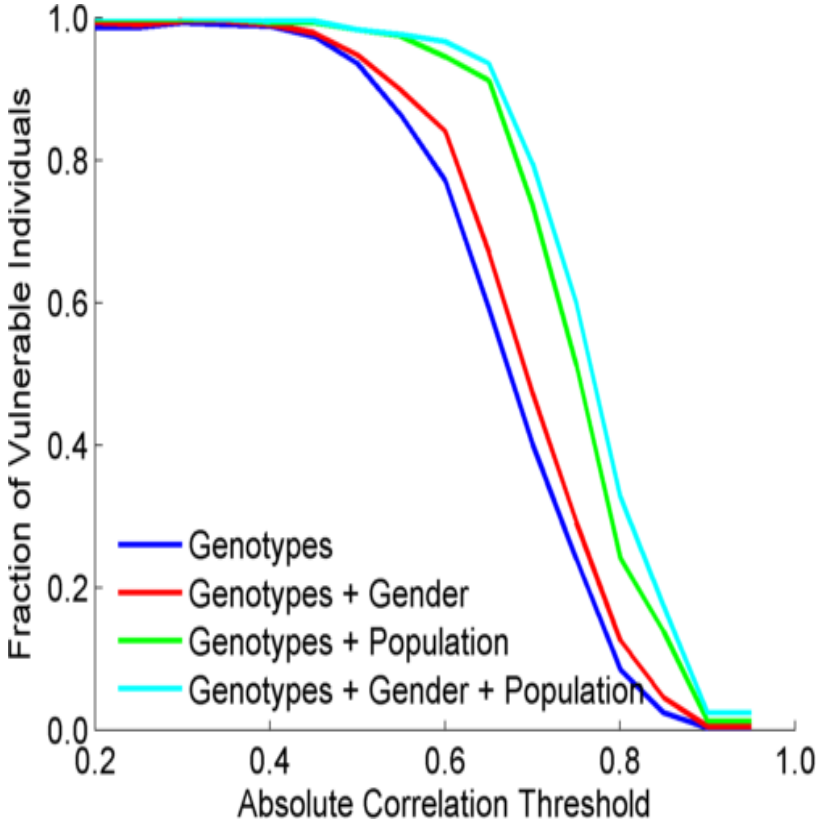
Levels of Expression-Genotype Model Simplifications:



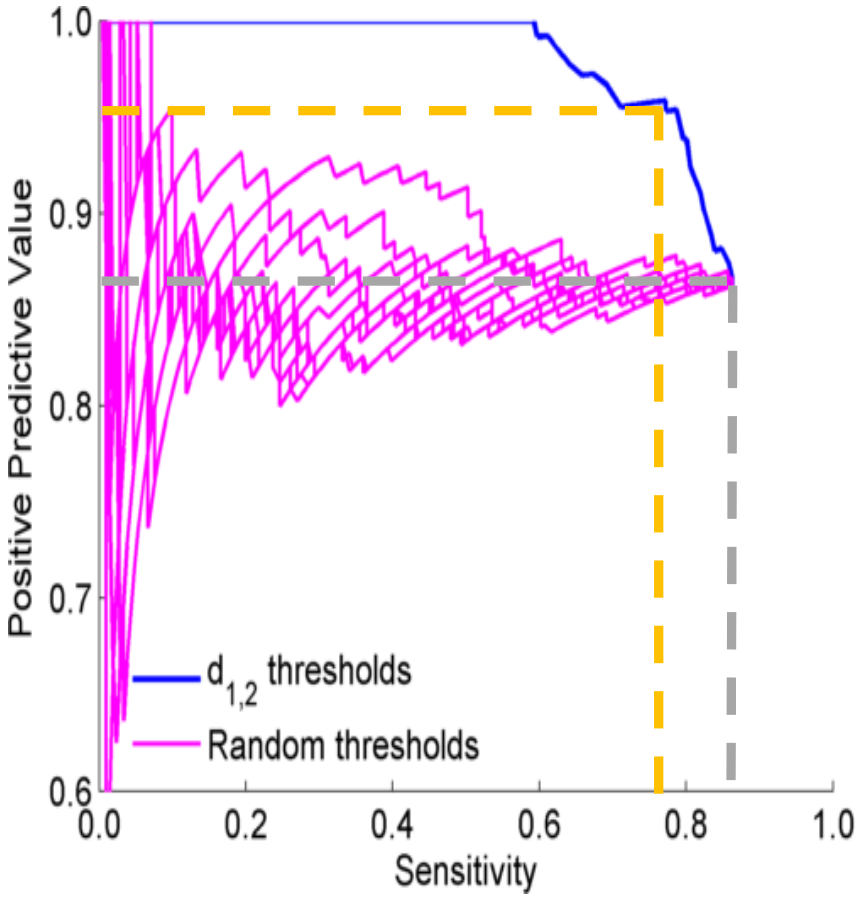
Levels of Expression-Genotype Model Simplifications:



Extremity based linking with homozygous genotypes



Attacker can estimate the reliability of linkings



Sensitivity: Fraction of correctly linked Individuals among all individuals

PPV: Fraction of correctly linked individuals among selected individuals

[Harmanciet al. Nat. Meth. (in revision)]

- **The Dilemma of Genomic Privacy**
  - Fundamental, inherited info that's very private vs the need for large-scale data-sharing to enable med. research
  - Current Social & Tech Approaches
    - Issues: burdensome security, inconsistencies + ways the solutions have been partially "hacked"
    - Strawman Hybrid Soc-Tech Proposal (Cloud Enclaves. Quantifying Leaks, & Closely Coupled priv.-public data)
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  - Quantifying & removing variant info from expression levels + eQTLs
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Large-scale Transcriptome Mining: Building Interpretative Models while Protecting Individual Privacy

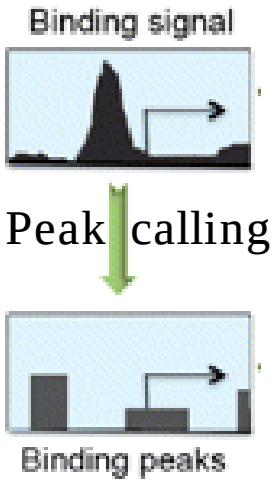
- **Large-scale Mining of RNA-seq to Determine State Space Models**
  - Using dimensionality reduction to help determine internal & external drivers
  - Decoupling expression changes into those driven by worm-fly conserved genes vs species-specific ones. Also, Conserved genes have similar canonical patterns (iPDPs) in contrast to species specific ones (Ex of ribosomal v signaling genes)
  - In human cell cycle, only conserved genes show matching periodic pattern

A gene can be regulated by multiple gene regulatory factors

Next generation sequencing techniques (e.g., ChIP-seq, CLIP-seq) predict **gene regulatory factors (RFs)** and their target genes

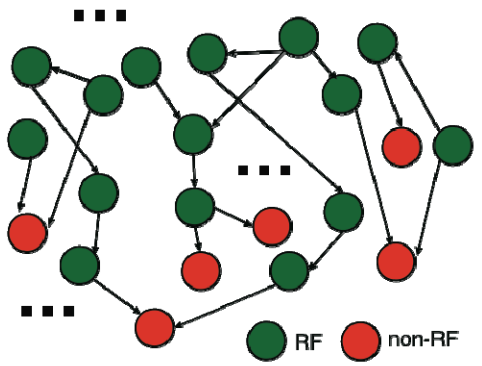
- transcription factors (TFs)
- micro-RNAs

…



Gene regulatory network

Regulatory Factor (RF)	Target (T)
TF 1	Gene 1
TF 2	Gene 1
TF 3	Gene 2
miRNA 1	Gene 1
miRNA 2	Gene 3
miRNA 3	Gene 2
…	…



Many genes are regulated by multiple RFs.

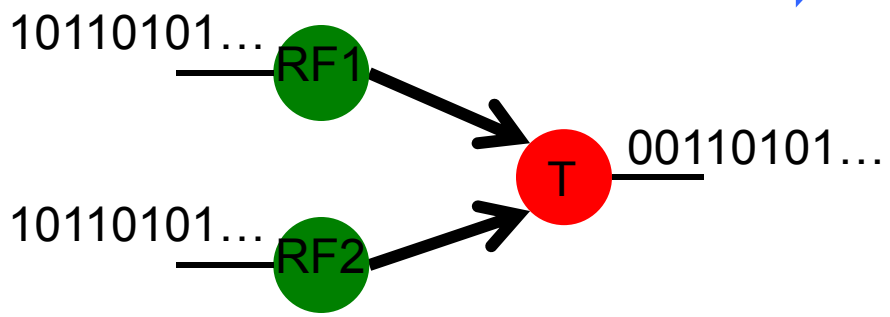
How RFs coordinate to regulate target gene expression?

- cooperative?
- competitive?
- independent?

…

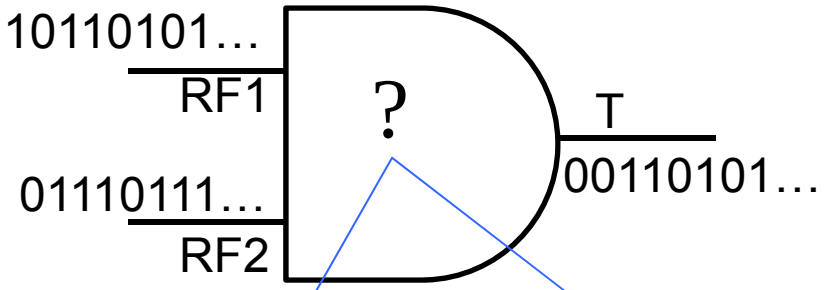
Modeling cooperativity between RFs to target gene using logic gates

A regulatory triplet



0 – gene off
1 – gene on
after binarizing gene expression data*

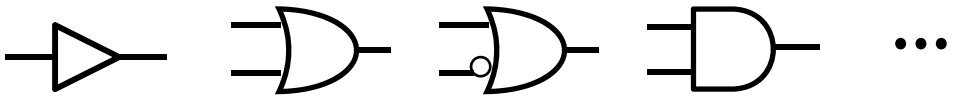
2-input-1-output logic gate



Input type (RF1, RF2)	RF1	0	0	1	1
	RF2	0	1	0	1
Output	T	*X*	*X*	*X*	*X*

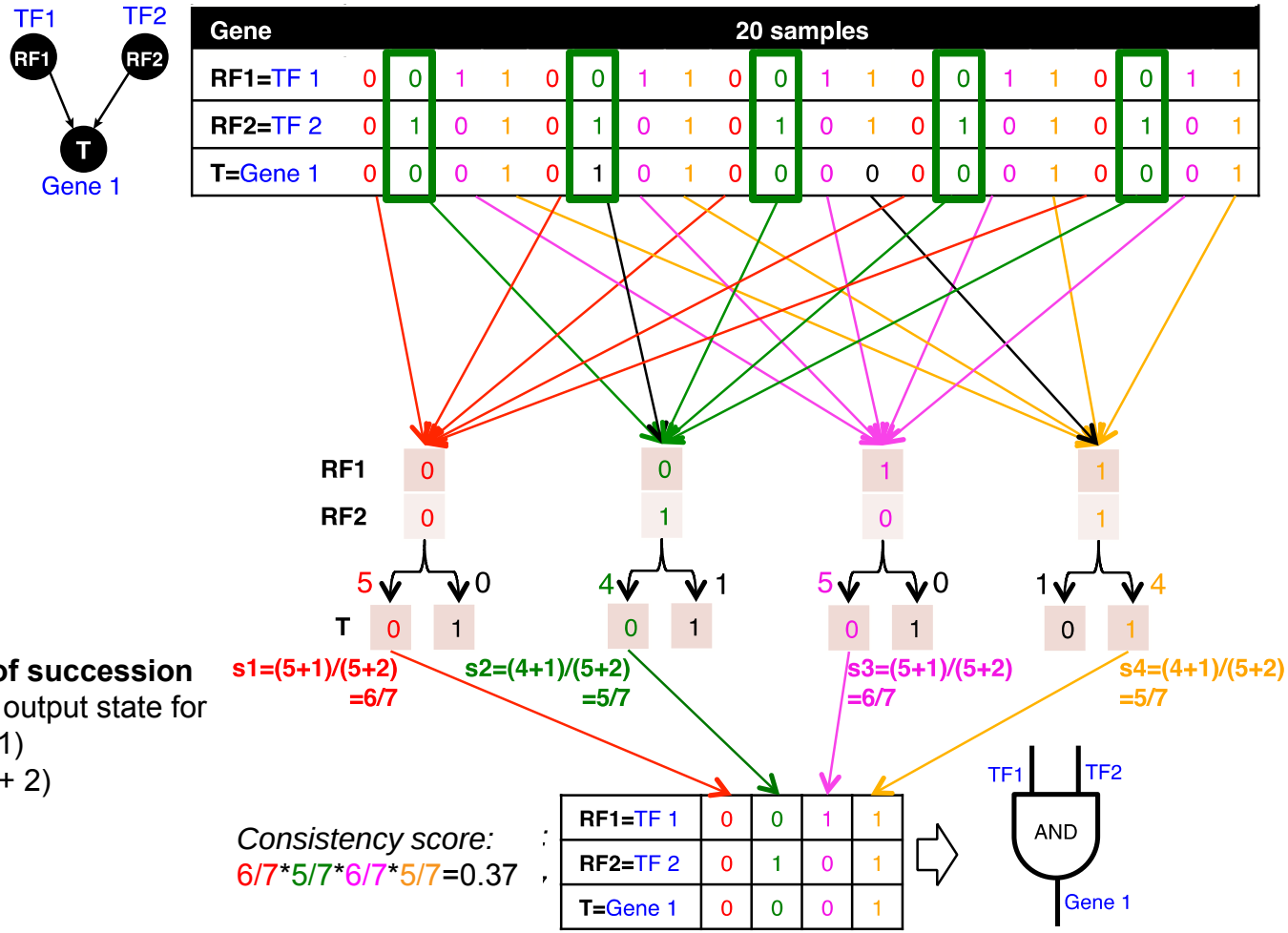
Binarized expression

X can be 0 or 1, so there are 2^4=16 possible output combinations, each of which corresponds to a unique 2-input-1-output logic gate



*BoolNet, R package

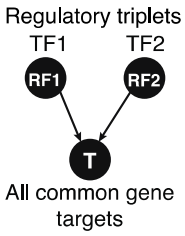
An example: selection of the best-matched logic gate



Laplace's rule of succession
s=(# of selected output state for the input type + 1)
/(# of input type + 2)

Wang, et al., *PLoS Computational Biology*, 2015

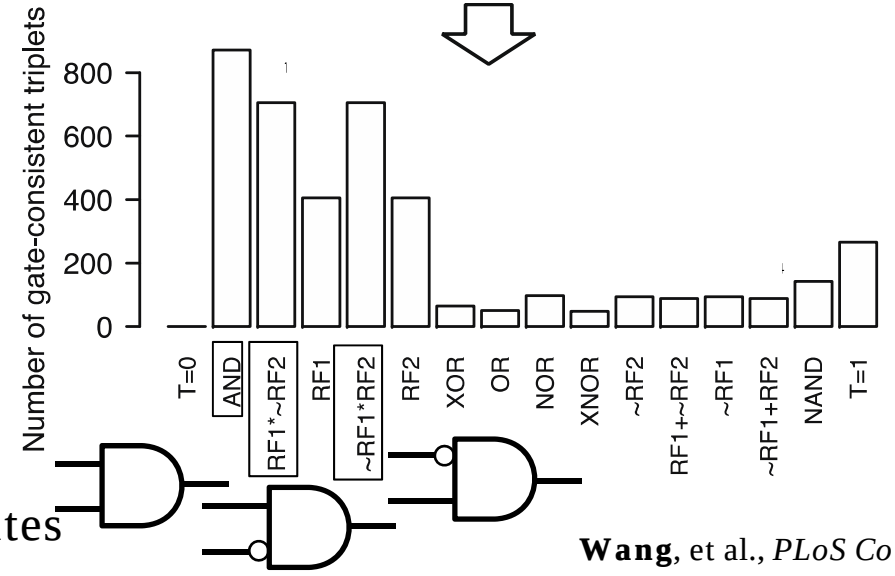
Application 1 – transcription factor cooperativity in Yeast cell cycle



Target gene	2464
TF	176
Triplet	39,011
Time point	59

Yeast Cell Cycle

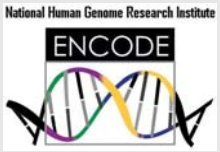
Triplet ID	RF1	RF2	Common Target Gene (T)	Matched logic gate
1	YHR084W	YBR083W	YBR082C	AND
2	YKL112W	YIL131C	YMR198W	OR
…	…	…	…	…
39011	YOR113W	YBL103C	YDR042C	XOR



AND-like gates

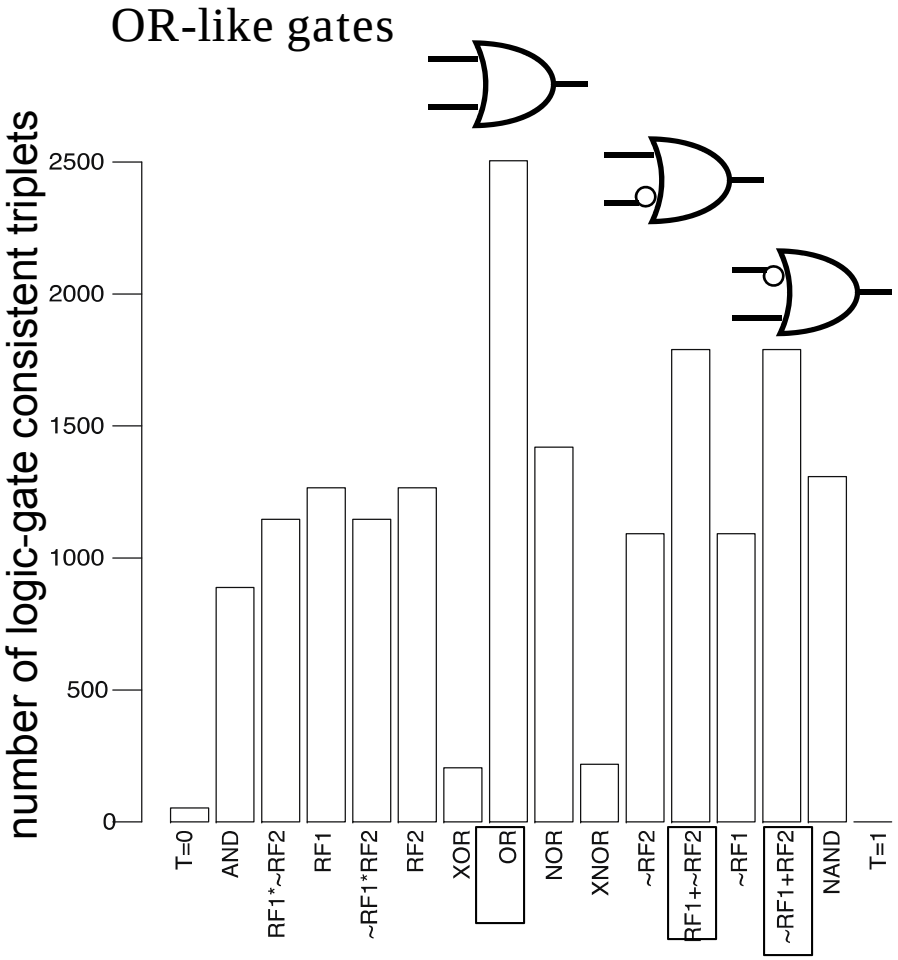
Wang, et al., *PLoS Computational Biology*, 2015

Application 2 – transcription factor cooperativity in Acute Myeloid Leukemia (AML)

Target gene	1824	ENCODE Data (K562, ChIP-seq) http://encodenets.gersteinlab.org/
TF	70	
Regulatory triplet	50,865	TCGA Data (AML, level 3, RNA-seq) https://tcga-data.nci.nih.gov/tcga/tcgaDownload.jsp
Patient sample	197	

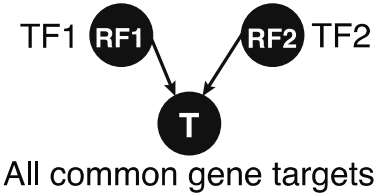
Wang, et al., *PLoS Computational Biology*, 2015

Application 2 – transcription factor cooperativity in Acute Myeloid Leukemia (AML)



Human TF-TF-target

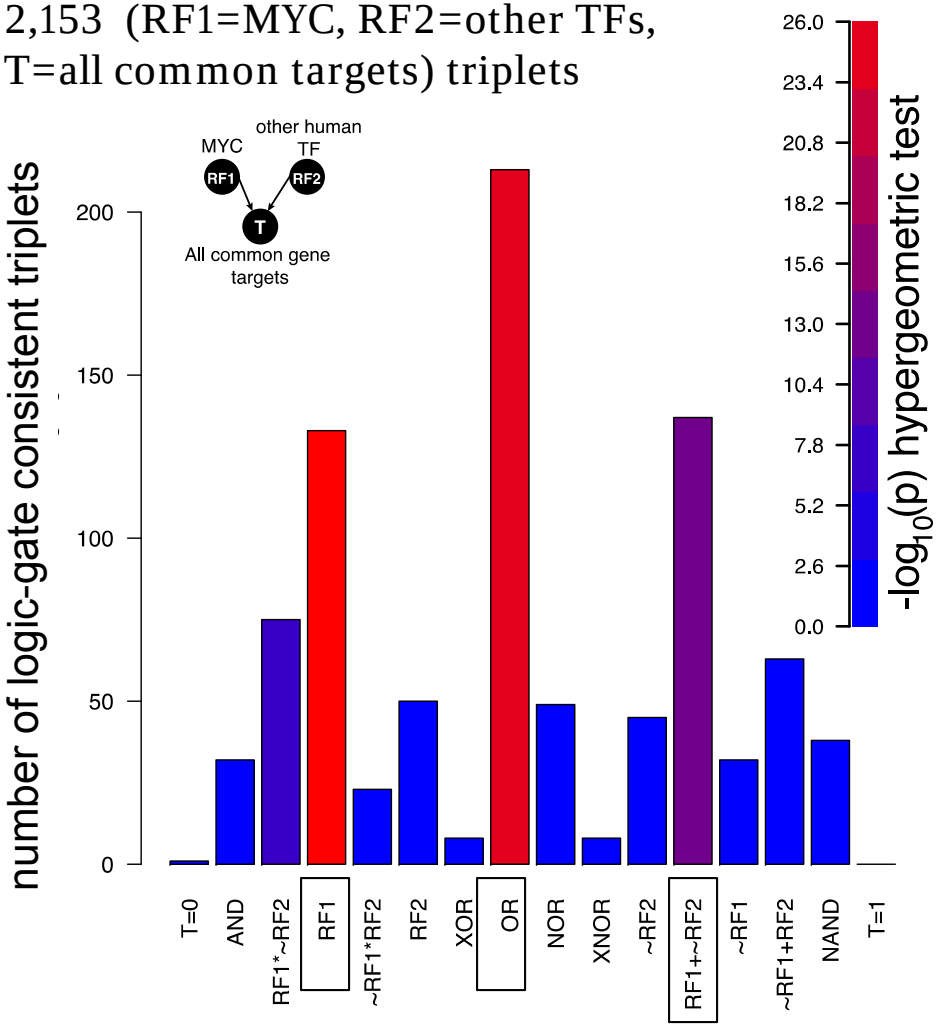
RF1	RF2	Common Target Gene (T)	Matched logic gate
ATF3	BDP1	YPEL1	AND
MYC	BCL3	BCR	T=RF1
ATF3	BRF2	AIF1L	AND
…	…	…	…

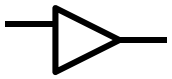
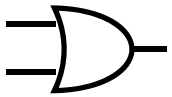
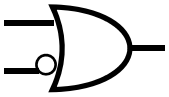


Wang, et al., *PLoS Computational Biology*, 2015

Cancer-related TF, MYC universally amplifies target expression

2,153 (RF1=MYC, RF2=other TFs, T=all common targets) triplets



- RF1 
- **OR**(RF1, RF2) 
- **OR**(RF1, **NOT** RF2) 

High expression of MYC is sufficient for high target gene expression

c-Myc Is a Universal Amplifier of Expressed Genes in Lymphocytes and Embryonic Stem Cells

Cell

Zuqin Nie,[1,6] Gangqing Hu,[2,6] Gang Wei,[2] Kairong Cui,[2] Arito Yamane,[3] Wolfgang Resch,[3] Ruoning Wang,[4] Douglas R. Green,[4] Lino Tessarollo,[5] Rafael Casellas,[3] Keji Zhao,[2,*] and David Levens[1,*]

Wang, et al., *PLoS Computational Biology*, 2015

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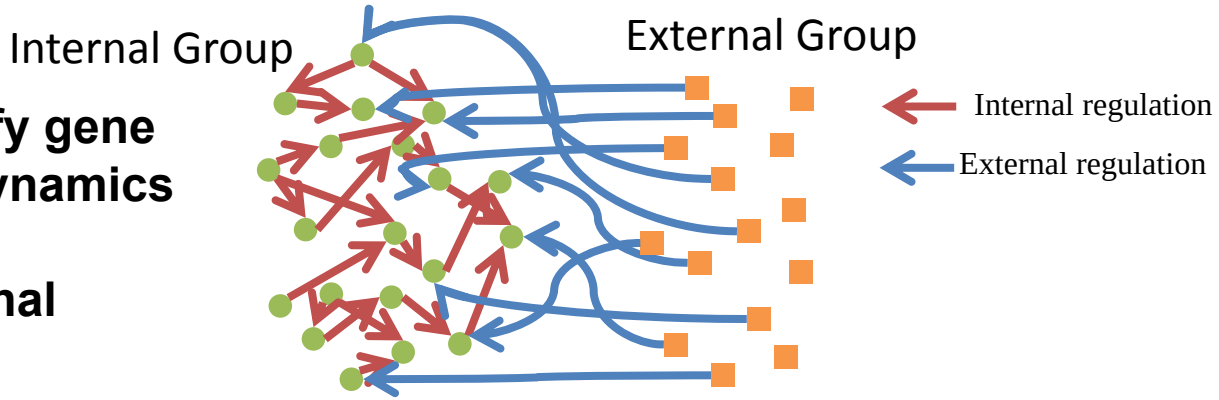
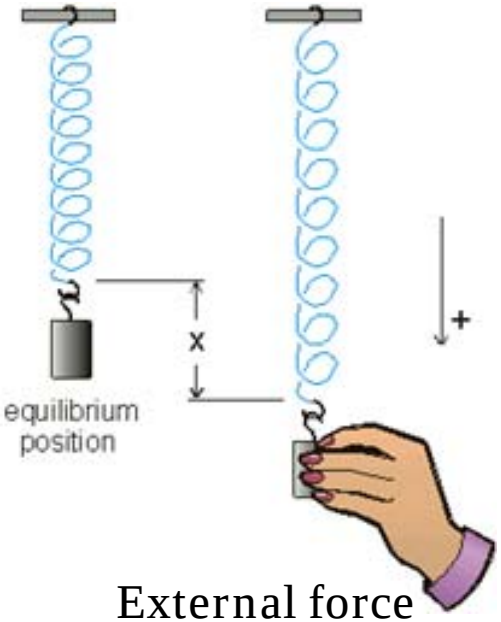
Internal and external gene regulatory networks



How to identify gene expression dynamics driven by internal/external regulation?

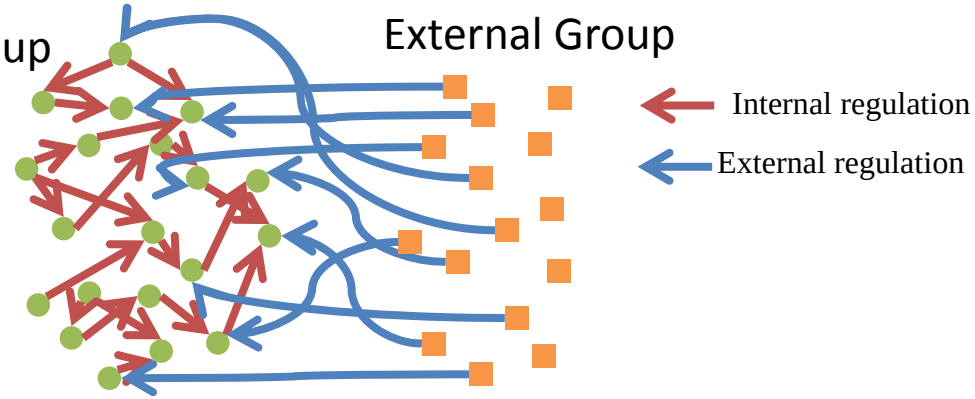


Interested system	Internal regulatory network	External regulatory network
Cross-species conserved genes	Conserved transcriptional factors (TFs)	Non-conserved TFs
Protein-coding genes	TFs	micro-RNAs
Individual's protein coding genes	Wild-type TFs	Somatic mutated TFs
Protein-coding genes in brain	Commonly expressed TFs	Brain-specific expressed TFs
Protein-coding genes in development	House-keeping TFs	Developmental TFs

[Wang et al. *PLOS CB* (in revision, '15)]

State-space model for internal and external gene regulatory networks

How to identify gene expression dynamics driven by internal/external regulation?



State space model

$$X_{t+1} = A X_t + B U_t$$

State: Gene expression vector of Group X at time t+1

A_{ij} captures temporal casual influence from Gene i to Gene j in internal group

State: Gene expression vector of internal group at time t

Control: Gene expression vector of external factors at time t

B_{kl} captures temporal casual influence from external factor k to Gene l in internal group

[Wang et al. *PLOS CB* (in revision, '15)]

Effective state space model for meta-genes

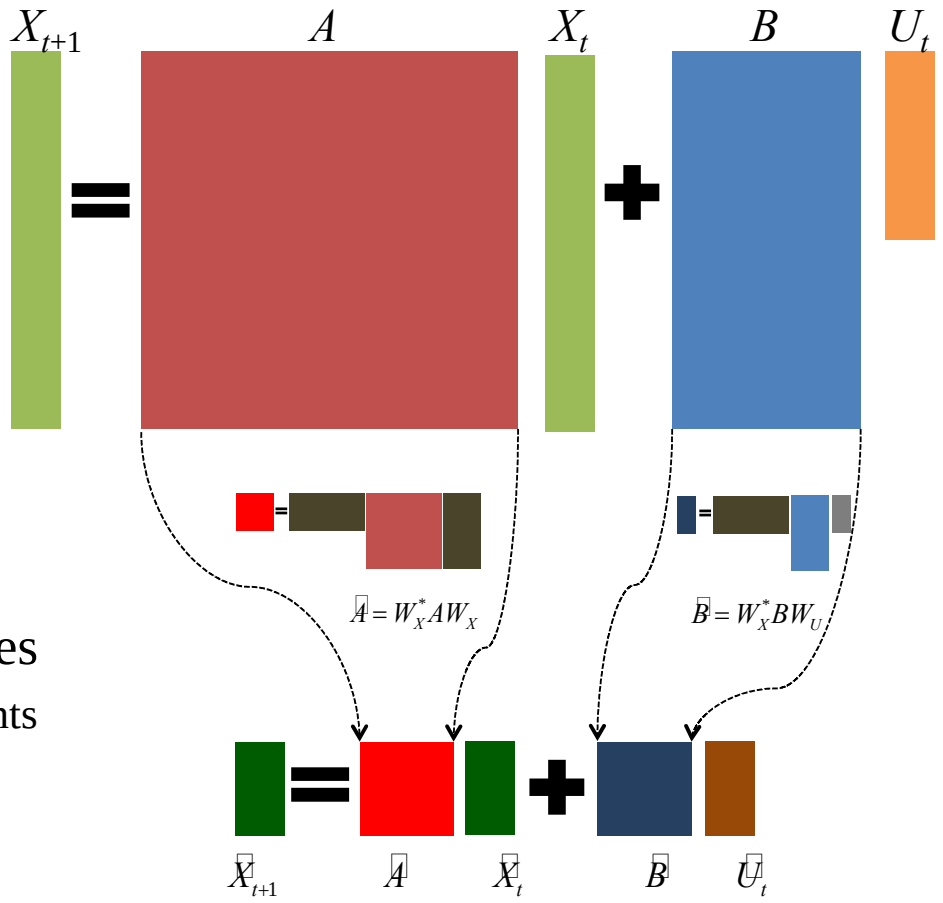
Not enough data to estimate state space model for genes
(e.g., 25 time points per gene to estimate 4 million elements of A or B for 2000 genes)

$$X_{t+1} = AX_t + BU_t$$

Dimensionality reduction from genes to meta-genes (e.g., SVD)

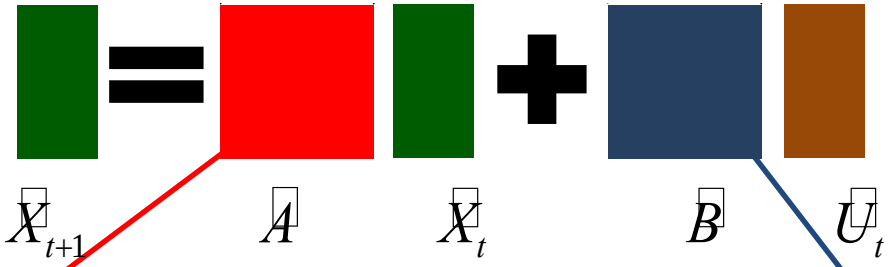
Effective state space model for meta-genes
(e.g., 250 time points to estimate 50 matrix elements if 5 meta-genes)

$$\tilde{X}_{t+1} = \tilde{A}\tilde{X}_t + \tilde{B}\tilde{U}_t$$



[Wang et al. *PLOS CB* (in revision, '15)]

Canonical temporal expression trajectories from effective state space model



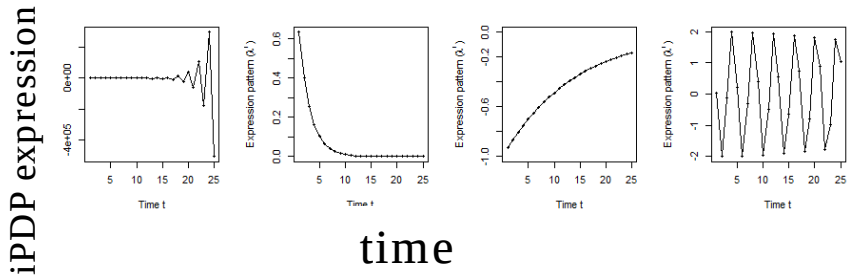
Internal driven dynamics

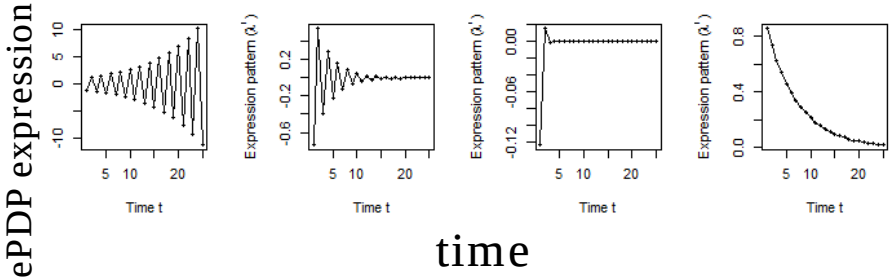
Externally driven dynamics

p^{th} internal principal dynamic pattern (iPDP): $[\lambda_p{}^1, \lambda_p{}^2, \ldots, \lambda_p{}^T]$, where λ_p is p^{th} eigenvalue of $\tilde{A}$.

q^{th} external principal dynamic pattern (ePDP): $[\sigma_q{}^1, \sigma_q{}^2, \ldots, \sigma_q{}^T]$, where σ_q is q^{th} eigenvalue of $\tilde{B}$.

Canonical temporal expression trajectories
(e.g., degradation, growth, damped oscillation, etc.)



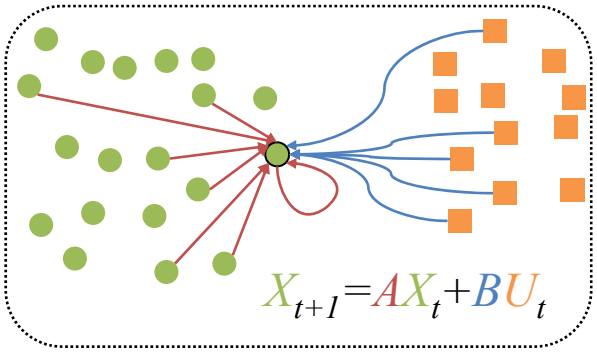


[Wang et al. *PLOS CB* (in revision, '15)]

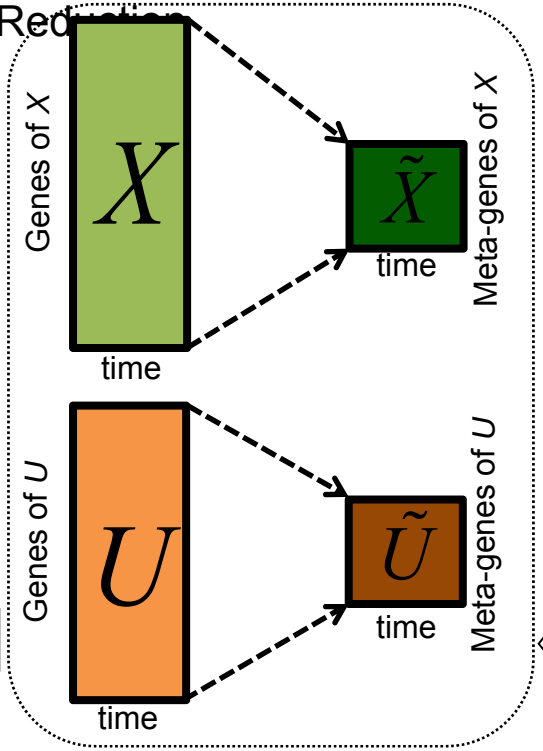
[Wang et al. *PLOS CB* (in revision, '15)]

Flowchart

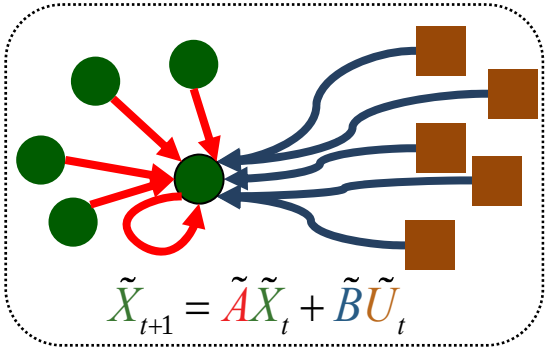
A. Gene state-space model



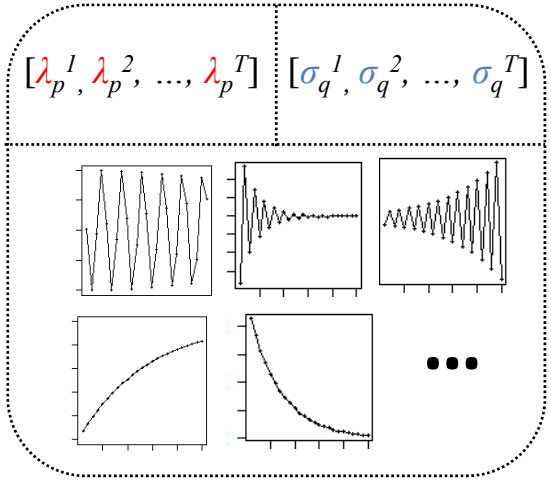
B. Dimensionality Reduction



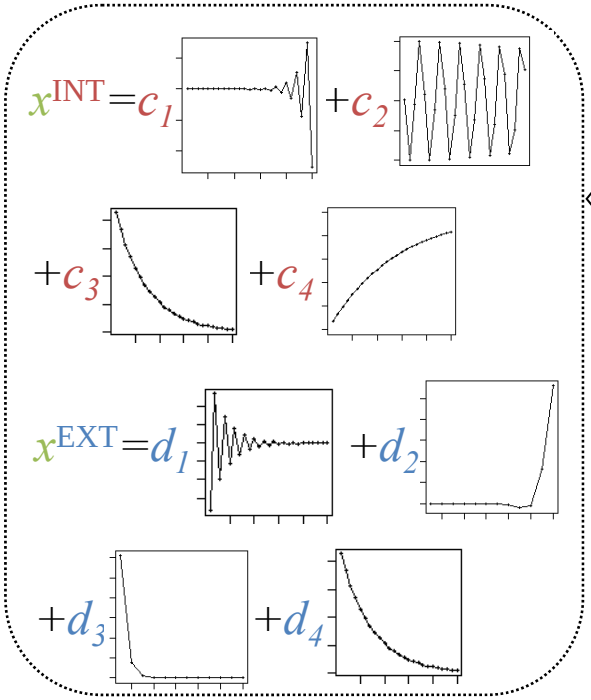
C. Meta-gene state-space model



D. Internal/External Principal Dynamic Patterns (PDPs)



E. Gene's internal (INT) and external (EXT) driven expression dynamics composed of PDPs



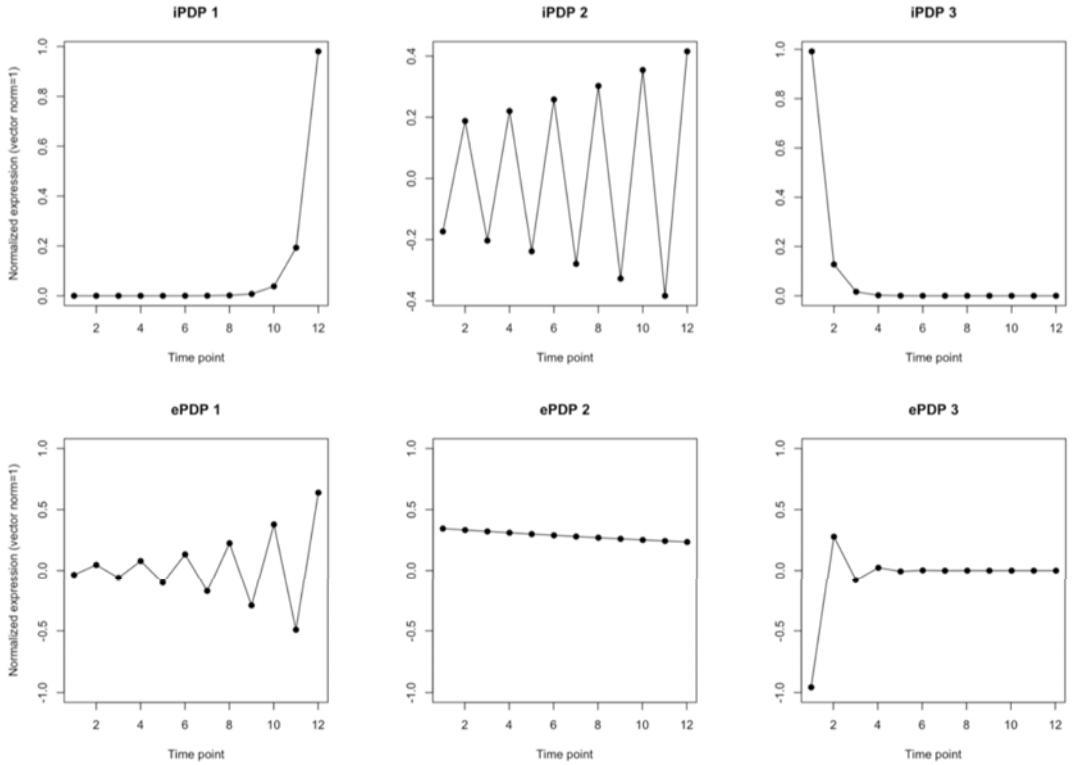
Internal regulation among genes/meta-genes Group X by $A/\tilde{A}$

External regulation from genes/meta-genes in Group U to genes/meta-genes in Group X by $B/\tilde{B}$

Genes/Meta-genes in Group X Genes/Meta-genes in Group U

Breast cancer cell cycle under hormonal stimulation

Dataset	Group X (internal)	Group U (external)	Time samples of a full cell cycle
Human breast cancer cell cycle under hormonal stimulation	1132 metazoan conserved genes incl. 150 orthologous TFs	1870 non-conserved metazoan transcription factors	T=12 time points: 0, 4, 6, 8, 12, …, 28, 32 hours



Oscillated iPDP by conserved TFs

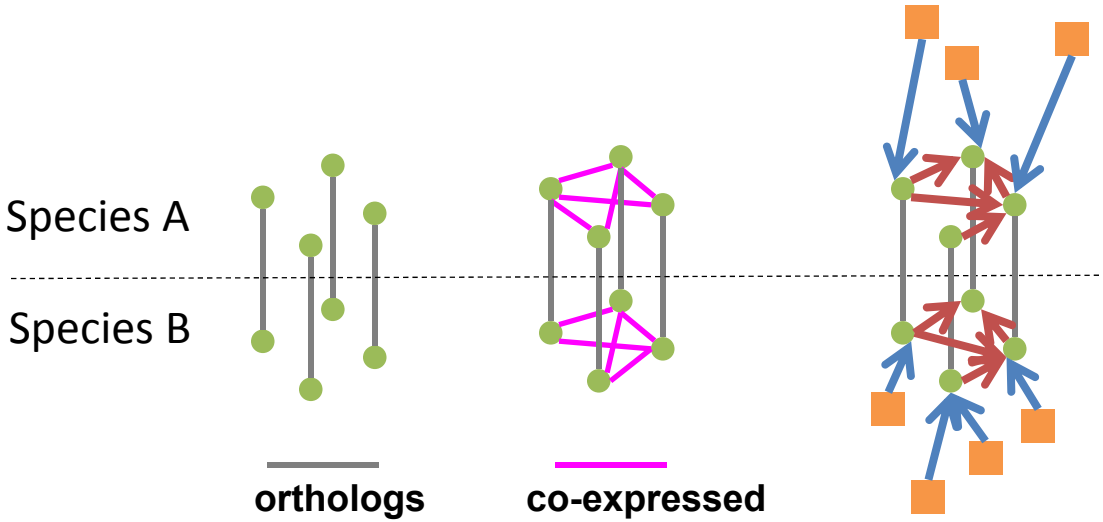
a full cell cycle

Oscillated ePDP by non-conserved TFs

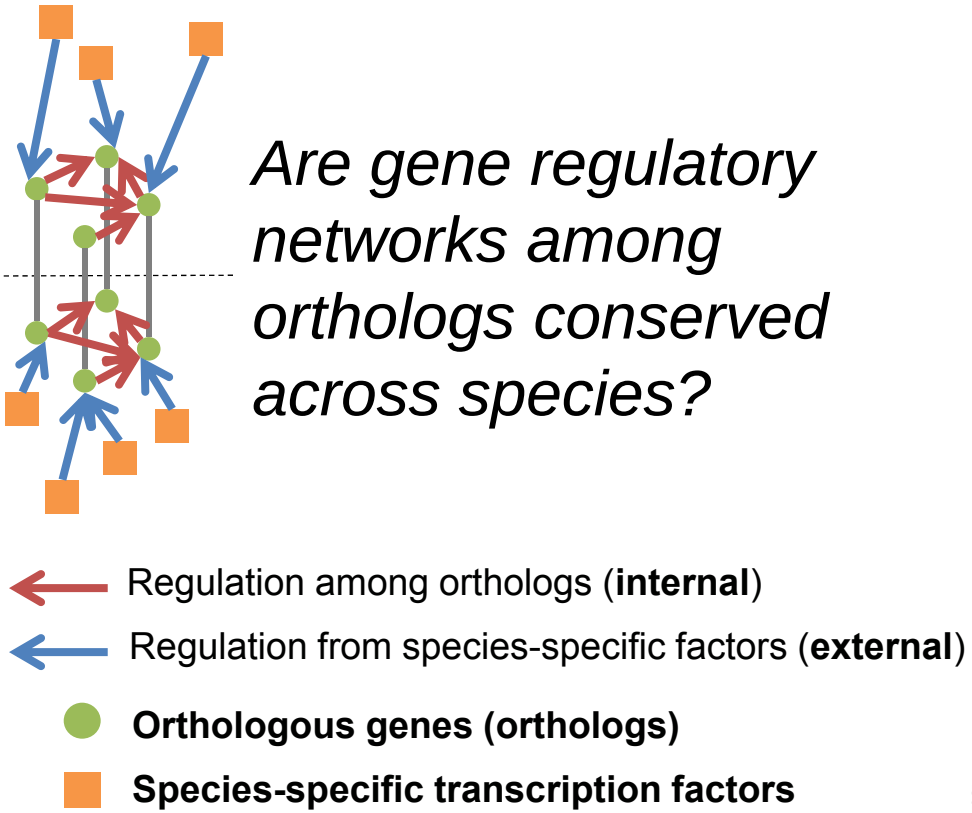
faster cycle due to hormone

[Wang et al. *PLOS CB* (in revision, '15)]

Are gene regulations among orthologs conserved across species?



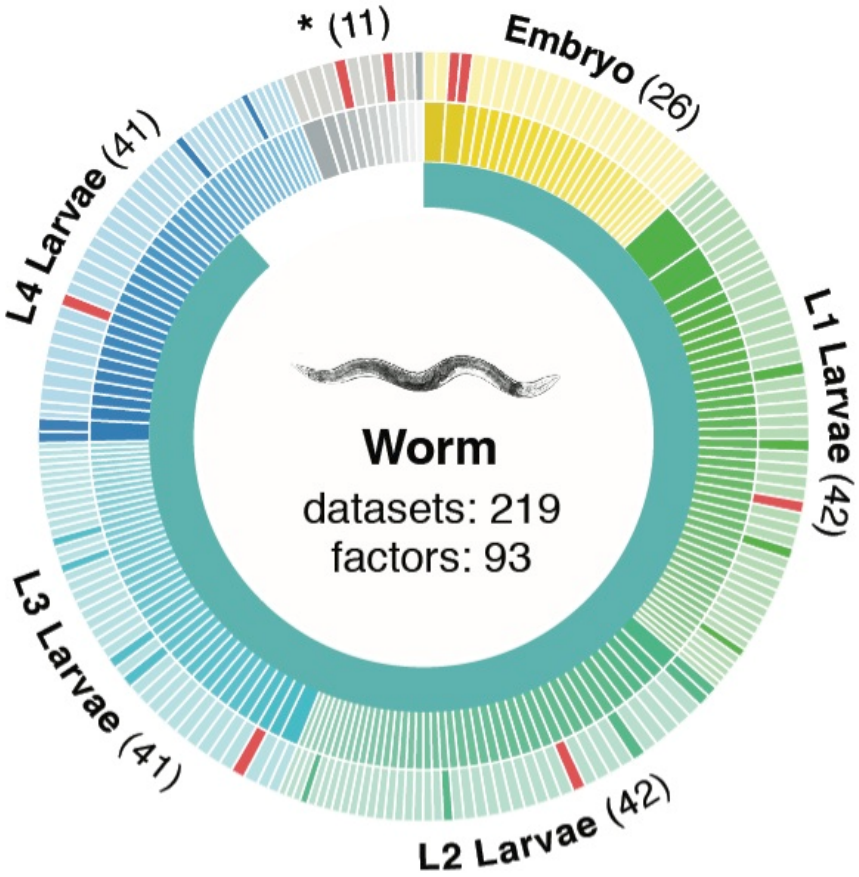
Are gene regulatory networks among orthologs conserved across species?

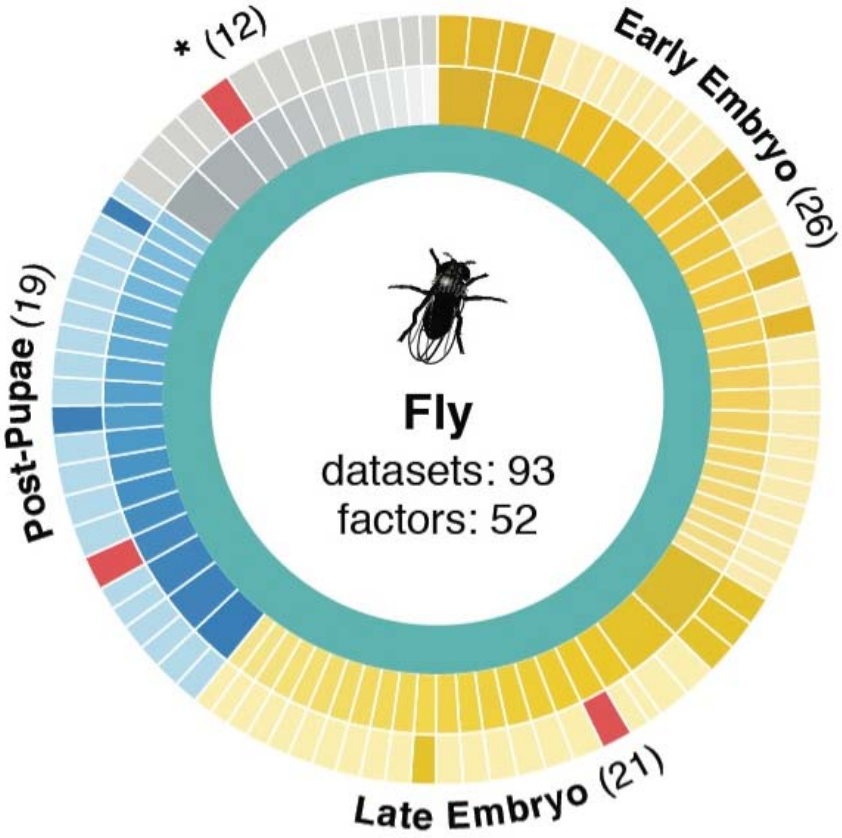


To what degree can't ortholog expression levels be predicted due to species-specific regulation

[Wang et al. *PLOS CB* (in revision, '15)]

Time-course gene expression data of worm & fly development





Organism	Major developmental stages
worm (*C. elegans*)	33 stages: 0, 0.5, 1, …, 12 hours, L1, L2, L3, L4, …, Young Adults, Adults
fly (*D. mel.*)	30 stages: 0, 2, 4, 6, 8,…, 20, 22 hours, L1-L4, Pupaes, Adults

[*Nature* 512:445 ('14); doi: 10.1038/nature13424]

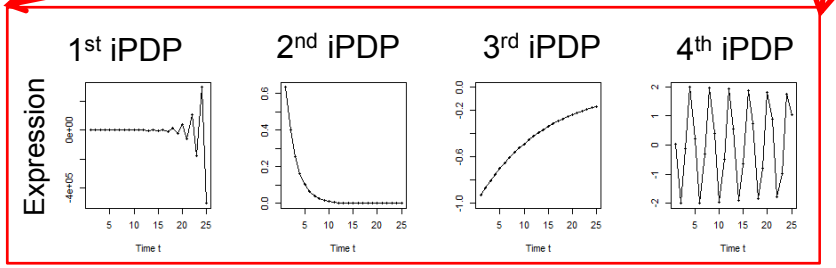
Orthologs have similar internal but different external dynamic patterns during embryonic development

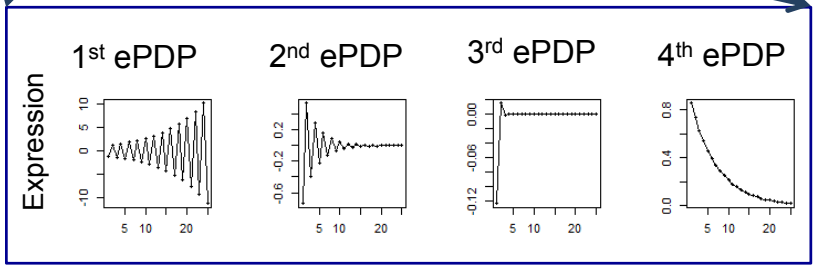
Worm's effective state space model

$$\tilde{X}_{t+1} = \tilde{A}\tilde{X}_t + \tilde{B}\tilde{U}_t$$

iPDPs: time exponentials of $\tilde{A}$ eigenvalues in worm

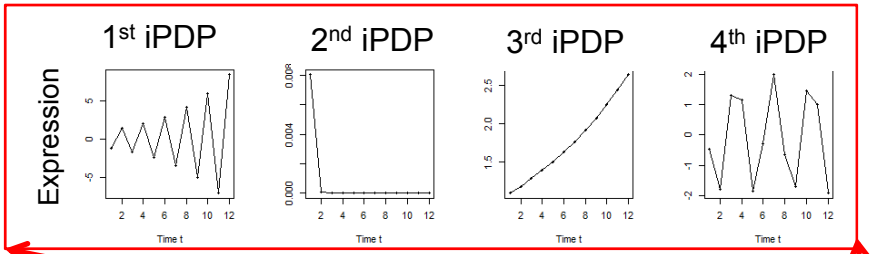
ePDPs: time exponentials of $\tilde{B}$ eigenvalues in worm

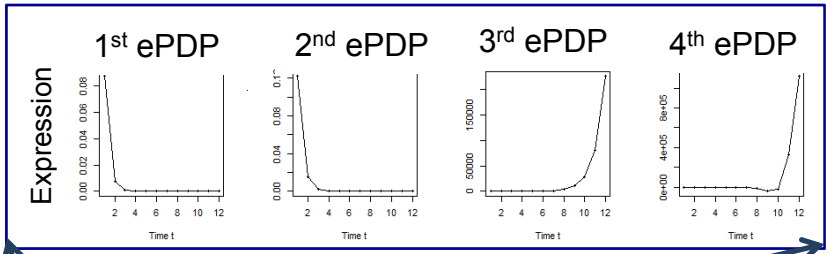




Similar iPDP canonical trajectories

Different ePDP canonical trajectories





iPDPs: time exponentials of $\tilde{A}$ eigenvalues in fly

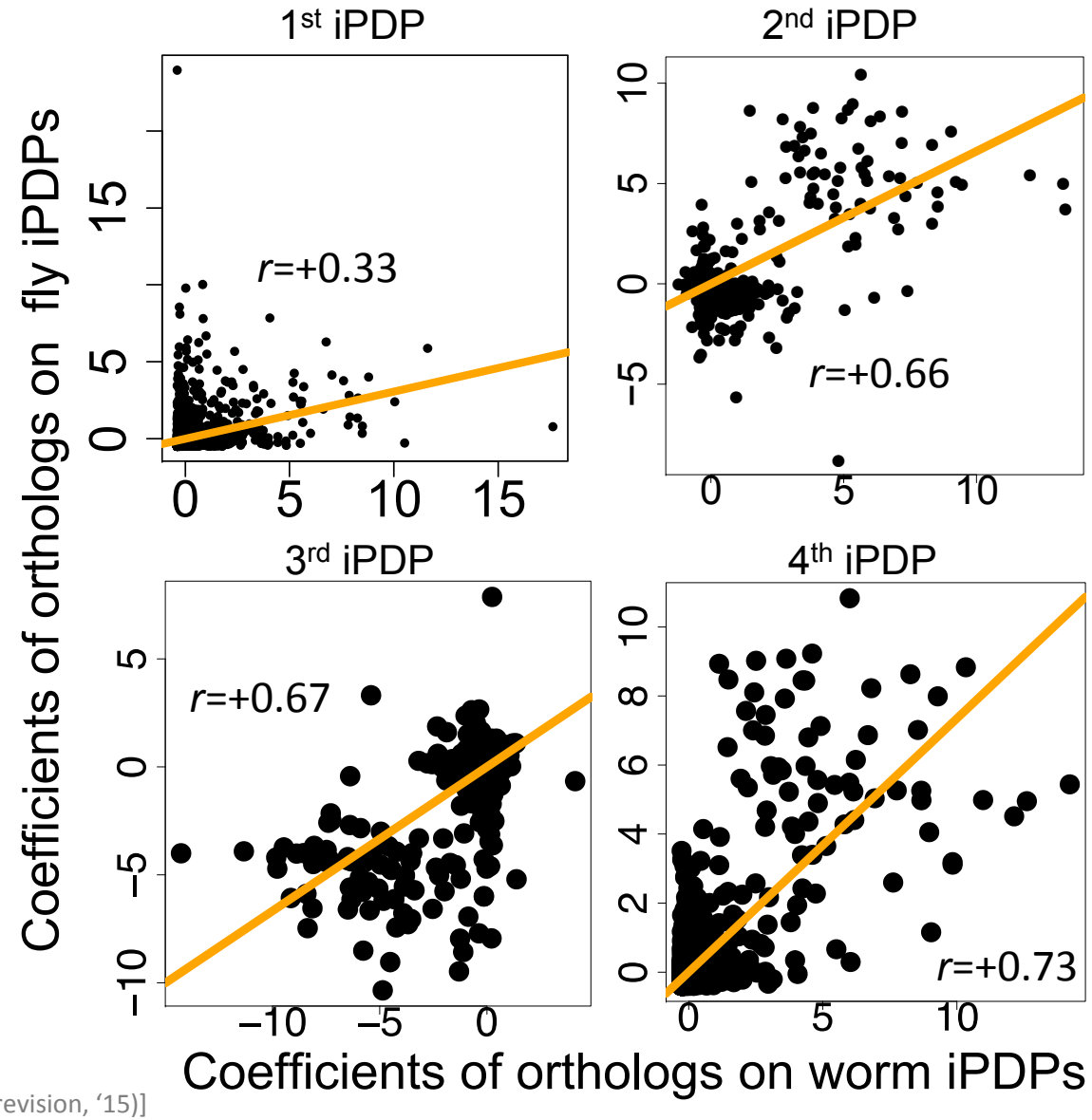
ePDPs: time exponentials of $\tilde{B}$ eigenvalues in fly

Fly's effective state space model

$$\tilde{X}_{t+1} = \tilde{A}\tilde{X}_t + \tilde{B}\tilde{U}_t$$

[Wang et al. *PLOS CB* (in revision, '15)]

Orthologs have correlated iPDP coefficients



[Wang et al. *PLOS CB* (in revision, '15)]

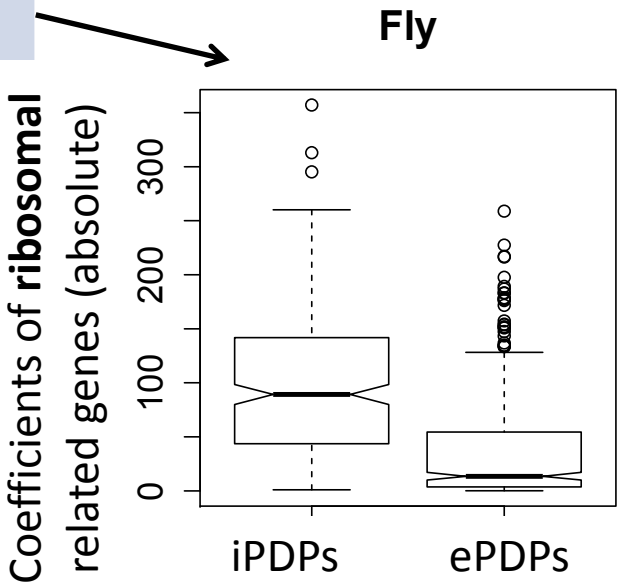
Evolutionarily conserved and younger genes exhibit the opposite internal and external PDP coefficients

iPDP coeffs > ePDP coeffs	Worm	Fly
Ribosomal genes	$p<0.001$	$p<2.2e-16$

Ribosomal genes have significantly larger coefficients for the internal than external PDPs, but signaling genes exhibit the opposite trend

iPDP coeffs < ePDP coeffs	Worm	Fly
Signaling genes	$p<7e-4$	$p<6e-4$

* *p*-values from KS-test



[Wang et al. *PLOS CB* (in revision, '15)]

- **The Dilemma of Genomic Privacy**
  - Fundamental, inherited info that's very private vs the need for large-scale data-sharing to enable med. research
  - Current Social & Tech Approaches
    - Issues: burdensome security, inconsistencies + ways the solutions have been partially "hacked"
    - Strawman Hybrid Soc-Tech Proposal (Cloud Enclaves. Quantifying Leaks, & Closely Coupled priv.-public data)
- **RNA-seq: How to Publicly Share Some of it**
  - Removing SNVs in reads using MRF
  - Quantifying & removing variant info from expression levels + eQTLs
  - Linking Attack using extreme expression levels

Large-scale Transcriptome Mining: Building Interpretative Models while Protecting Individual Privacy

- **Large-scale Mining of RNA-seq to Determine State Space Models**
  - Using dimensionality reduction to help determine internal & external drivers
  - Decoupling expression changes into those driven by worm-fly conserved genes vs species-specific ones. Also, Conserved genes have similar canonical patterns (iPDPs) in contrast to species specific ones (Ex of ribosomal v signaling genes)
  - In human cell cycle, only conserved genes show matching periodic pattern

Acknowledgements

DREISS.gersteinlab.org

D Wang, F He, S Maslov

papers.gersteinlab.org/subject/**privacy**

D Greenbaum

PrivaSeq.gersteinlab.org

A Harmanci

RSEQtools.gersteinlab.org

L Habegger, A Sboner, TA Gianoulis, J Rozowsky, A Agarwal, M Snyder

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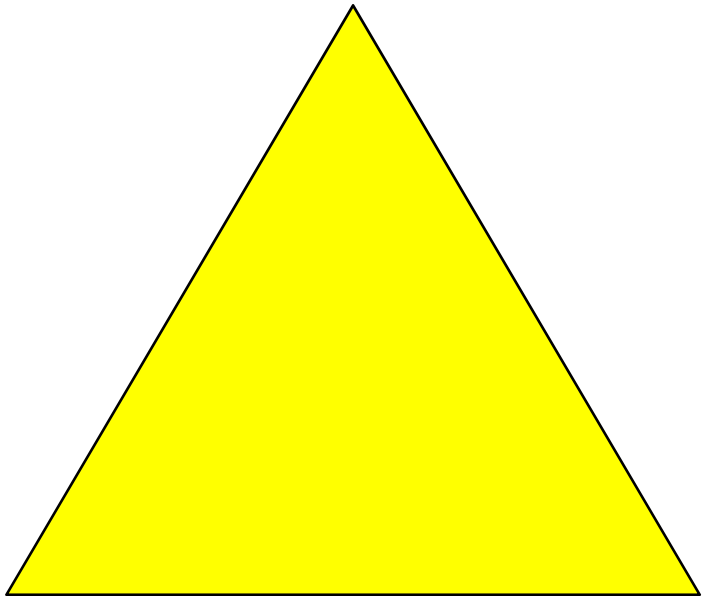
Hiring Postdocs. See gersteinlab.org/jobs !

Default Theme

- Default Outline Level 1
  - Level 2



More Information on this Talk

SUBJECT: Networks

DESCRIPTION:

NOTES:
This PPT should work on mac & PC. Paper references in the talk were mostly from Papers.GersteinLab.org.

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