Making Deep Learning Interpretable for Analyzing Sequential Data about Gene Regulation

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Department of Computer Science
University of Virginia

Today

- Deep Learning: a quick review
- Background Biology: a quick review

https://github.com/qdata

- Deep Learning for analyzing Sequential Data about Regulation:
  - DeepChrome
  - AttentiveChrome
  - DeepMotif

https://www.deepchrome.org

MIT Technology Review

10 Breakthrough Technologies 2013

Think of the most frustrating, intractable, or simply annoying problems you can imagine. Now think about what technology is doing to fix them. That's what we did in coming up with our annual list of 10 Breakthrough Technologies. We're looking for technologies that we believe will expand the scope of human possibilities.

Deep Learning

10 Breakthrough Technologies 2017

These technologies all have staying power. They will affect the economy and our politics, improve medicine, or influence our culture. Some are unfolding now; others will take a decade or more to develop. But you should know about all of them right now.

Deep Reinforcement Learning

Generative Adversarial Network (GAN)

Why breakthrough ?

Breakthrough from 2012 Large-Scale Visual Recognition Challenge (ImageNet)

10% improve with deepCNN

72%, 2010

74%, 2011

85%, 2012

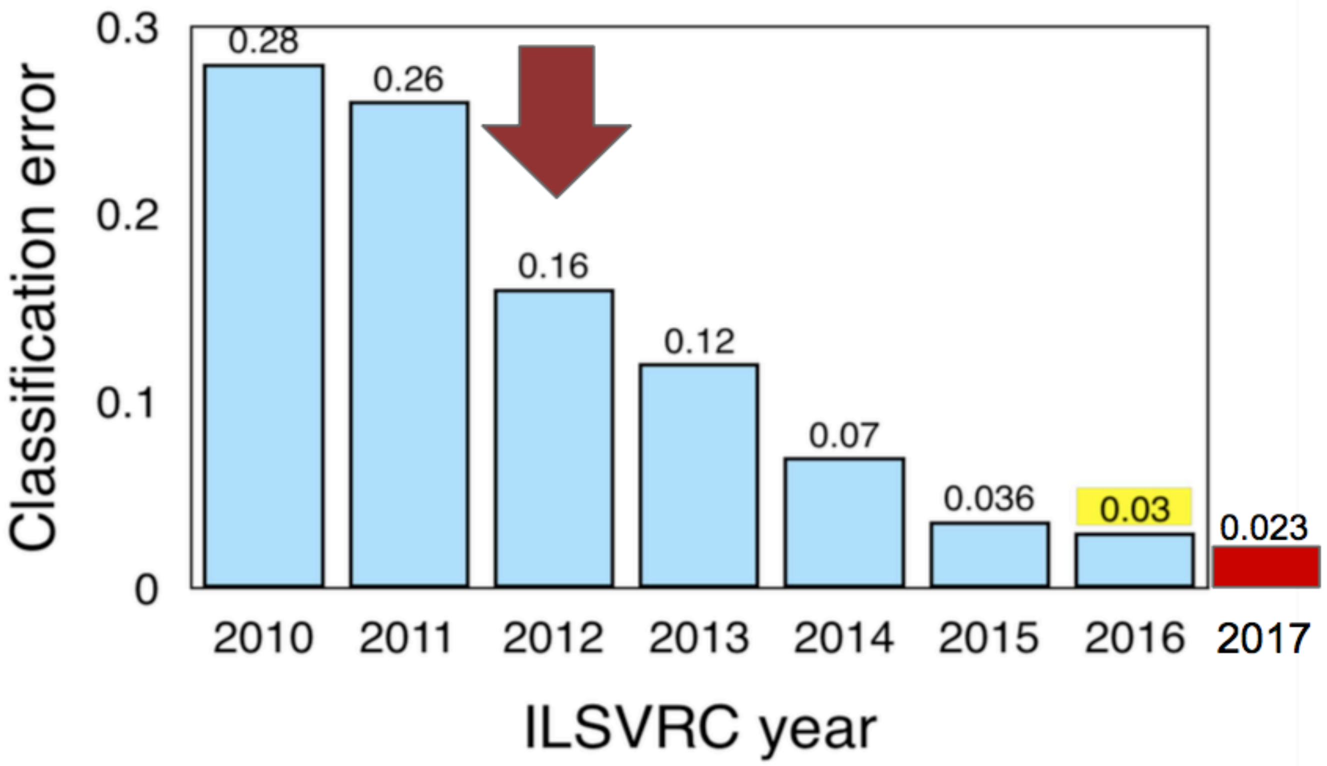
In one "very large-scale" benchmark competition

(**1.2 million images [X] vs.1000 different word labels [Y]**)

ImageNet Challenge

Arch

- 2010-11: hand-crafted computer vision pipelines
- 2012-2016: ConvNets
  - 2012: AlexNet
    - major deep learning success
  - 2013: ZFNet
    - improvements over AlexNet
  - 2014
    - VGGNet: deeper, simpler
    - InceptionNet: deeper, faster
  - 2015
    - ResNet: even deeper
  - 2016
    - ensembled networks
  - 2017
    - Squeeze and Excitation Network



Adapt from From NIPS 2017 DL Trend Tutorial

DNNs help us build more intelligent computers

- Perceive the world,
  - e.g., objective recognition, speech recognition, …
- Understand the world,
  - e.g., machine translation, text semantic understanding
- Interact with the world,
  - e.g., AlphaGo, AlphaZero, self-driving cars, …
- Being able to think / reason,
  - e.g., learn to code programs, learn to search deepNN, …
- Being able to imagine / to make analogy,
  - e.g., learn to draw with styles, ……

Some Recent Trends

https://qdata.github.io/deep2Read/

- 1. Autoencoder / layer-wise training
- 2. CNN / Residual / Dynamic parameter
- 3. RNN / Attention / Seq2Seq, …
- 4. Neural Architecture with explicit Memory
- 5. NTM 4program induction / sequential decisions
- 6. Learning to optimize / Learning DNN architectures
- 7. Learning to learn / meta-learning/ few-shots
- 8. DNN on graphs / trees / sets
- 9. Deep Generative models, e.g., autoregressive
- 10. Generative Adversarial Networks (GAN)
- 11. Deep reinforcement learning
- 12. Validate / Evade / Test / Understand / Verify DNNs

Deep Learning Way: Learning Representation from data

Feature Engineering

- ✓ Most critical for accuracy
- ✓ Account for most of the computation
- ✓ Most time-consuming in development cycle
- ✓ Often hand-craft and task dependent in practice

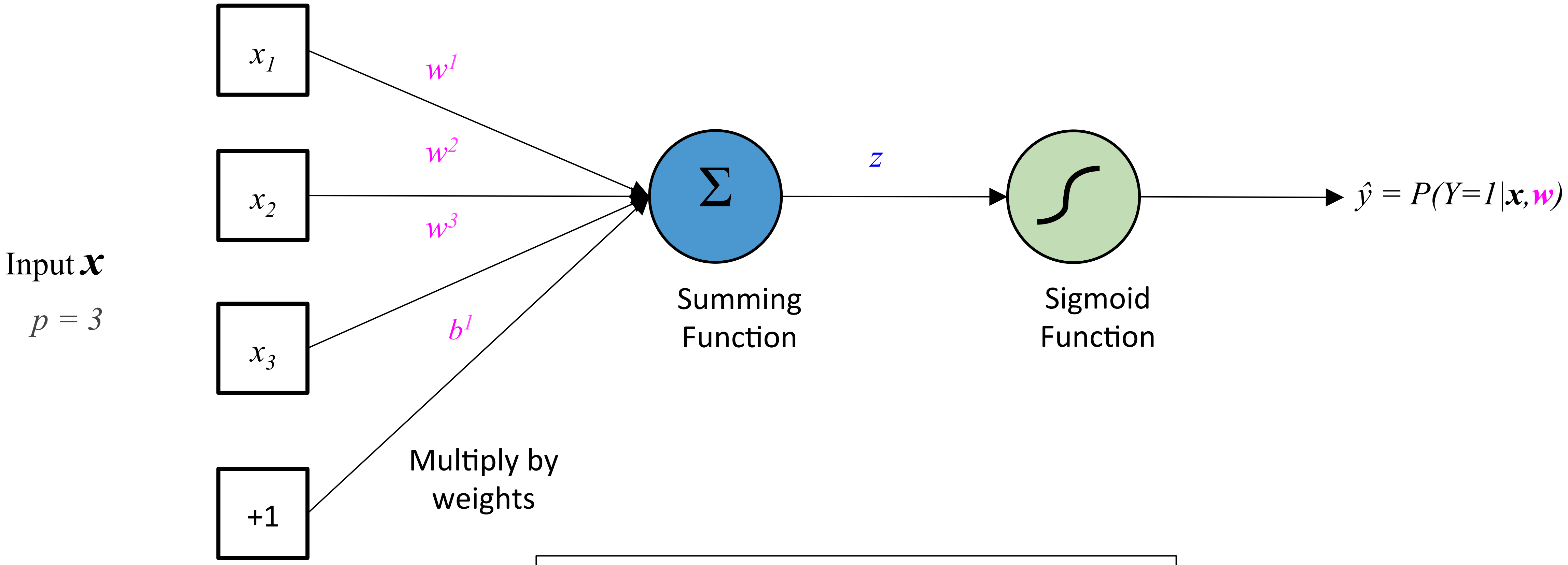
Feature Learning

- ✓ Easily adaptable to new similar tasks
- ✓ Learn layerwise representation from data

Basics

- Basic Neural Network (NN)
  - single neuron, e.g. logistic regression unit
  - multilayer perceptron (MLP)
  - various loss function
    - E.g., when for multi-class classification, softmax layer
  - training NN with backprop algorithm

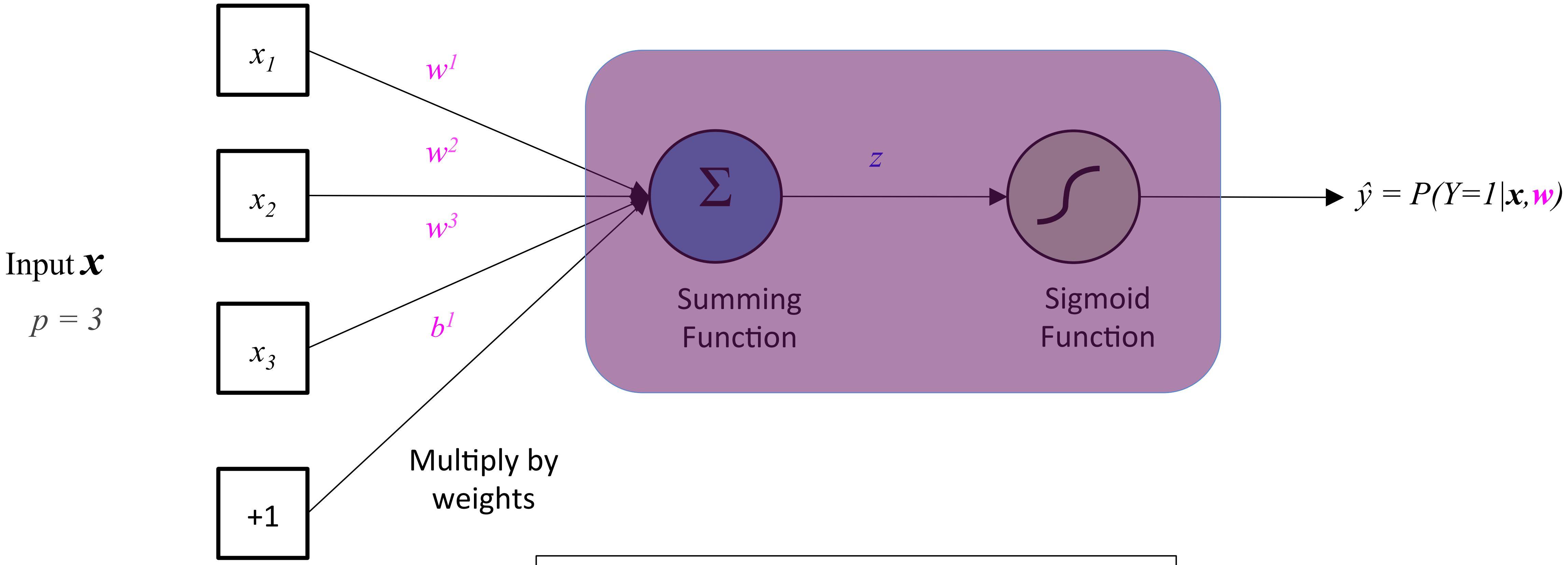
One “Neuron”: Expanded Logistic Regression



$$z = \boldsymbol{w}^T \cdot \boldsymbol{x} + \boldsymbol{b}$$

$$y = sigmoid(z) \quad = \frac{e^z}{1 + e^z}$$

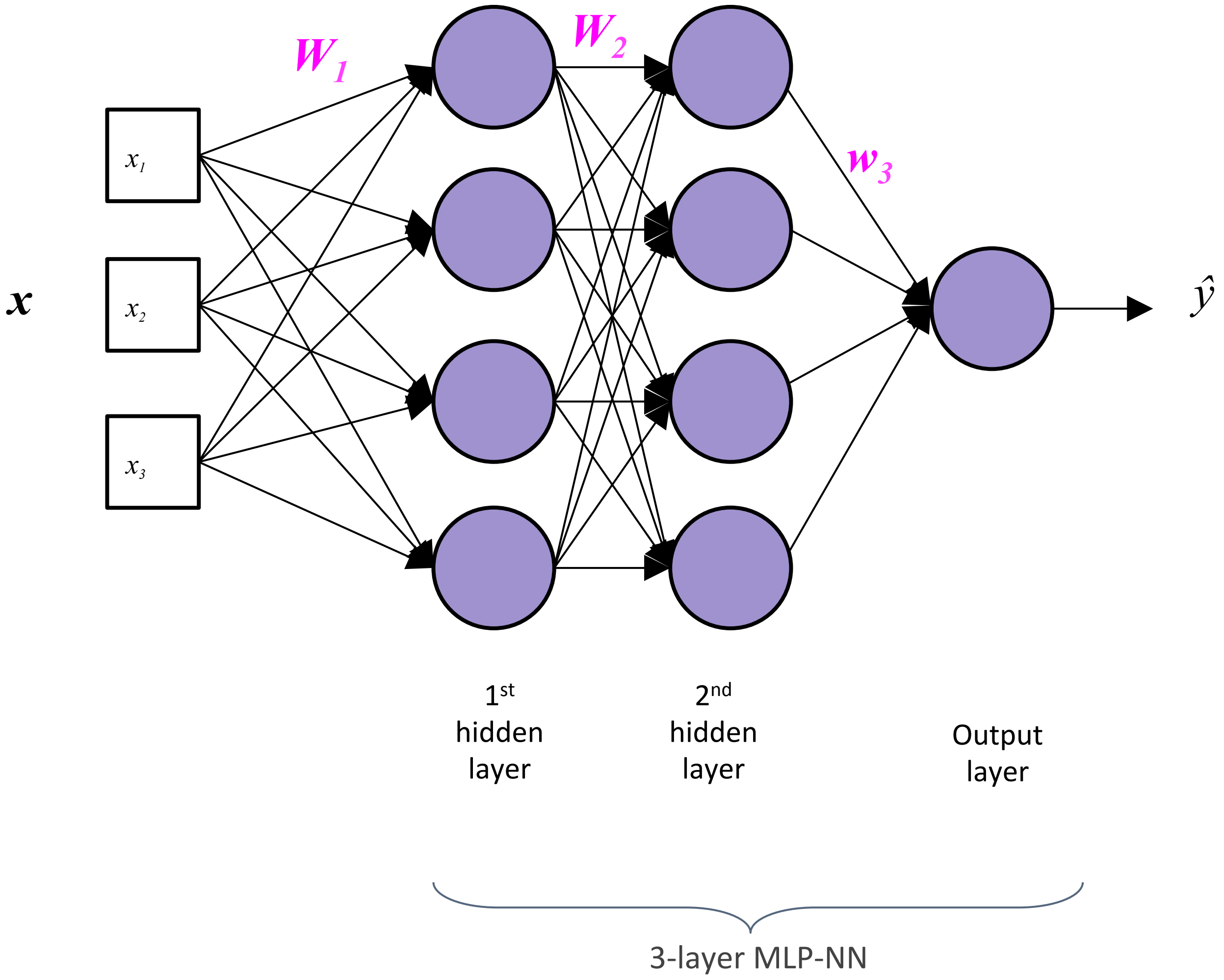
One “Neuron”: Expanded Logistic Regression



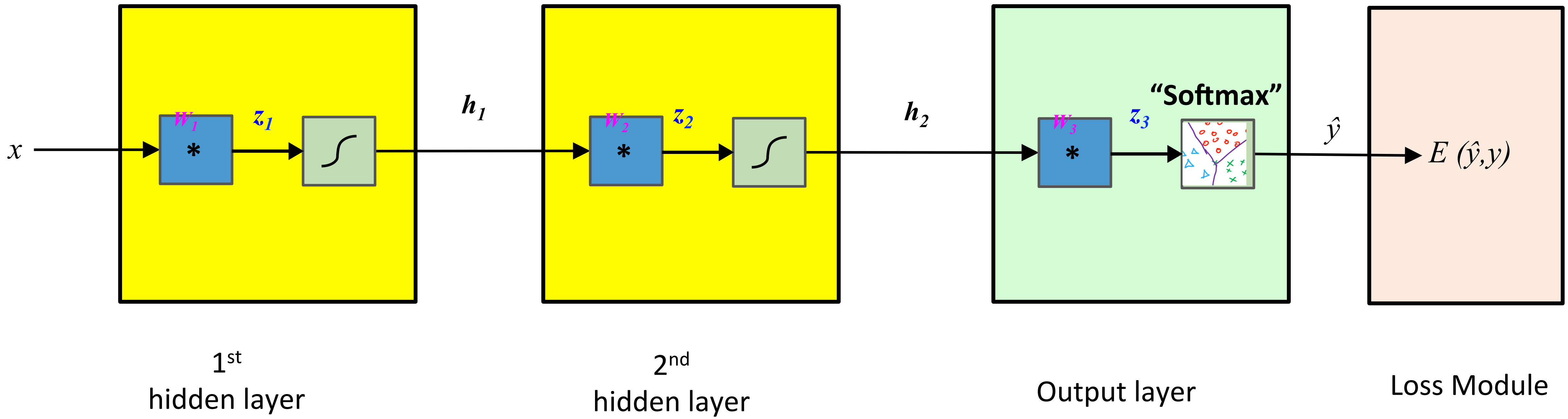
$$z = \mathbf{w}^T \cdot \mathbf{x} + \mathbf{b}$$

$$y = sigmoid(z) = \frac{e^z}{1 + e^z}$$

Multi-Layer Neural Network (MLP)- (Feed-Forward)



"Block View"



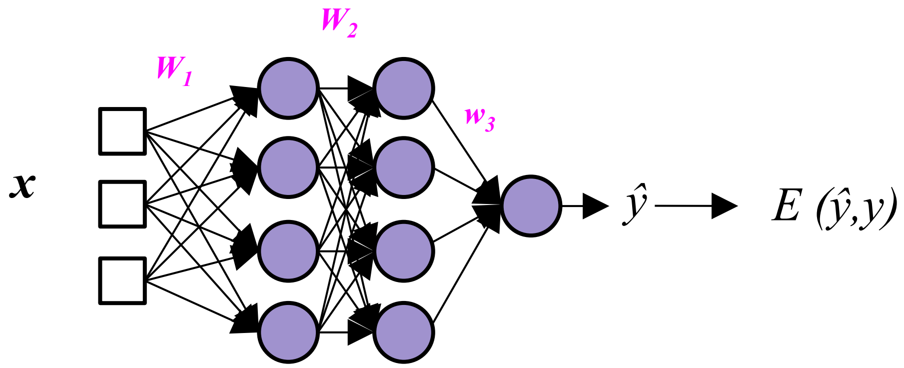
x
W_1
z_1
h_1
W_2
z_2
h_2
W_3
z_3
"Softmax"
$\hat{y}$
$E\ (\hat{y}, y)$
1^{st} hidden layer
2^{nd} hidden layer
Output layer
Loss Module

Training Neural Networks

How do we learn the optimal weights W_L for our task??

- **Stochastic Gradient descent:**

$$W_L^{t} = W_L^{t-1} - \eta \frac{\partial E}{\partial W_L}$$



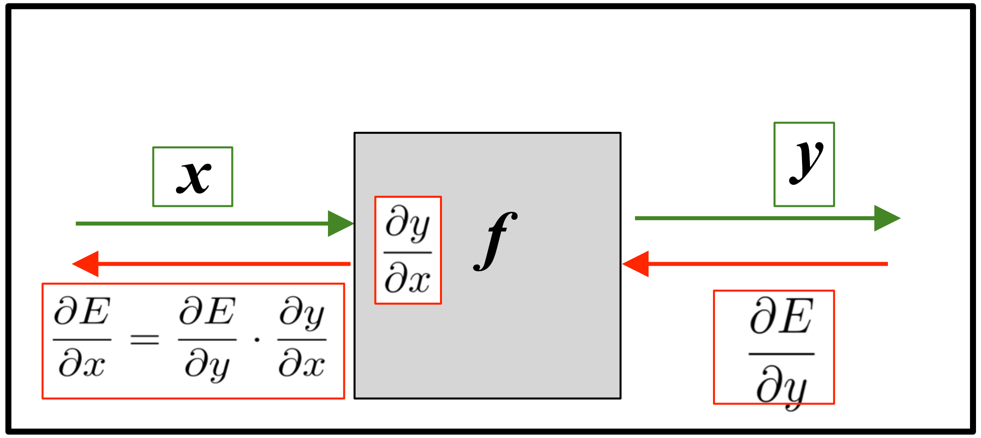
But how do we get gradients of lower layers?

- **Backpropagation!**
  - Repeated application of chain rule of calculus
  - Locally minimize the objective
  - Requires all “blocks” of the network to be differentiable

– Main Idea: error in hidden layers

LeCun et. al. *Efficient Backpropagation*. 1998

Building Deep Neural Nets



http://cs231n.stanford.edu/slides/winter1516_lecture5.pdf

Important Block: Convolutional Neural Networks (CNN)

- Prof. Yann LeCun invented CNN in 1998
- First NN successfully trained with many layers

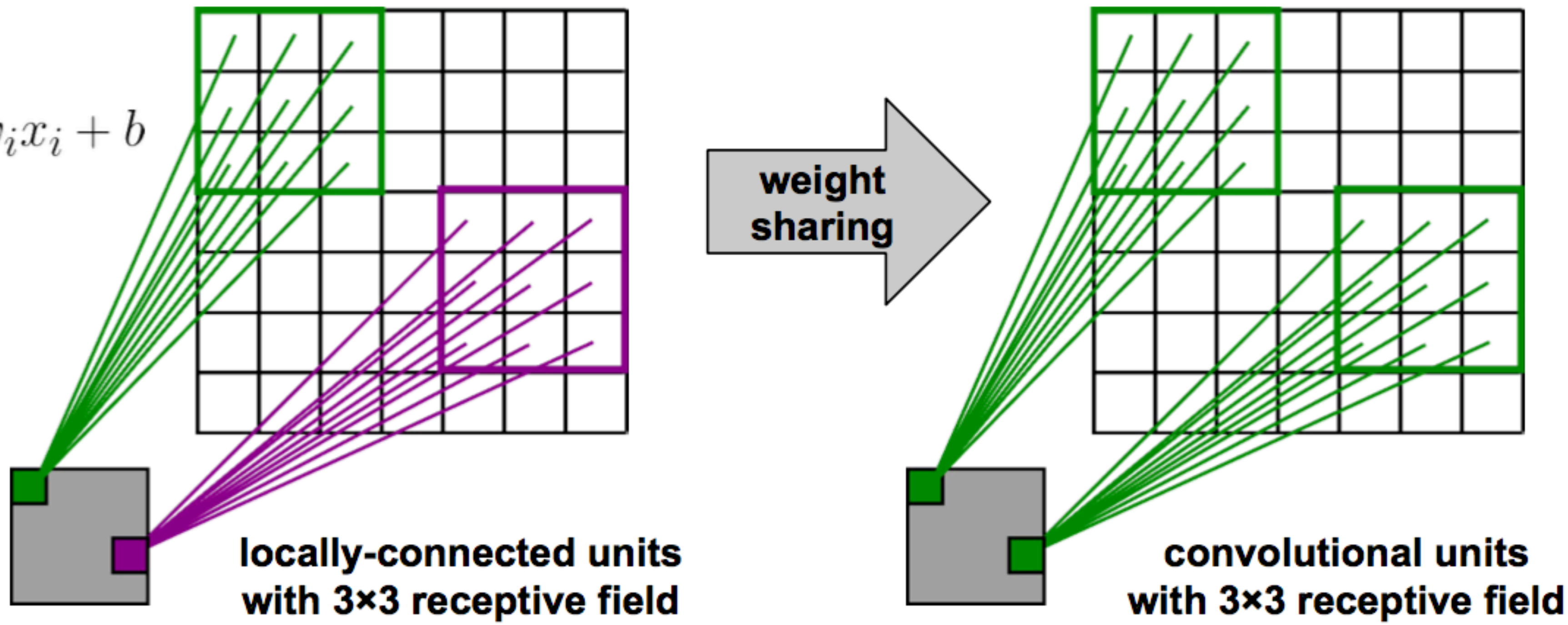
The bird occupies a local area and looks the same in different parts of an image.
We should construct neural nets which exploit these properties!

Y. LeCun, L. Bottou, Y. Bengio, and P. Haffner, Gradient-based learning applied to document recognition, Proceedings of the IEEE 86(11): 2278–2324, 1998.

CNN models Locality and Translation Invariance

Make fully-connected layer locally-connected and sharing weight

$$y = \sum_{i \in \substack{receptive \\ field}} w_i x_i + b$$

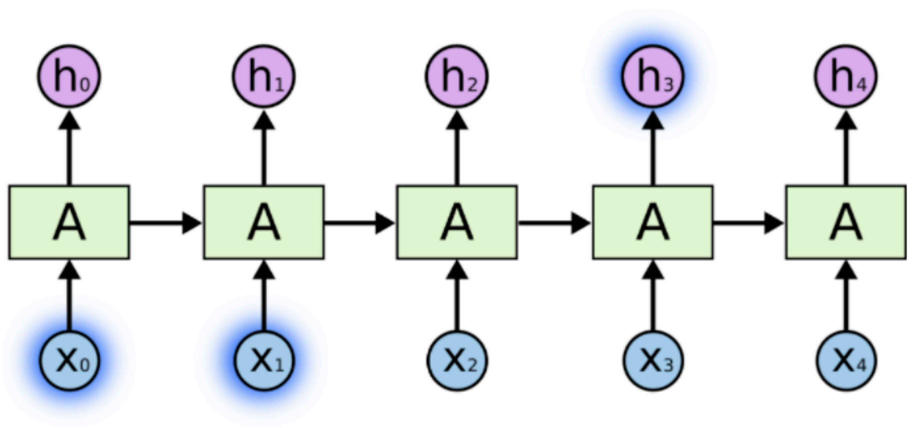


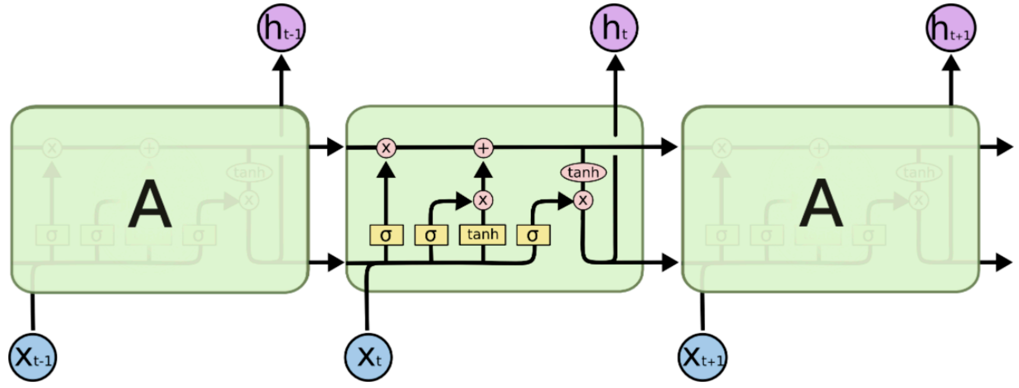
$$y = w * x + b$$

Adapt from From NIPS 2017 DL Trend Tutorial

Important Block: Recurrent Neural Networks (RNN)

- Prof. Schmidhuber invented "Long short-term memory" – Recurrent NN (LSTM-RNN) model in 1997





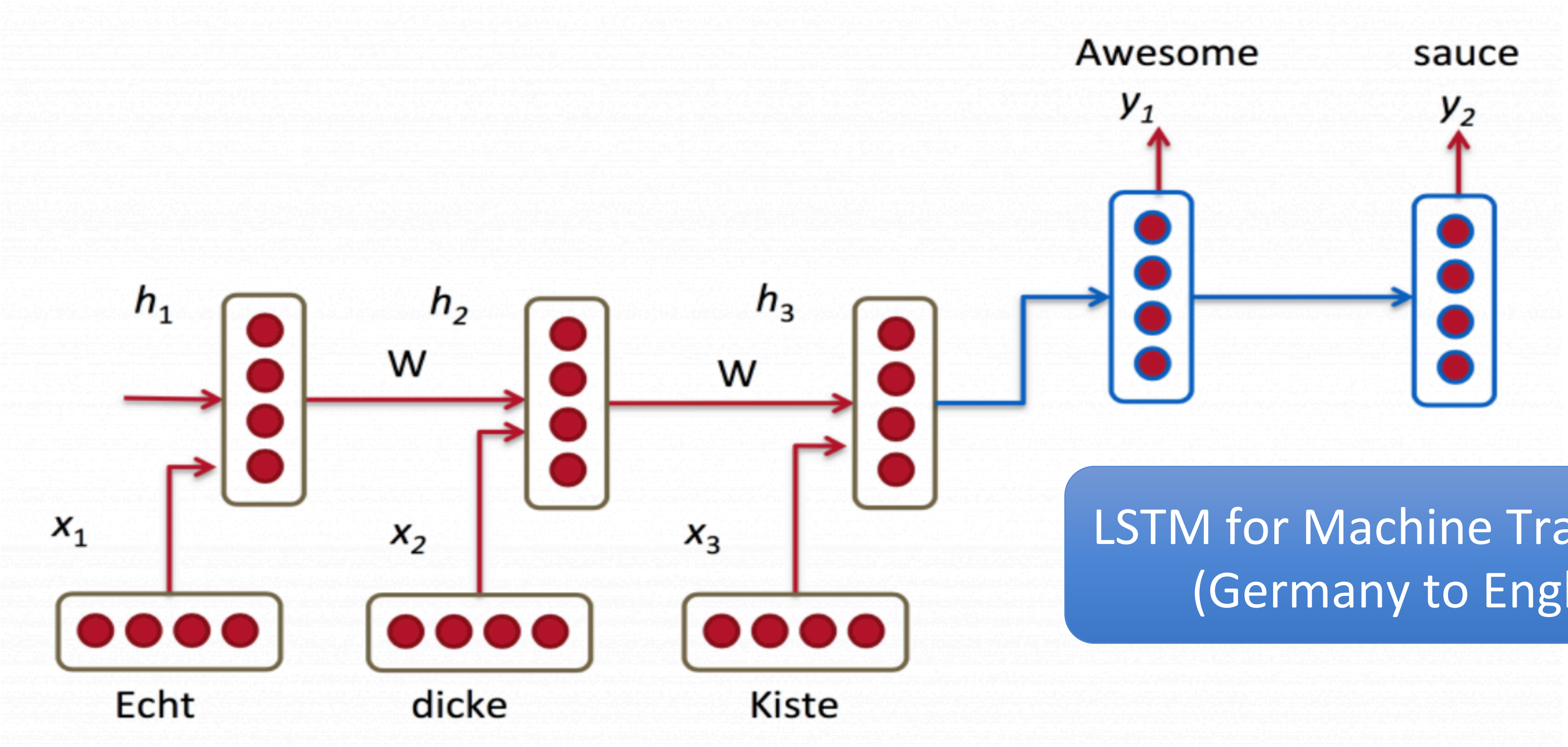
The repeating module in an LSTM contains four interacting layers.

Sepp Hochreiter; Jürgen Schmidhuber (1997). "Long short-term memory". Neural Computation. 9 (8): 1735–1780.

Image Credits from Christopher Olah

RNN models dynamic temporal dependency

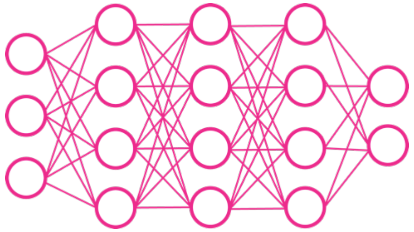
- Make fully-connected layer model each unit recurrently
- Units form a directed chain graph along a sequence
- Each unit uses recent history and current input in modeling



LSTM for Machine Translation (Germany to English)

Image credit : wildML

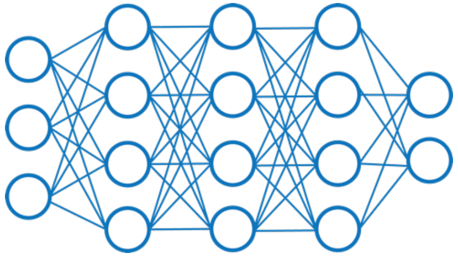
State-of-the-art: Deep Neural Networks (DNNs)



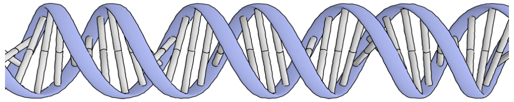
"Dog"

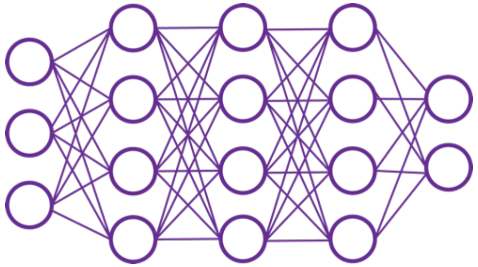
Can get overly sentimental at times, but Gus Van Sant's sensitive direction... and his excellent use of the city make it a hugely entertaining and effective film.

Full Review... | May 25, 2006



ATGCGATCAAGTCTG

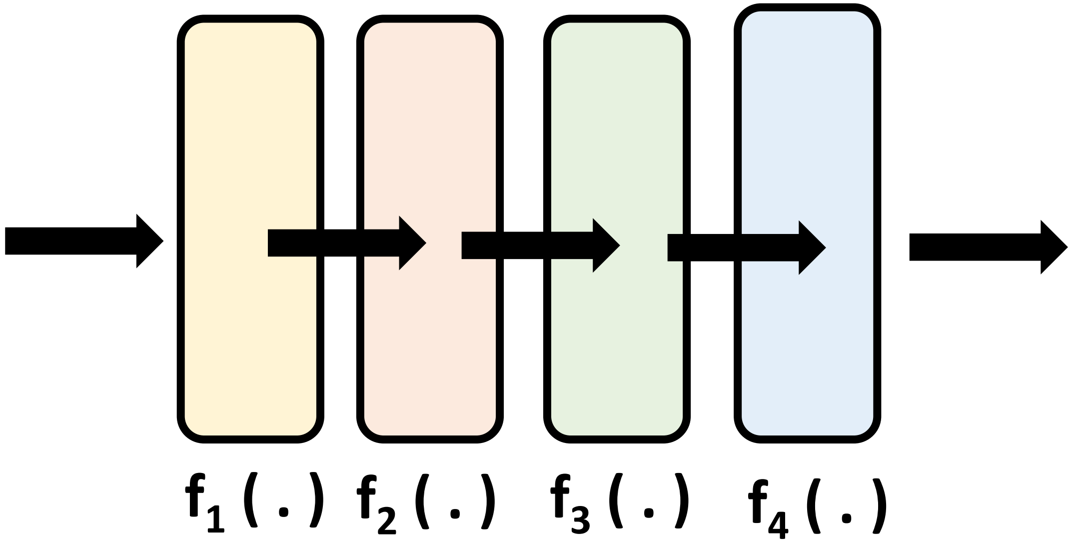




"Protein-binding Site"

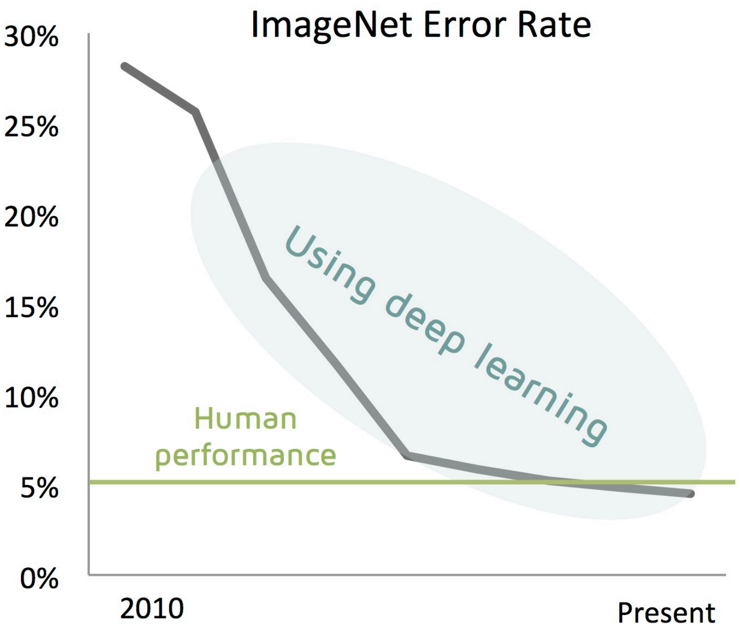
Challenge : DNNs are hard to Interpret

X

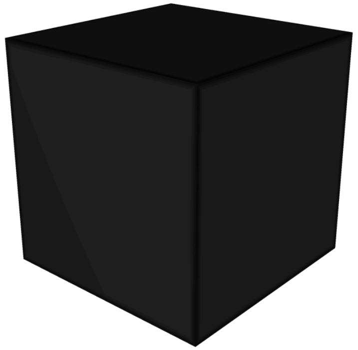


Y

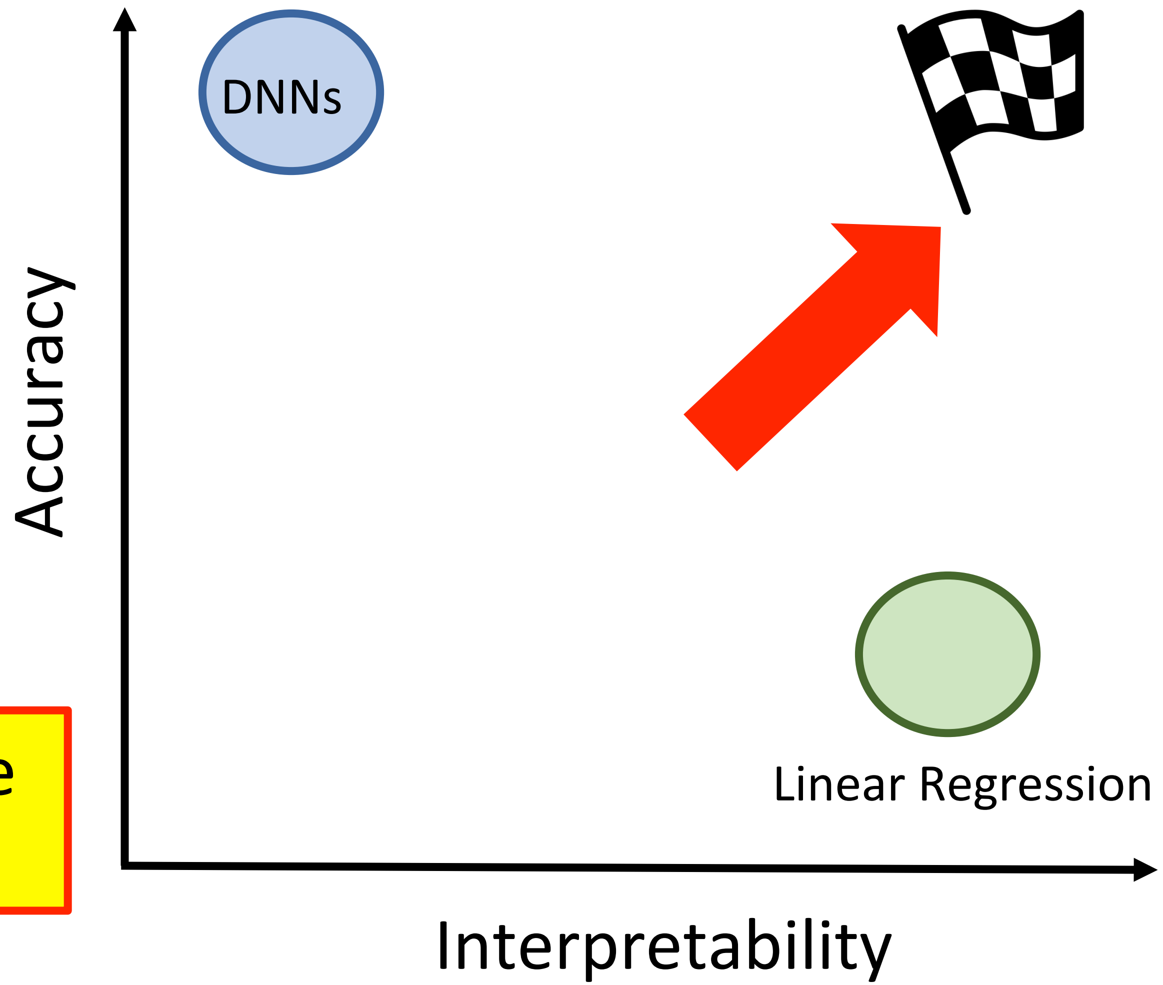
"Dog"



$$Y=f_4(f_3(f_2(f_1(X))))$$

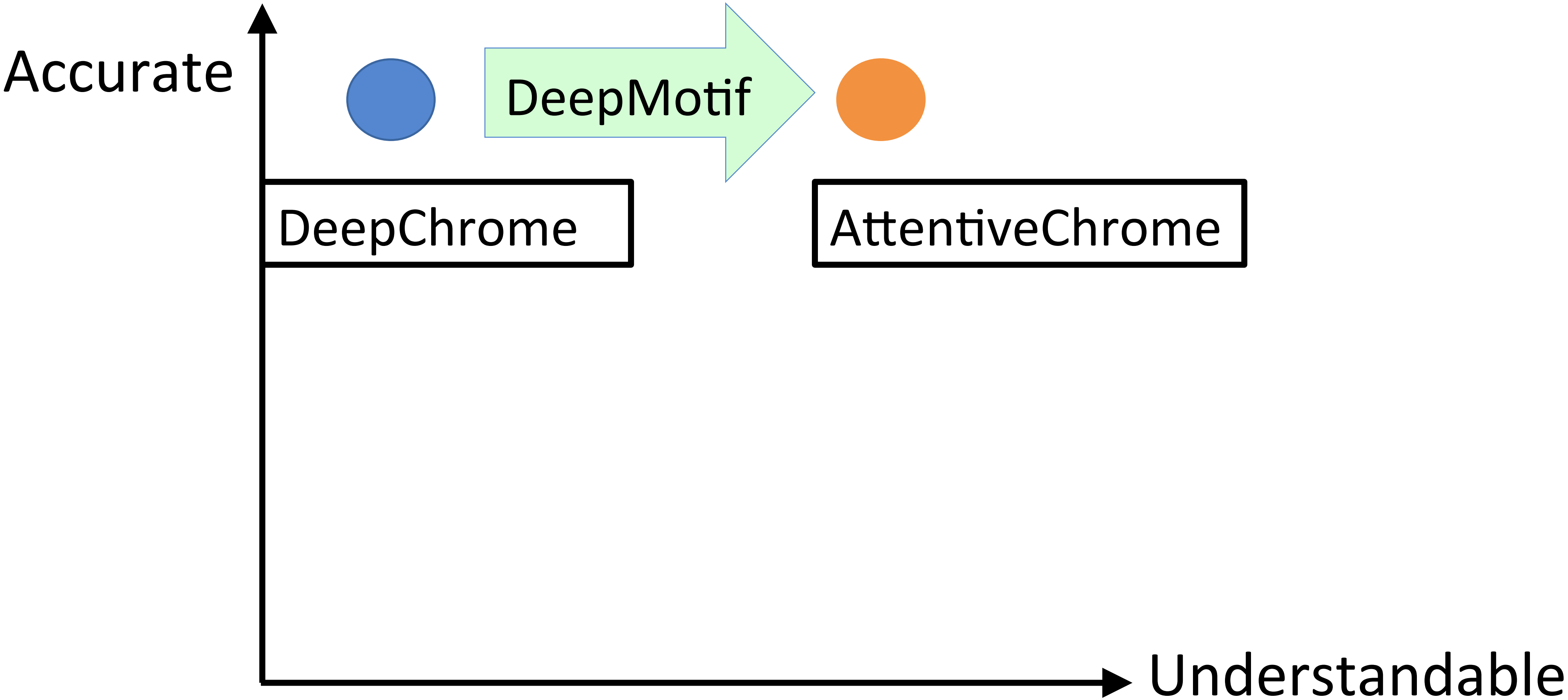


Our Goal: Interpretable DNNs



Challenge : DNNs are hard to Interpret

Summary of our tools



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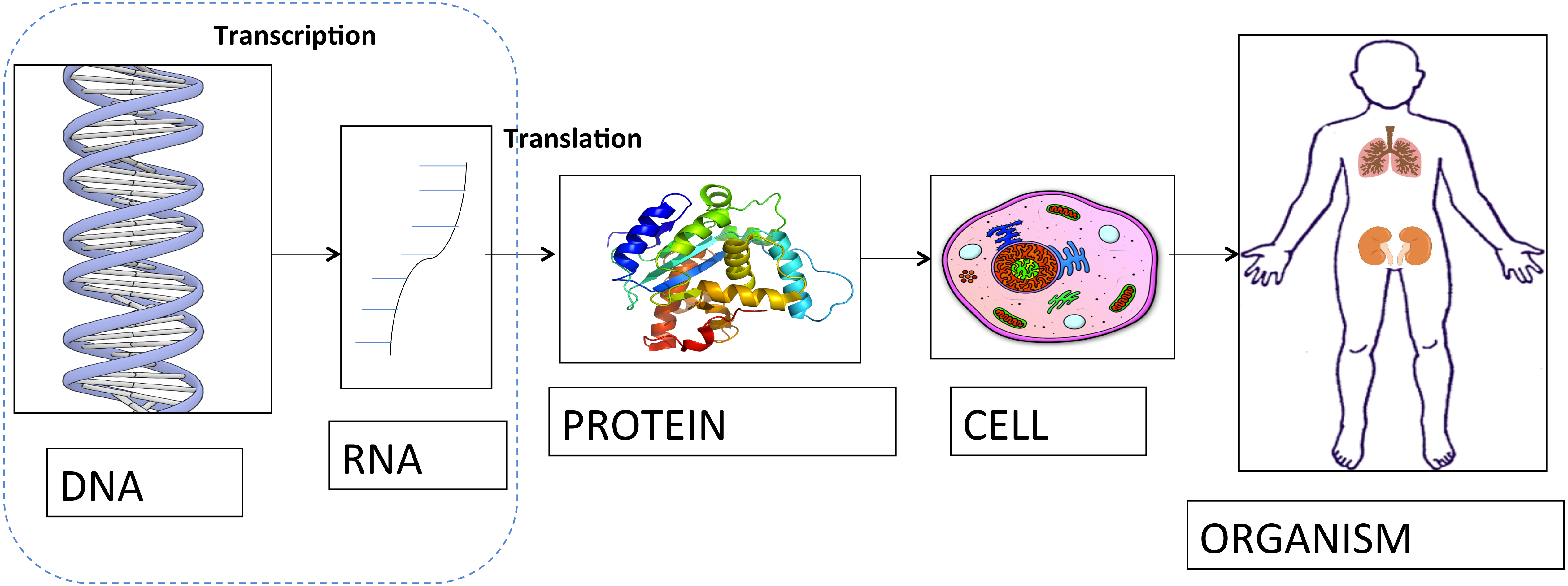
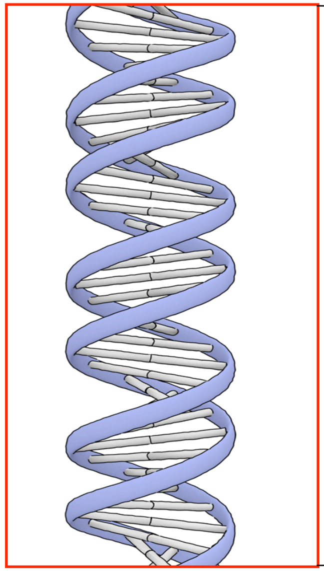
Biology in a Slide



DNA and Diseases



DNA

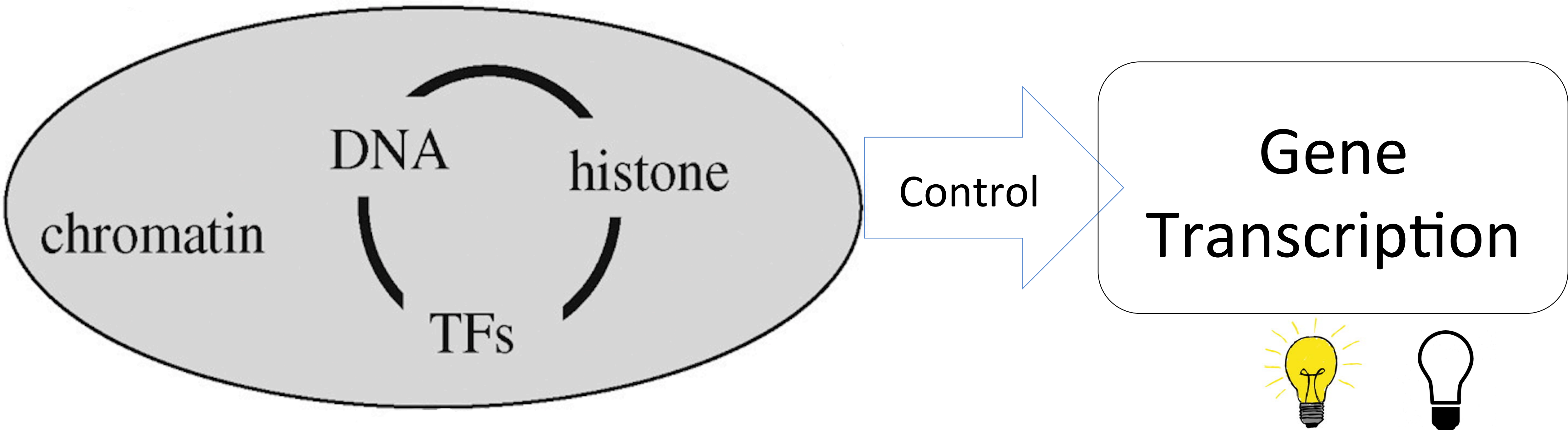
- Down Syndrome
- Parkinson’s Disease
- Autism
- Muscular Atrophy
- Sickle Cell Disease

……….

………..

Epigenetics
“Environment of the DNA”

Chromatin



Histone Proteins

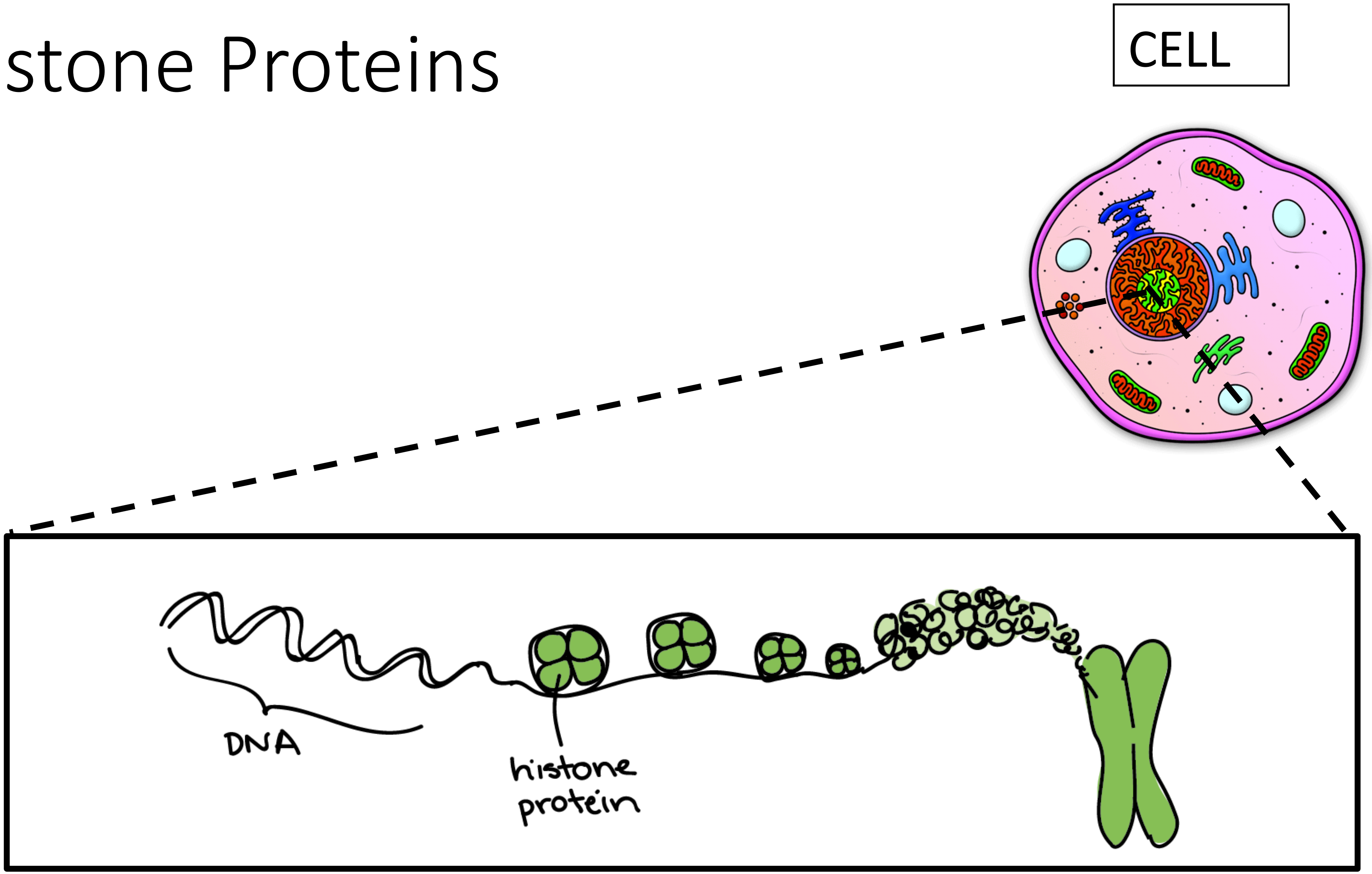
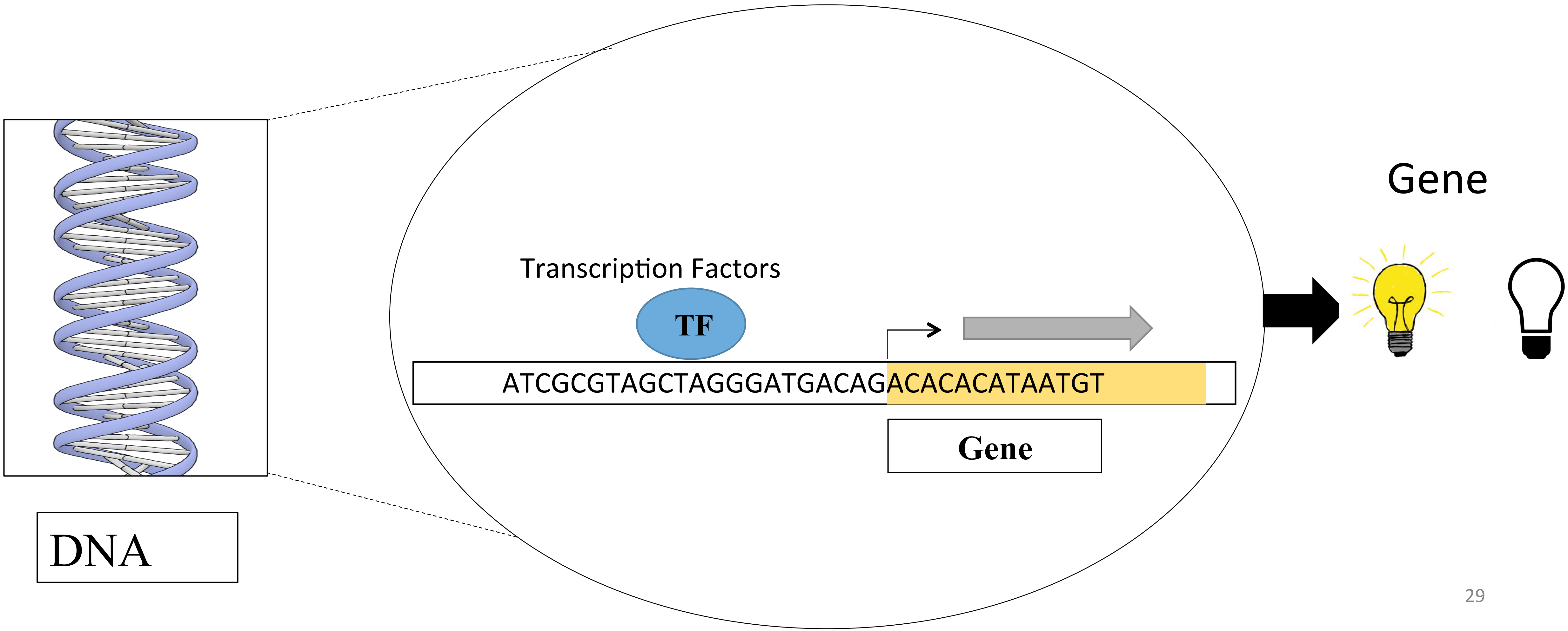
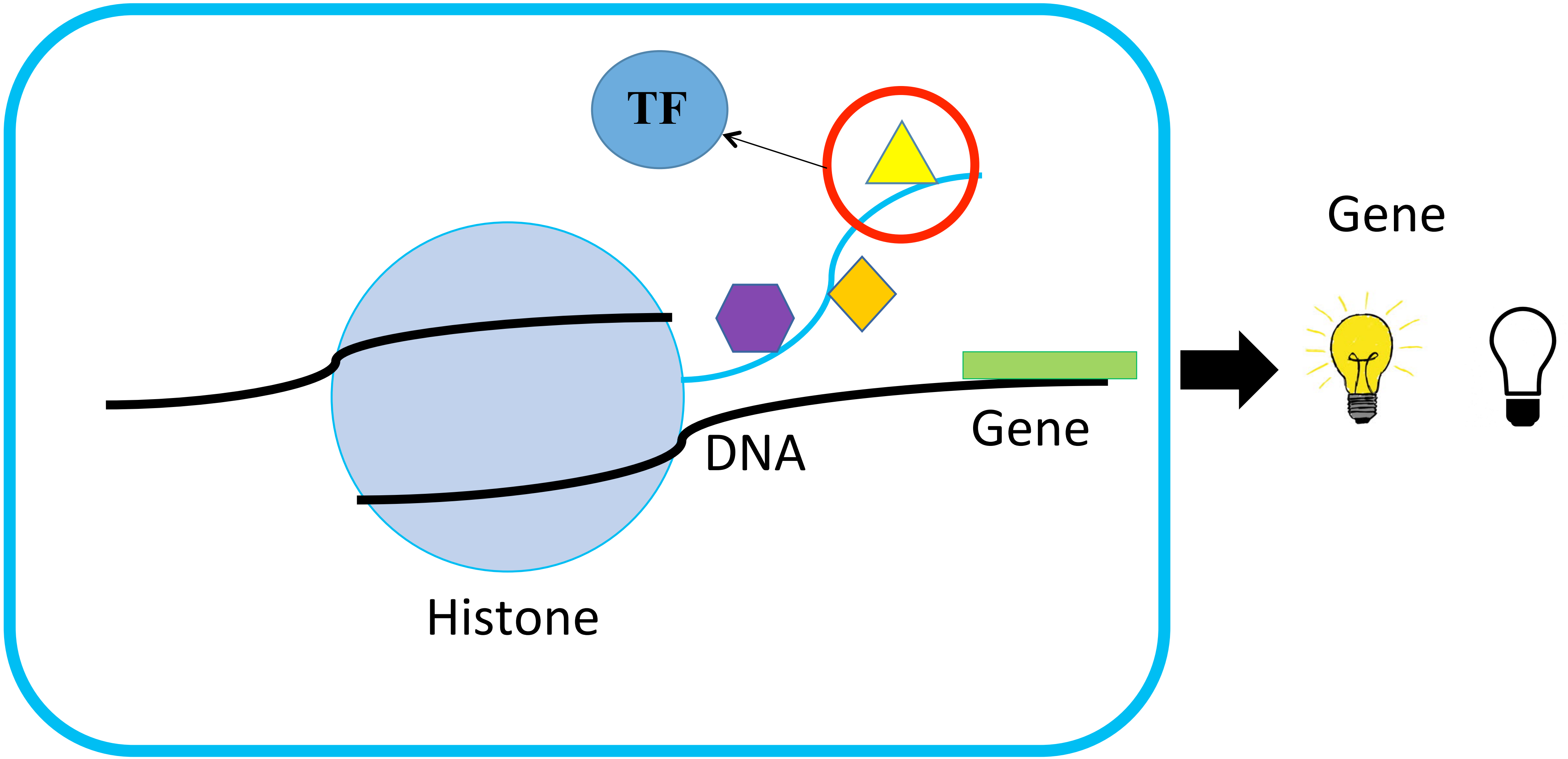


Image:https://www.khanacademy.org/science/biology/cellular-molecular-biology/intro-to-cell-division/a/dna-and-chromosomes-article

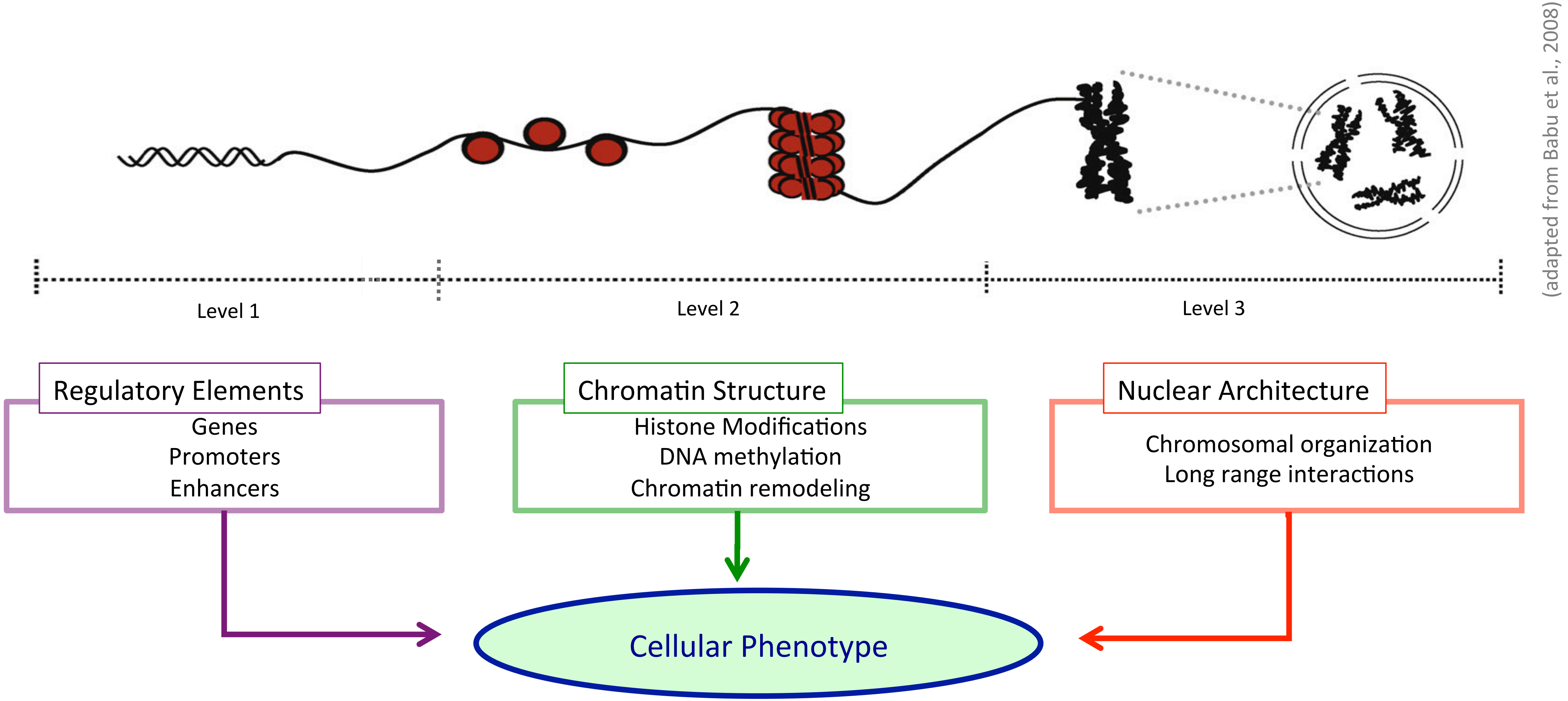
Transcription Factor Binding => Gene Transcription

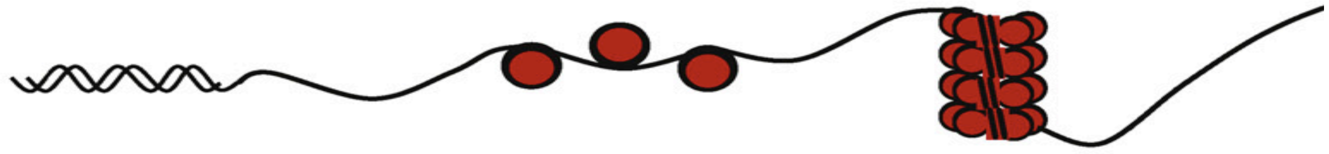


Histone Modifications (HM)



Genome Organization and Gene Regulation





Level 1

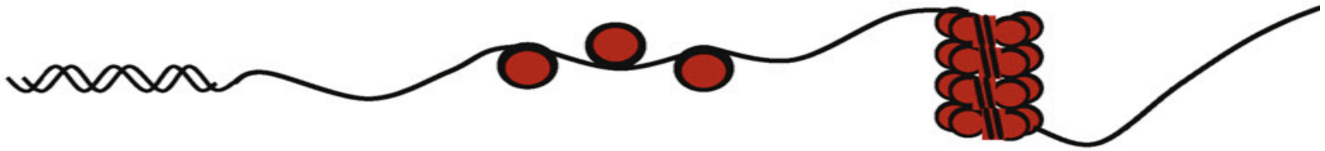
Level 2

Regulatory Elements
Genes
Promoters
Enhancers

Chromatin Structure
Histone Modifications
DNA methylation
Chromatin remodeling

ENCODE Project (2003-Present)

Describe the functional elements encoded in human DNA



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Regulatory Elements

Genes
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ENCODE Project (2003-)

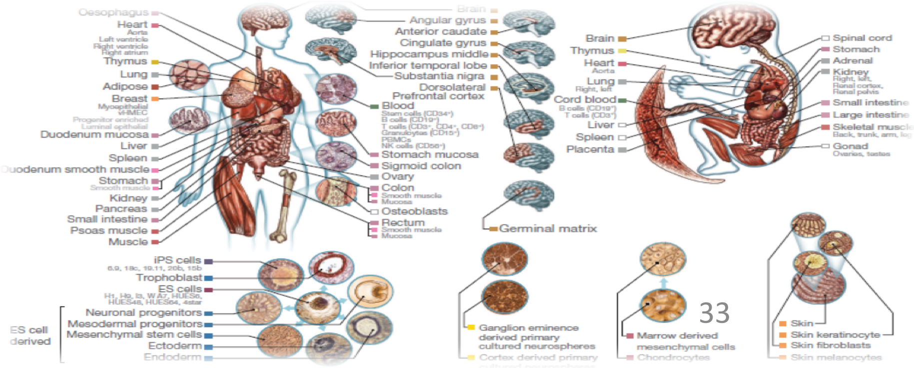
Describe the functional elements encoded in human DNA

Roadmap Epigenetics Project (REMC, 2008-)

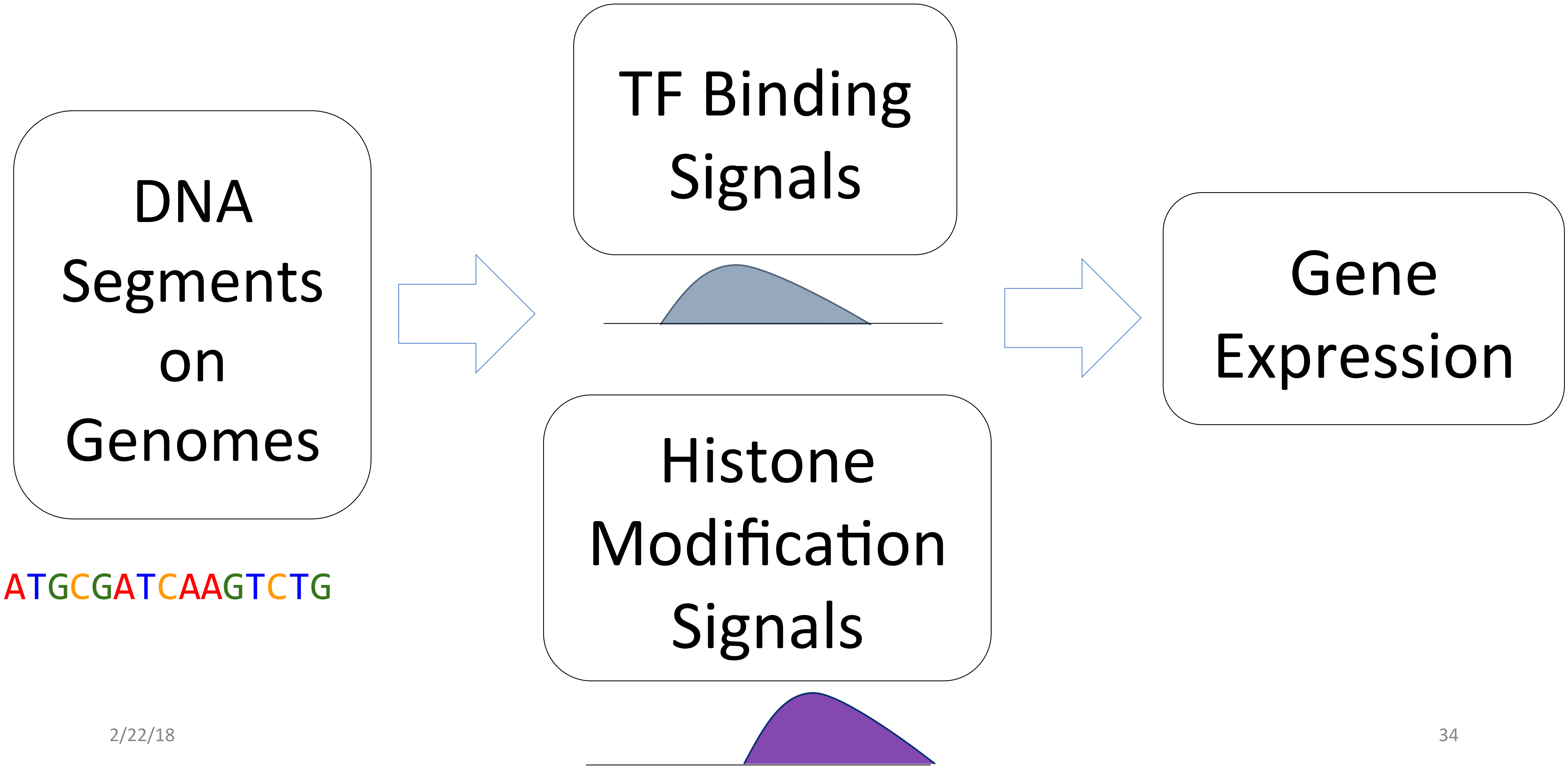
To produce a public resource of epigenomic maps for stem cells and primary ex vivo tissues selected to represent the normal counterparts of tissues and organ systems frequently involved in human disease.

Nature
February 18, 2015

Integrative analysis of 111 reference human epigenomes (Abstract)



Many Possible Computational Tasks



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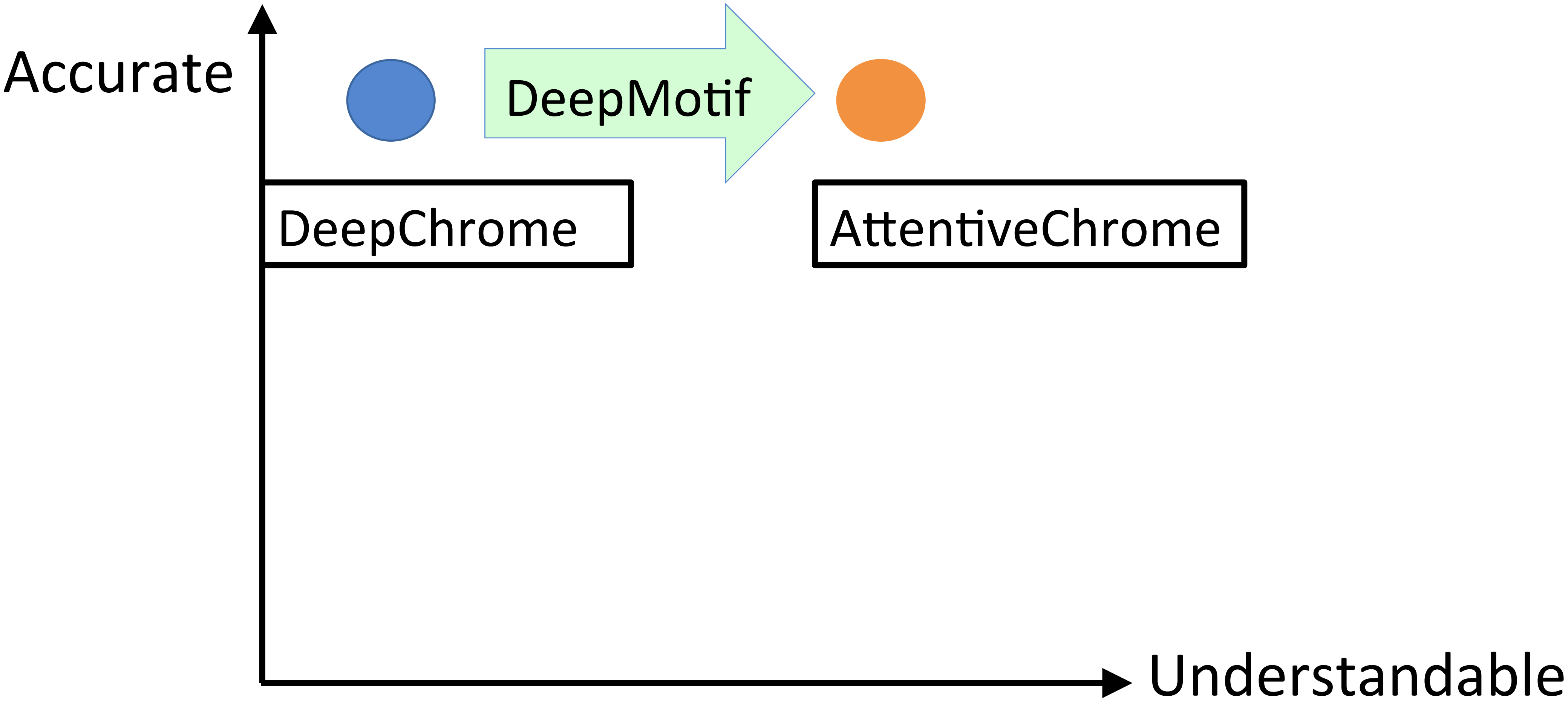
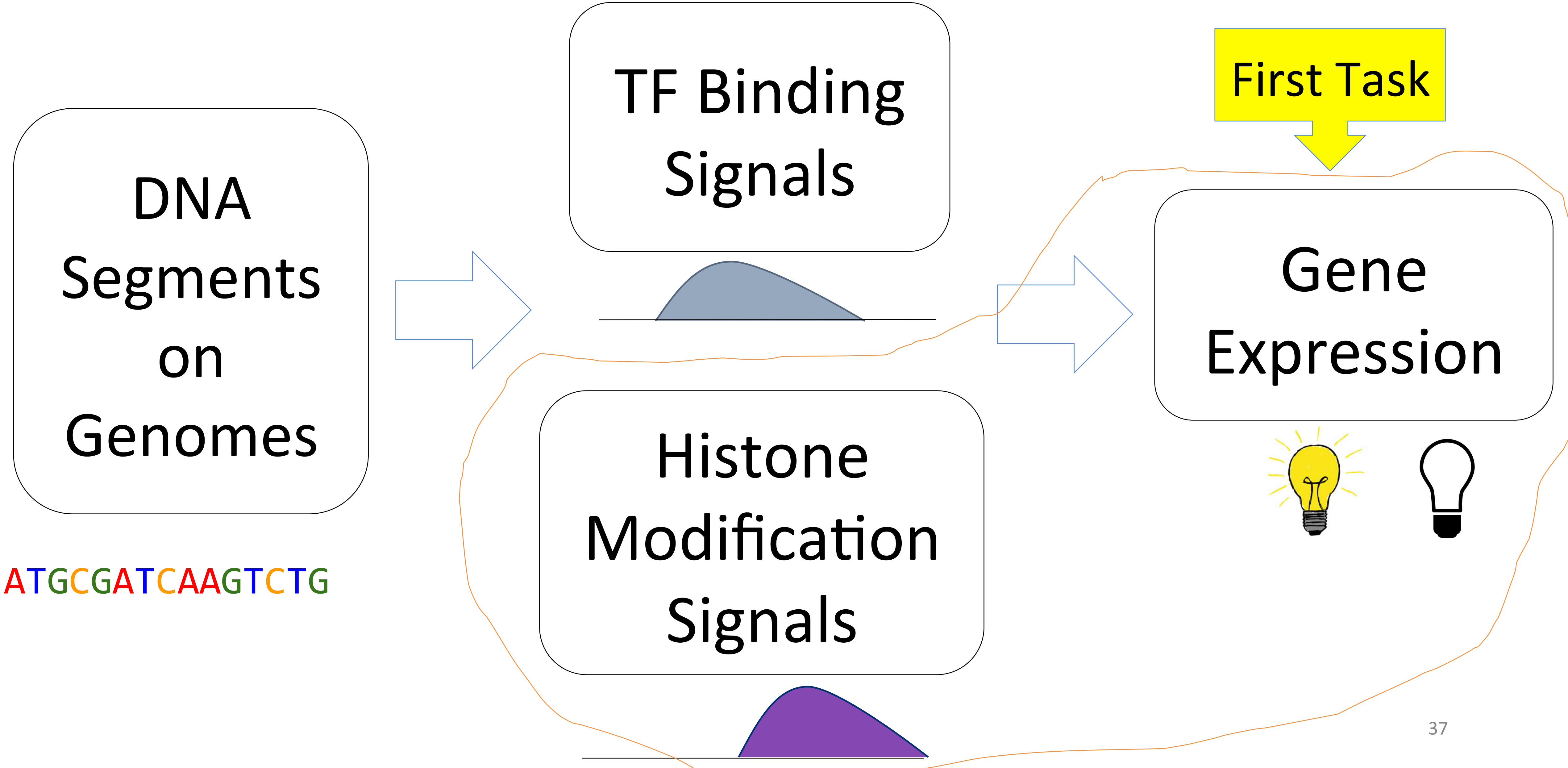
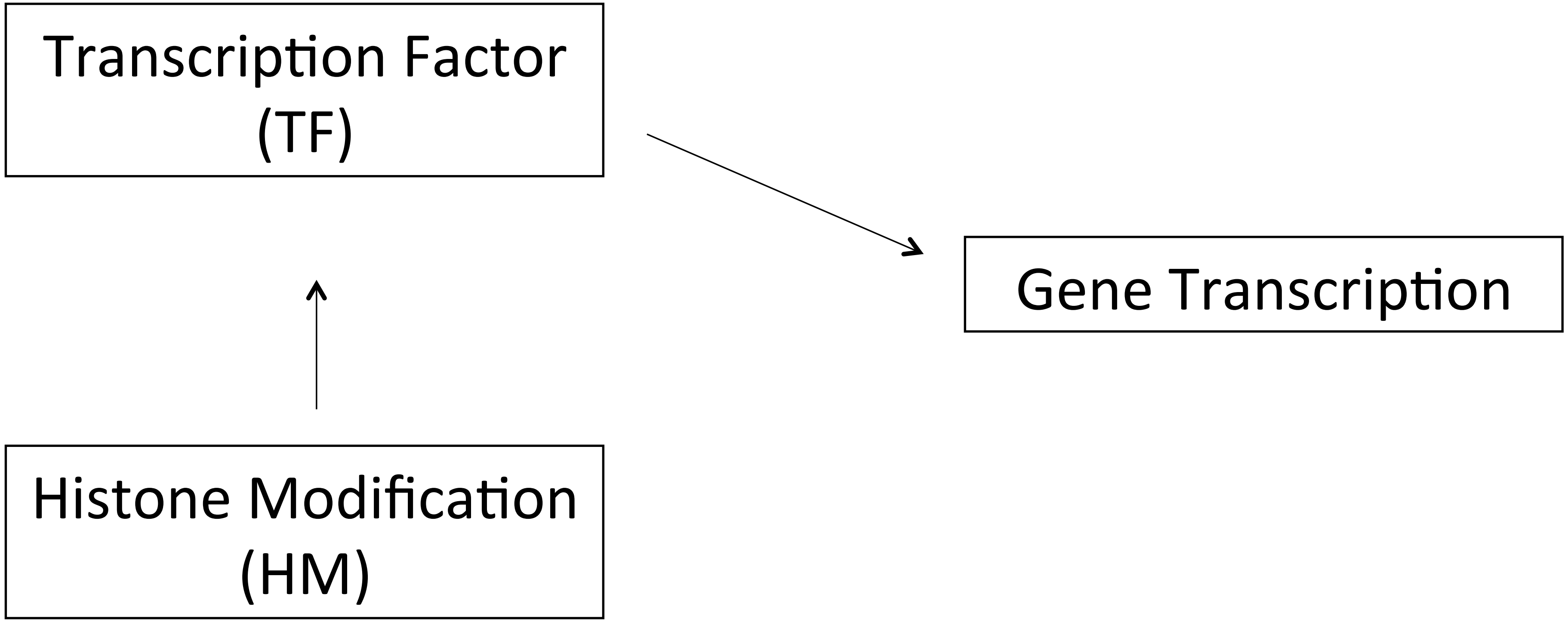


Many Important Data-Driven Computational Tasks



Histone Modification and Gene Transcription



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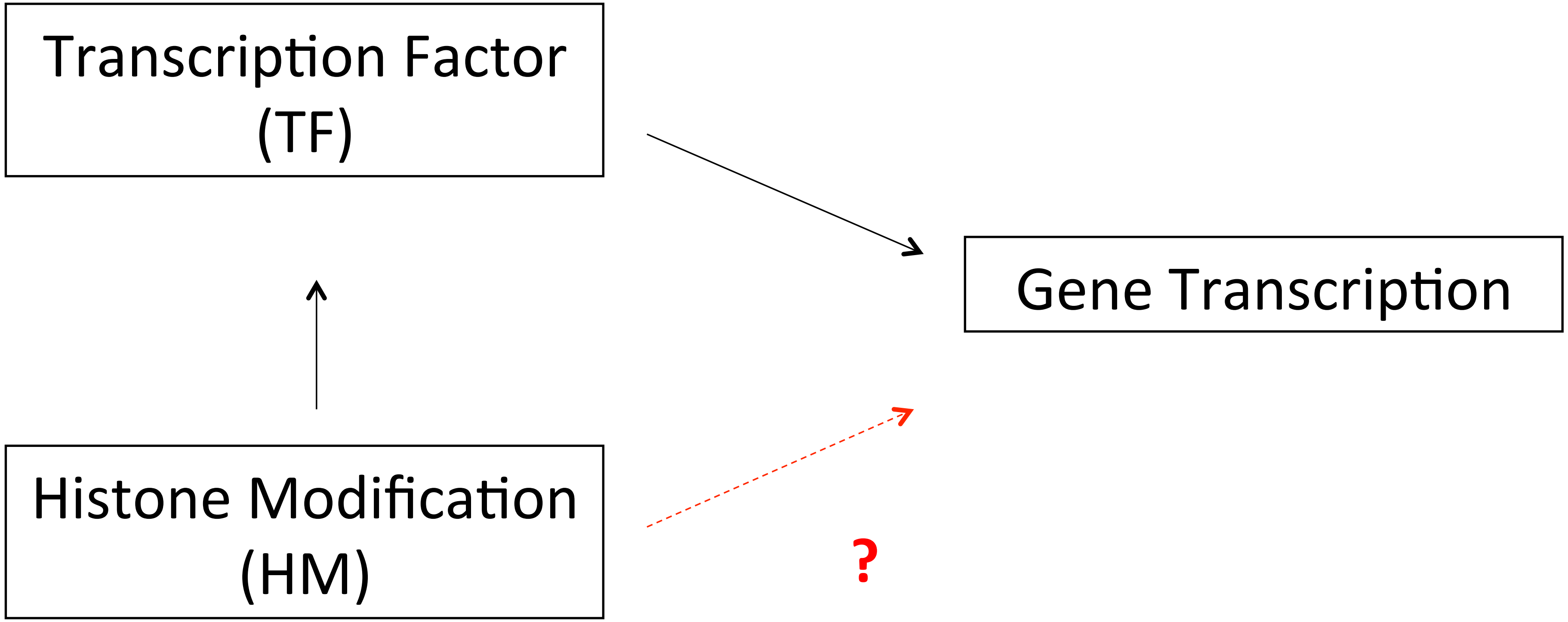


Histone Modification and Gene Transcription

Transcription Factor
(TF)

Gene Transcription

Histone Modification
(HM)

?

Why Studying [HM => Gene Expression] ?

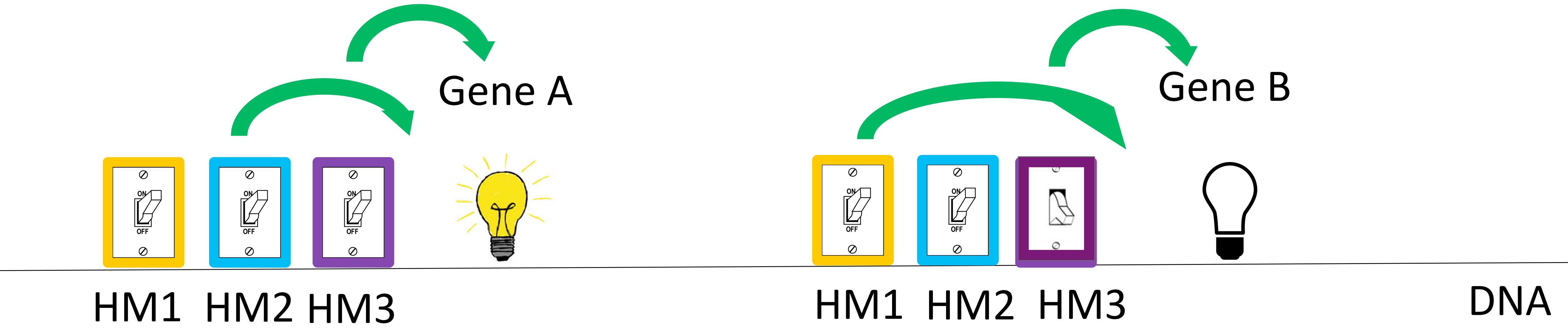
- Epigenomics:
  - Study of chemical changes in DNA and histones (without altering DNA sequence)
  - Inheritable and involved in regulating gene expression, development, tissue differentiation and suppression …

- Modification in DNA/histones (changes in chromatin structure and function)
  - => influence how easily DNA can be accessed by TF

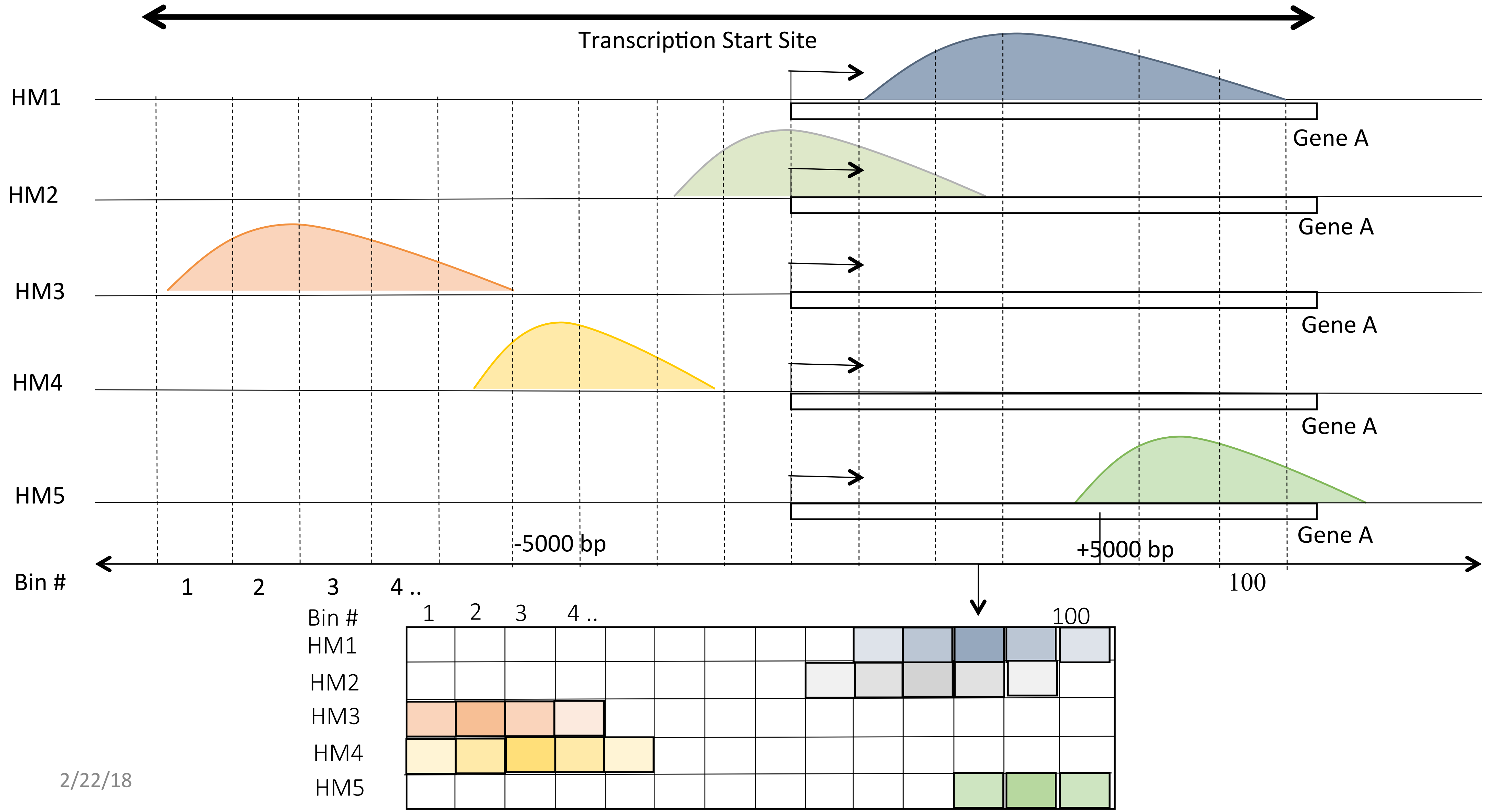
- Epigenome is dynamic
  - Can be altered by environmental conditions
  - Unlike genetic mutations, chromatin changes such as histone modifications are potentially reversible => Epigenome Drug for Cancer Cells?

Study how HMs influence genes?

~56 Cell Types

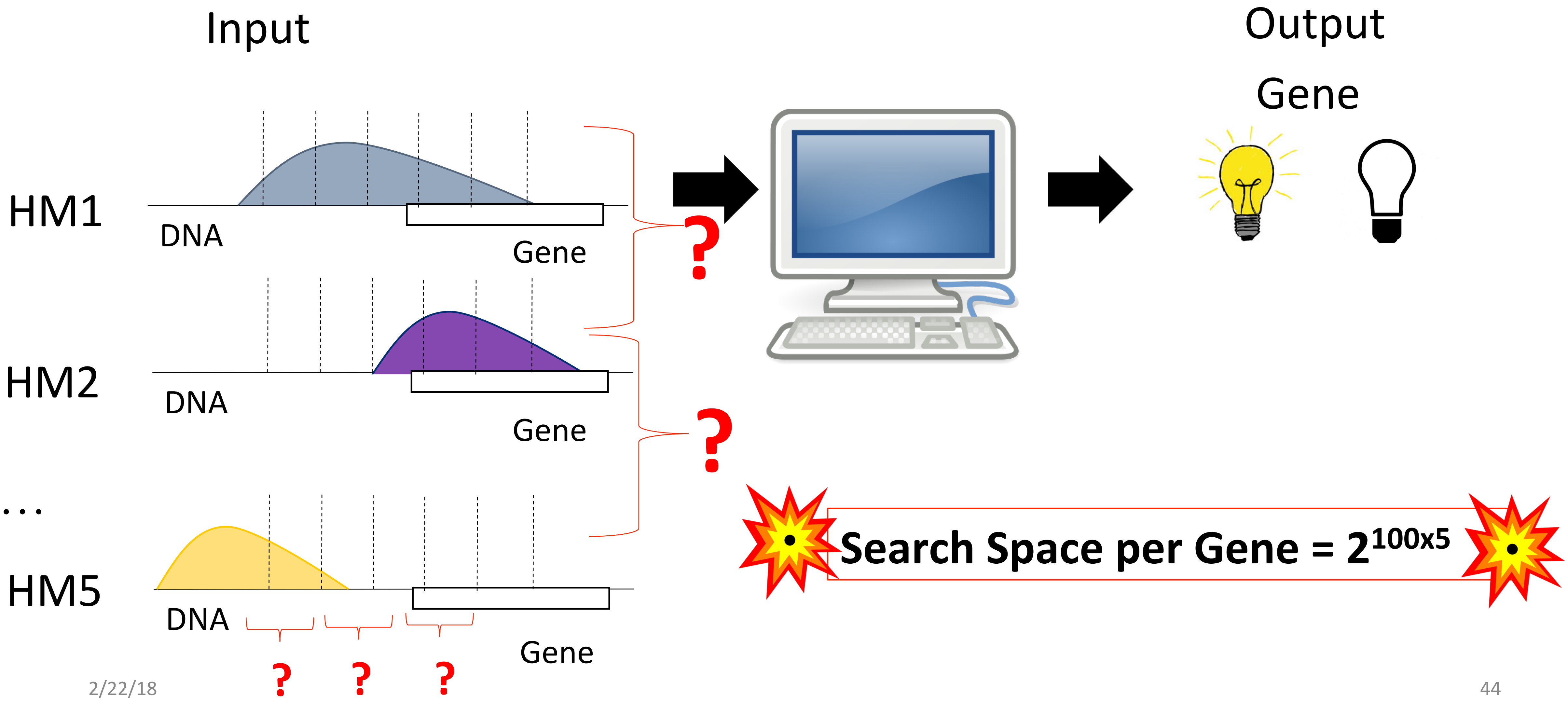


Input

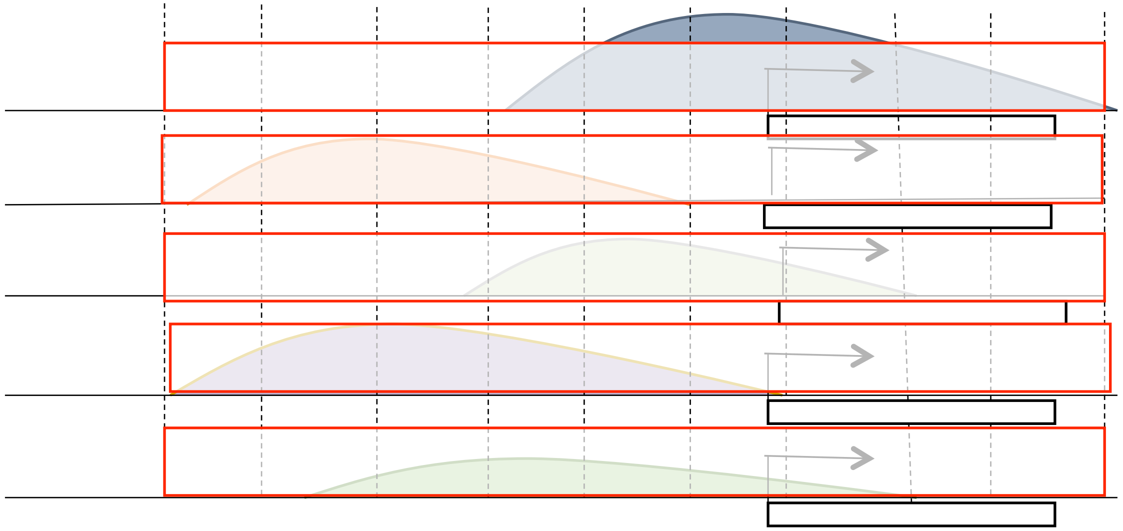


Transcription Start Site
HM1
HM2
HM3
HM4
HM5
Gene A
Gene A
Gene A
Gene A
Gene A
-5000 bp
+5000 bp
Bin #
1
2
3
4 ..
100
Bin #
1
2
3
4 ..
100
HM1
HM2
HM3
HM4
HM5

Computational Challenge



Related Work



Linear Regression,
SVM,
Random Forest

Gene Expression On/Off

[1] Karli´c, R. et al, Histone modification levels are predictive for gene expression. Proceedings of the National Academy of Sciences (2010)
[2] Cheng, C. et al, A statistical framework for modeling gene expression using chromatin features and application to modENCODE datasets. Genome Biology (2011)
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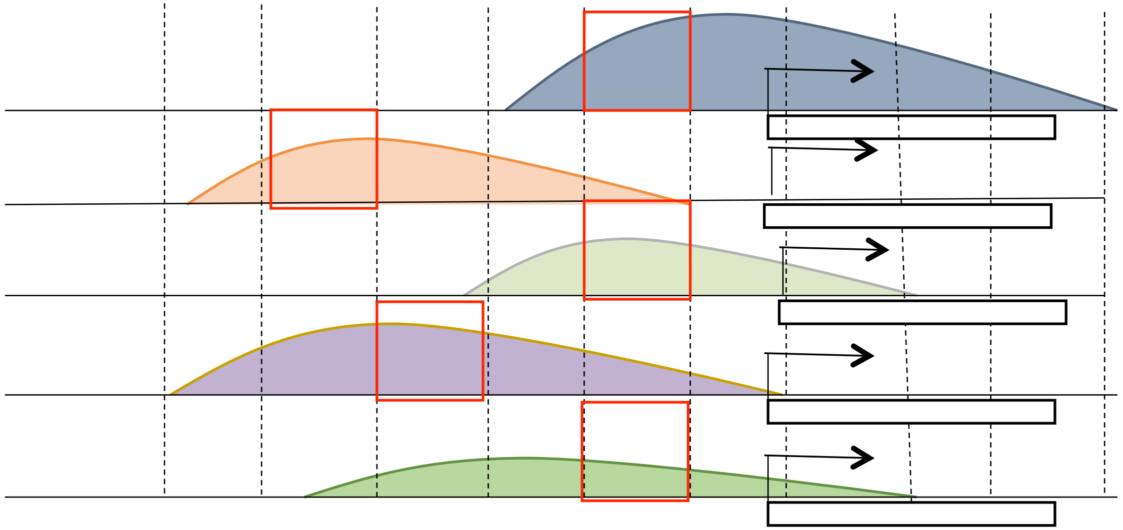
Related Work



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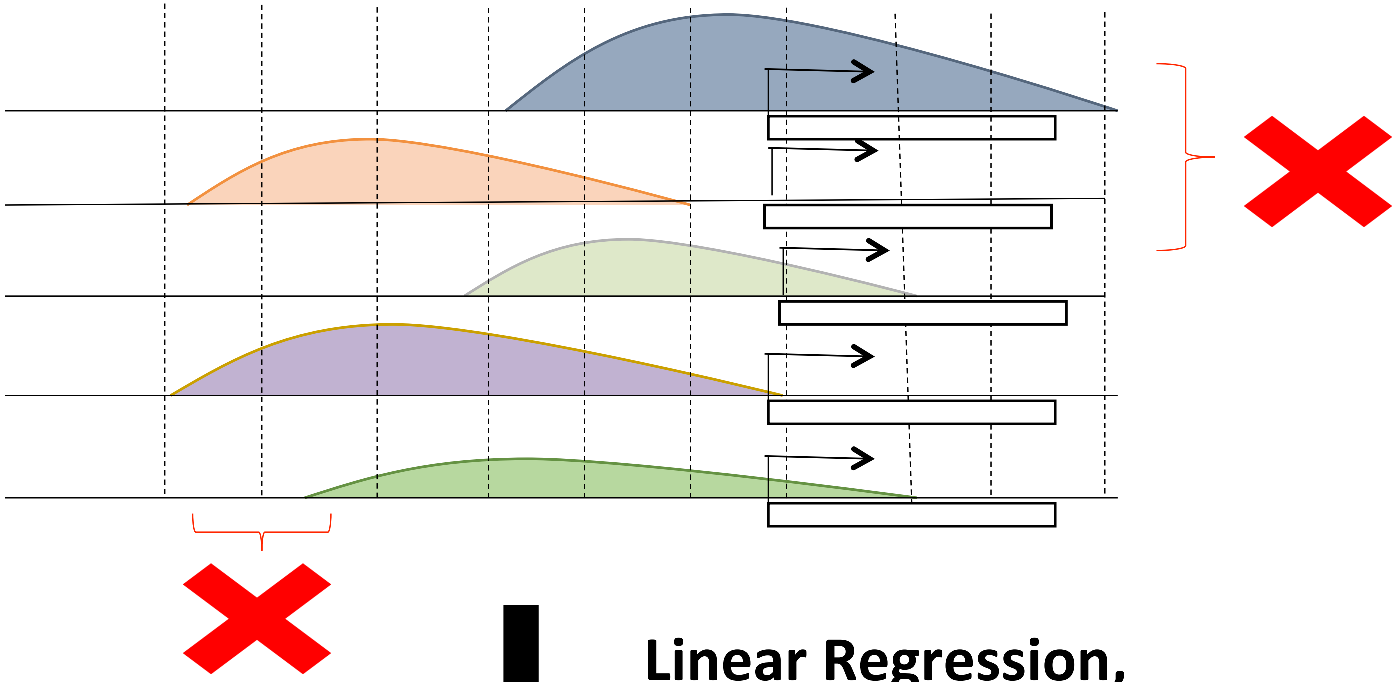
Drawback of Related Works



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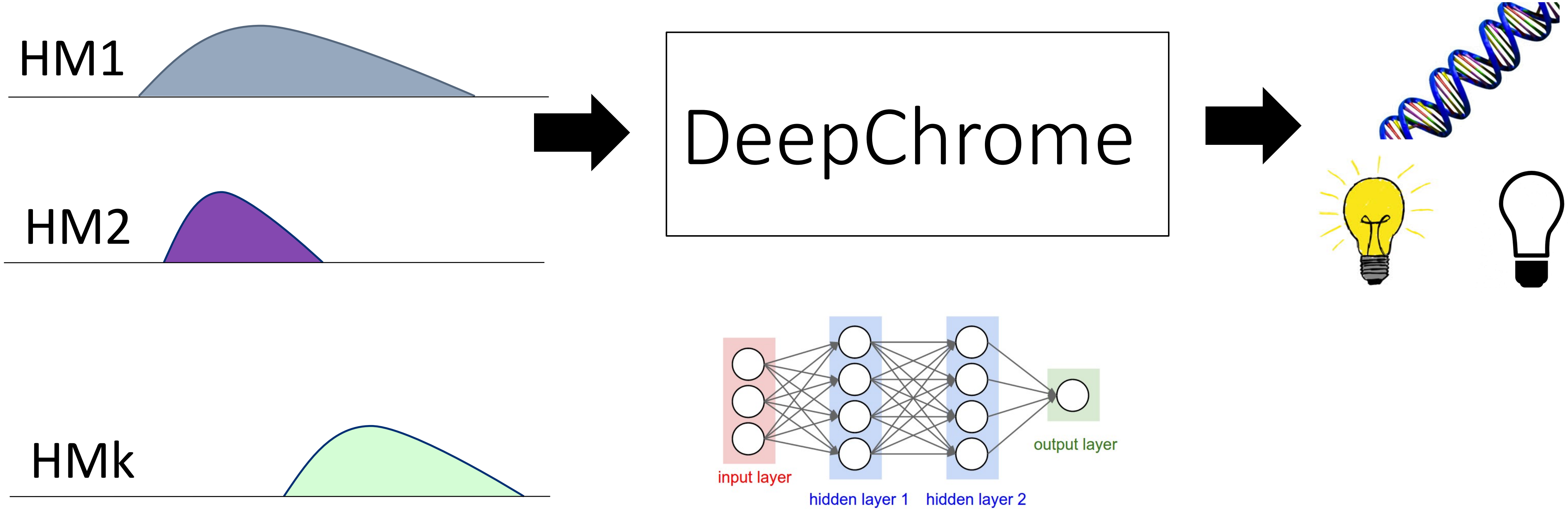
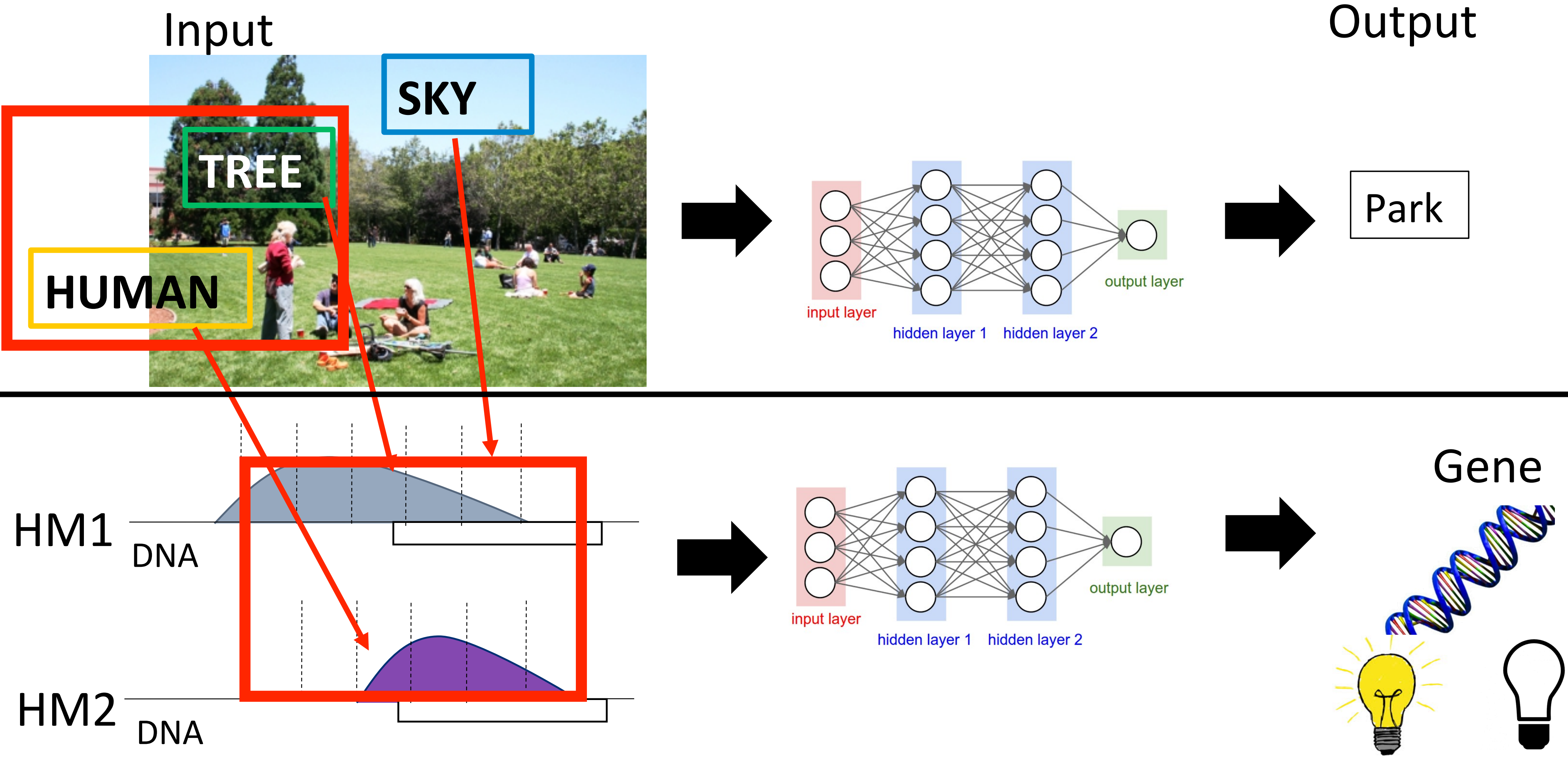
Our First Solution: DeepChrome : CNN



R. Singh, et al. "Deep-learning for predicting gene expression from histone modifications". *Bioinformatics.* (ECCB) (2016)

Our First Solution : CNN

HM signals occupy a local region and look similar in different parts?



Experimental Setup

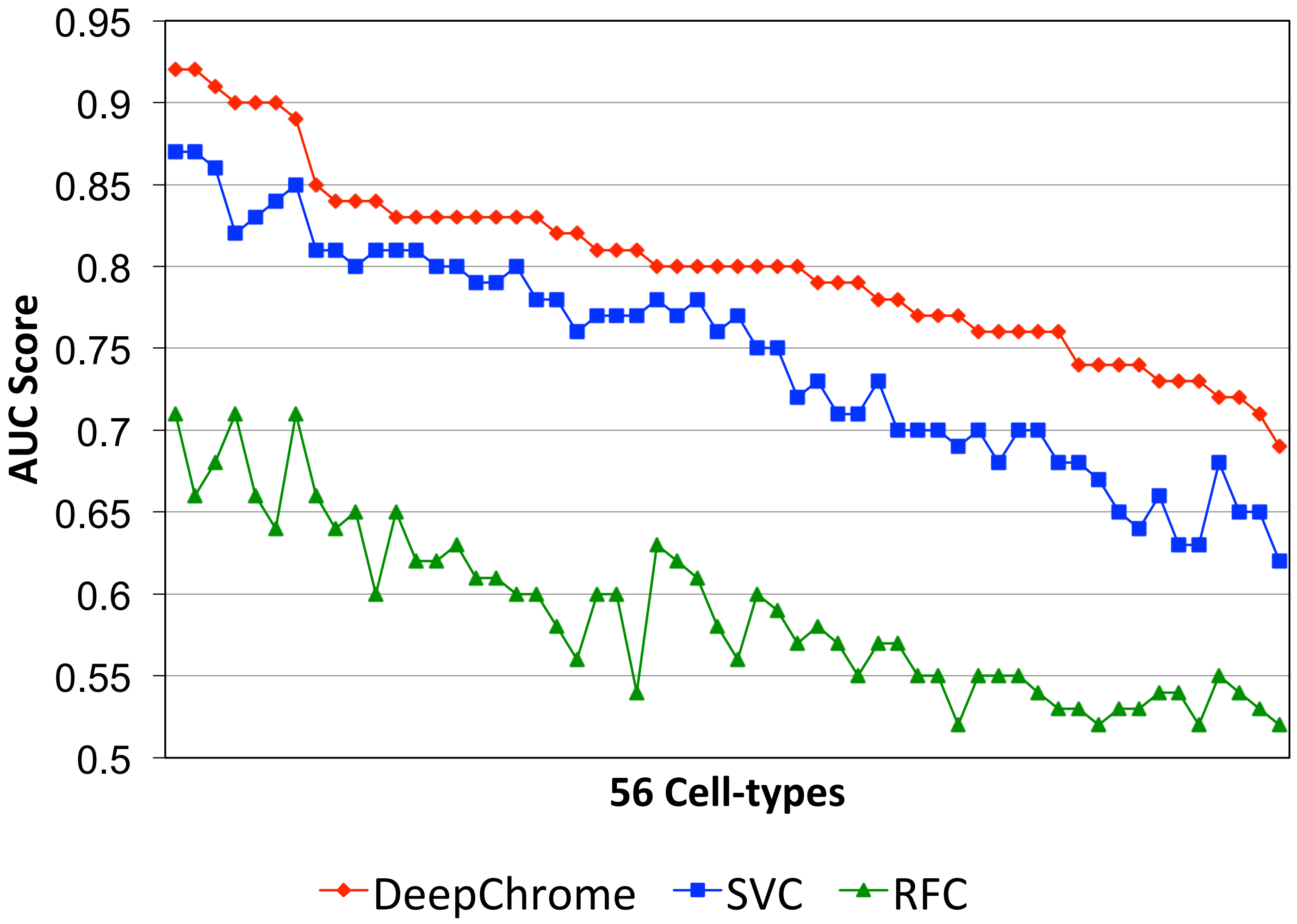
- Roadmap Epigenetics Project (REMC)
- **Cell-types:** 56
- **Input (HM):** ChIP-Seq Maps / 5 Tier-1 HMs

Histone Mark	Functional Category
H3K27me3	Repressor
H3K36me3	Structural Promoter
H3K4me1	Distal Promoter
H3K4me3	Promoter
H3K9me3	Repressor

- **Output (Gene Expression):** Discretized RNA-Seq
- **Baselines:** Support Vector Classifier (SVC) and Random Forest Classifier (RFC)

Training Set	Validation Set	Test Set
6601 Genes	6601 Genes	6600 Genes

Results: Accuracy



https://www.deepchrome.org

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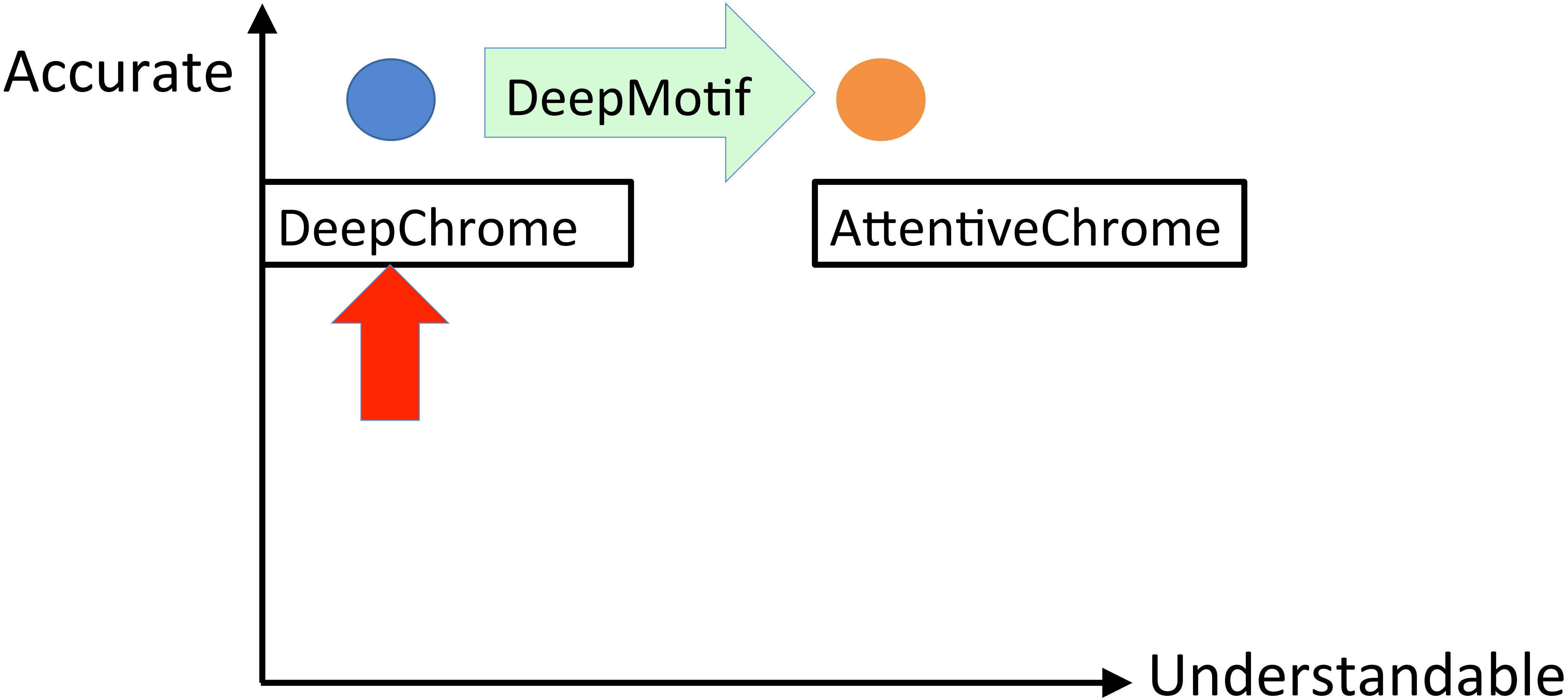
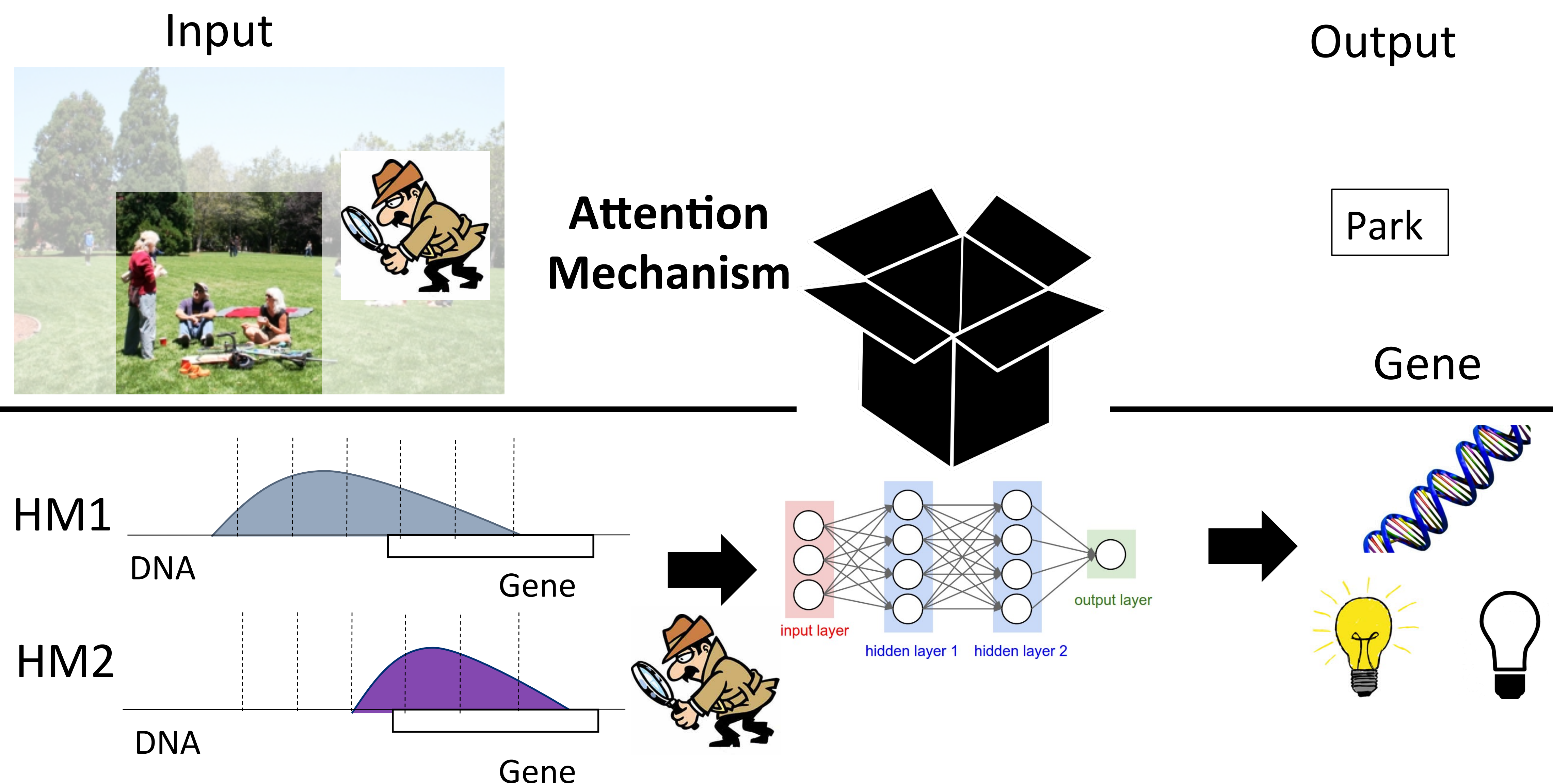


R. Singh, et al. Deep-learning for predicting gene expression from histone modifications". *Bioinformatics.* (2016)

Our 2nd Solution: Interpretability by Hierarchical Attention



Our 2nd Solution: Interpretability by Hierarchical Attention

Input

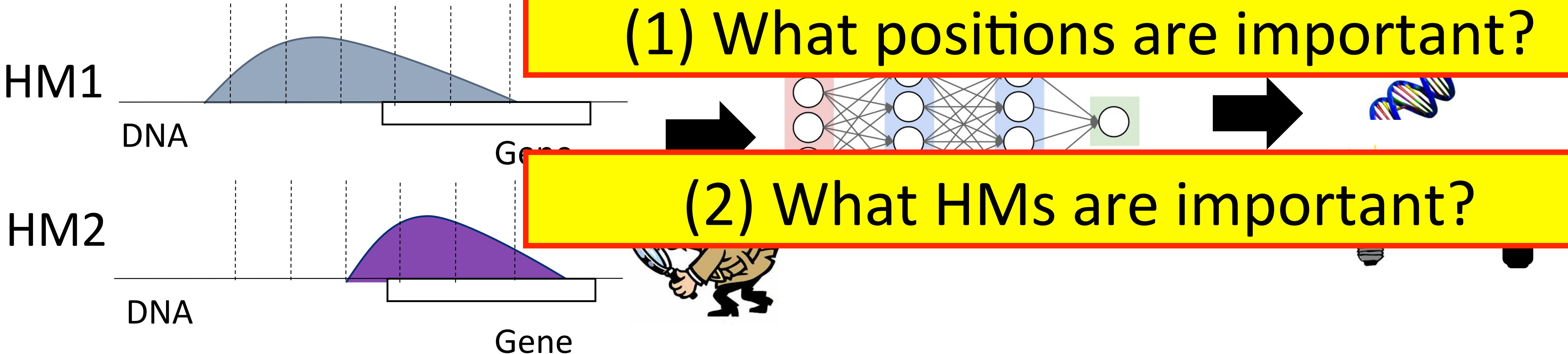
Output

Attention Mechanism

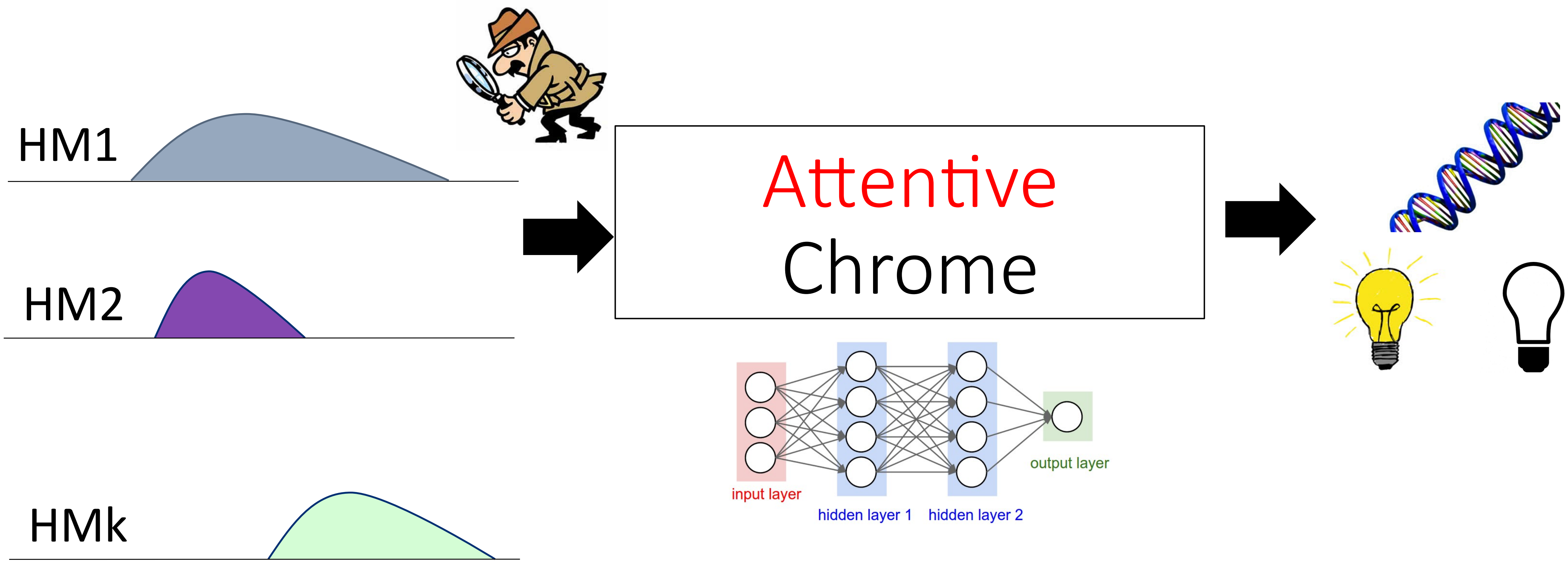
Park

Gene

(1) What positions are important?

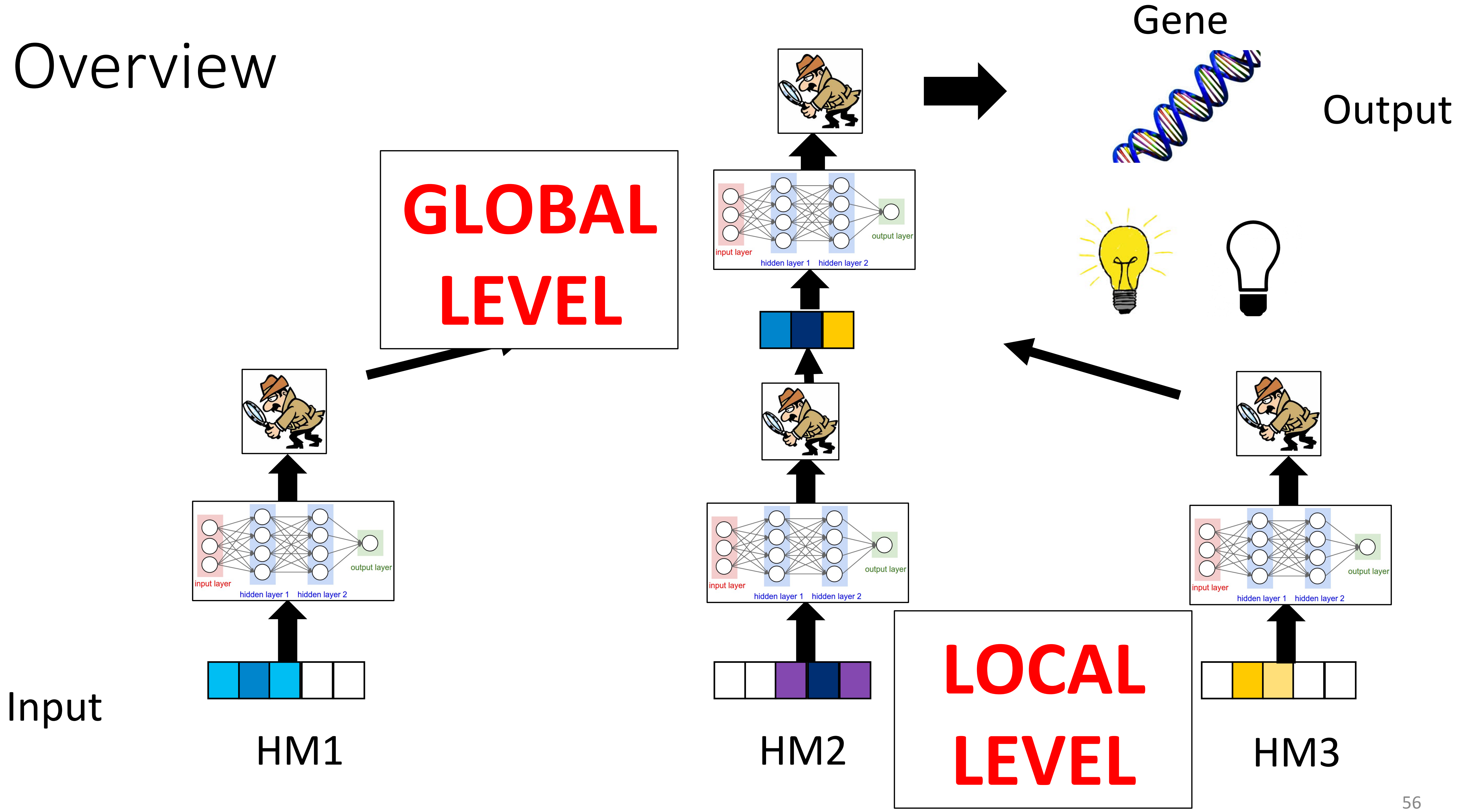


(2) What HMs are important?

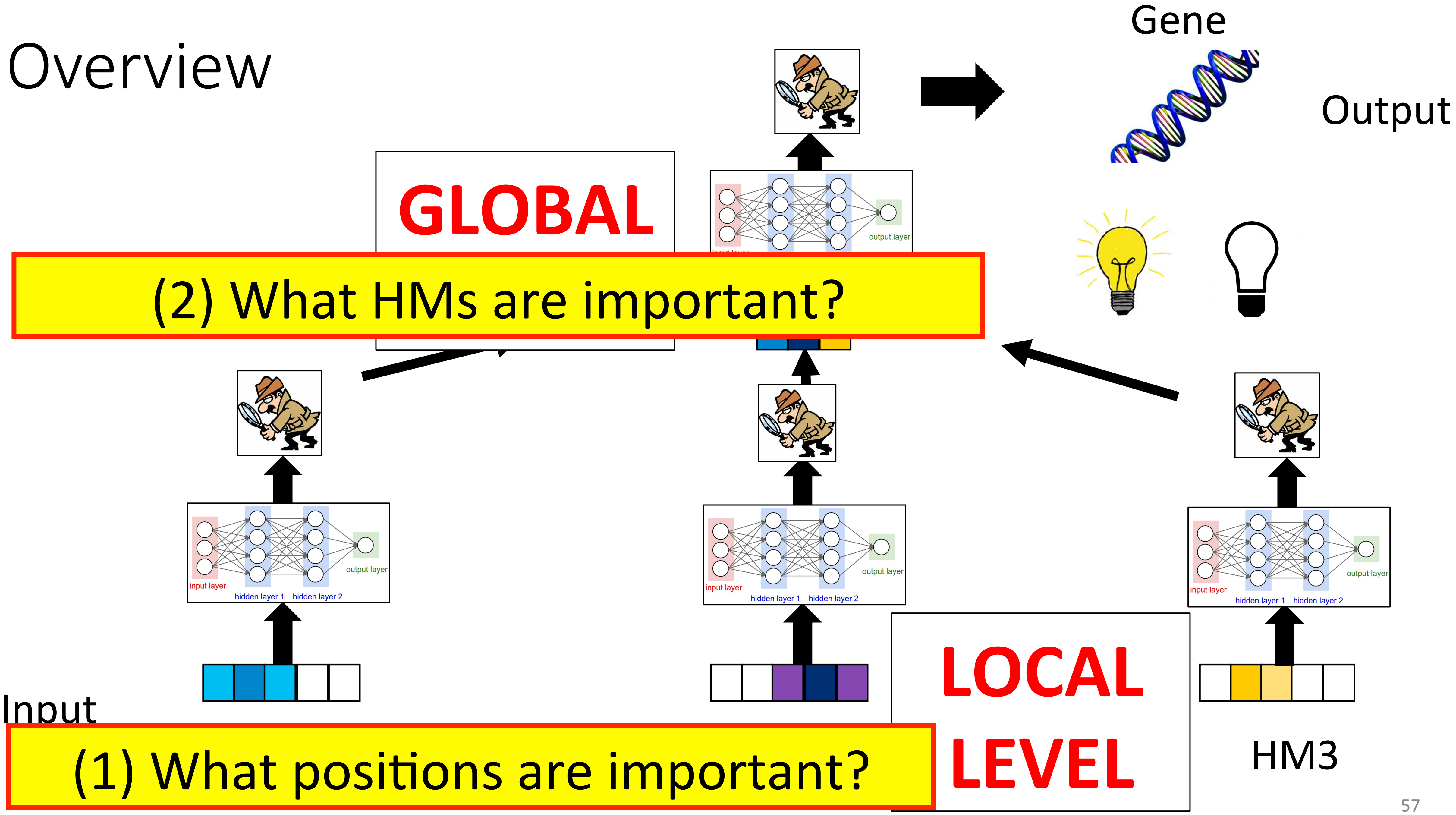


R. Singh, et al. "Attend and Predict: Understanding Gene Regulation by Selective Attention on Chromatin". *NIPS (2017)*

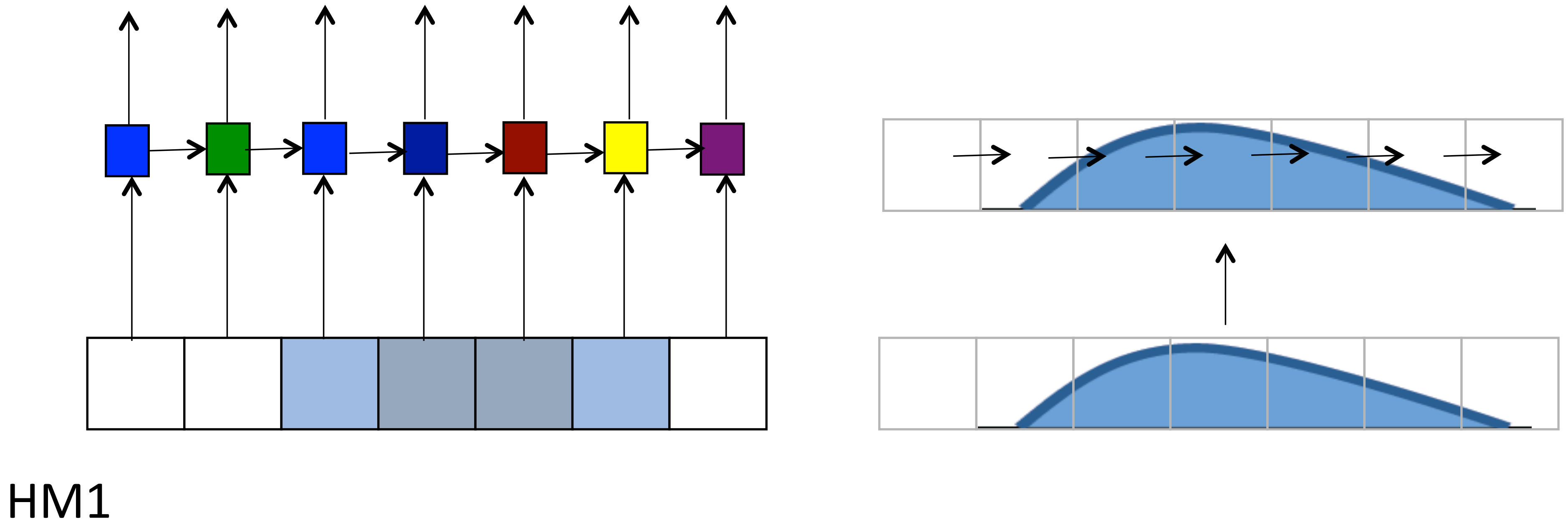
Overview


Gene
Output
GLOBAL LEVEL
input layer
hidden layer 1
hidden layer 2
output layer
LOCAL LEVEL
Input
HM1
HM2
HM3

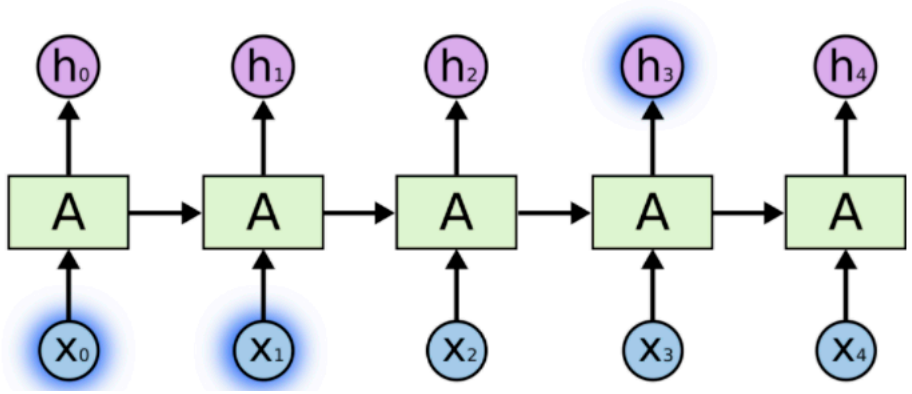
Overview


Gene
Output
GLOBAL
(2) What HMs are important?
output layer
input layer
hidden layer 1
hidden layer 2
Input
(1) What positions are important?
LOCAL
LEVEL
HM3

Multiple Recurrent Neural Networks (Hierarchical RNNs) to model each HM and the Combination of all HMs : for example on HM1



Using Attention to Select RNN per-unit outputs



$$\boxed{h_t} = \boxed{f_W}(\boxed{h_{t-1}}, \boxed{x_t})$$

new state

some function with parameters W

old state

input vector at some time step

$$\boldsymbol{\alpha}_t^j = \frac{exp(\mathbf{W}_b \mathbf{h}_t^j)}{\sum_{i=1}^{T} exp(\mathbf{W}_b \mathbf{h}_i^j)}$$

W_b is learned

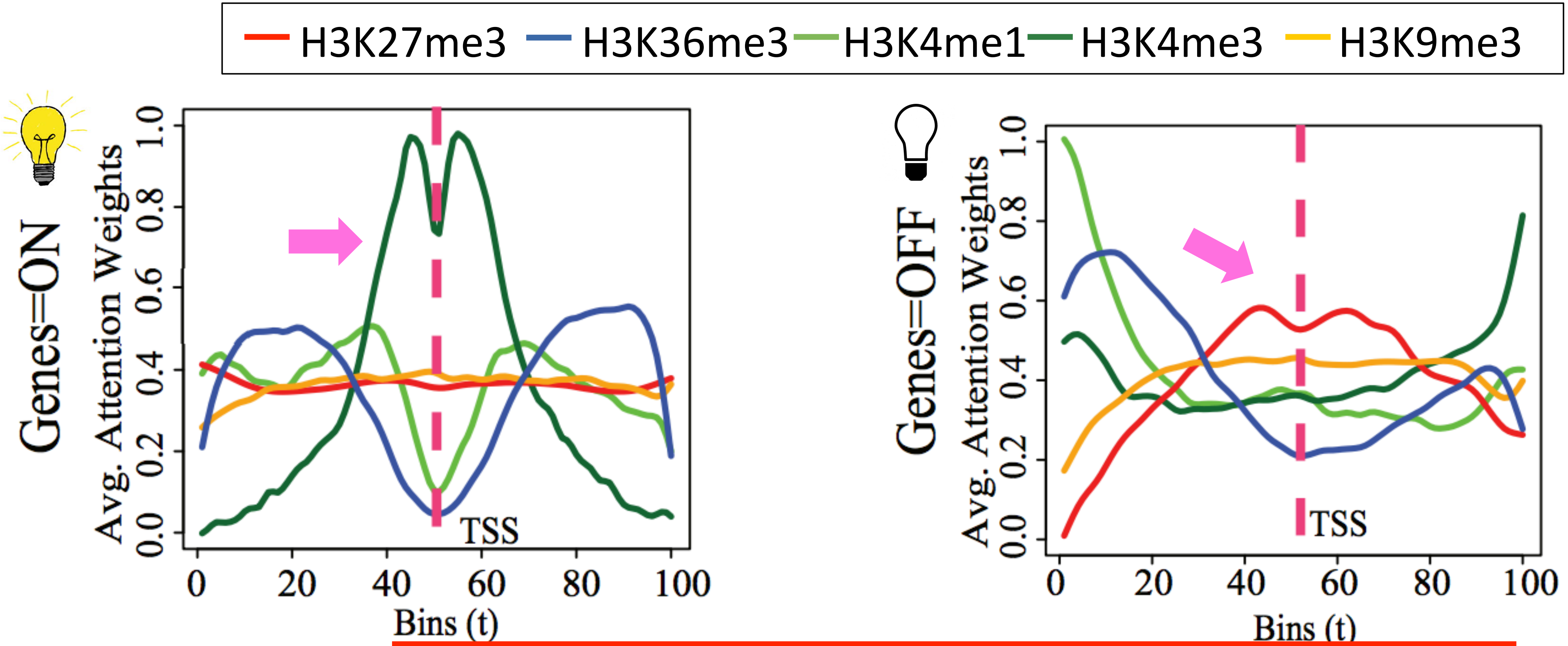
Image Credits from Christopher Olah

Results

	Baselines		Our Model
Models	**DeepChrome (CNN)**	**RNN**	**AttentiveChrome**
Mean	0.8008	0.8052	**0.8115**
Median	0.8009	0.8036	**0.8123**
Max	**0.9225**	0.9185	0.9177
Min	0.6854	0.7073	**0.7215**
Improvement over DeepChrome (out of 56 cell types)		36	**49**

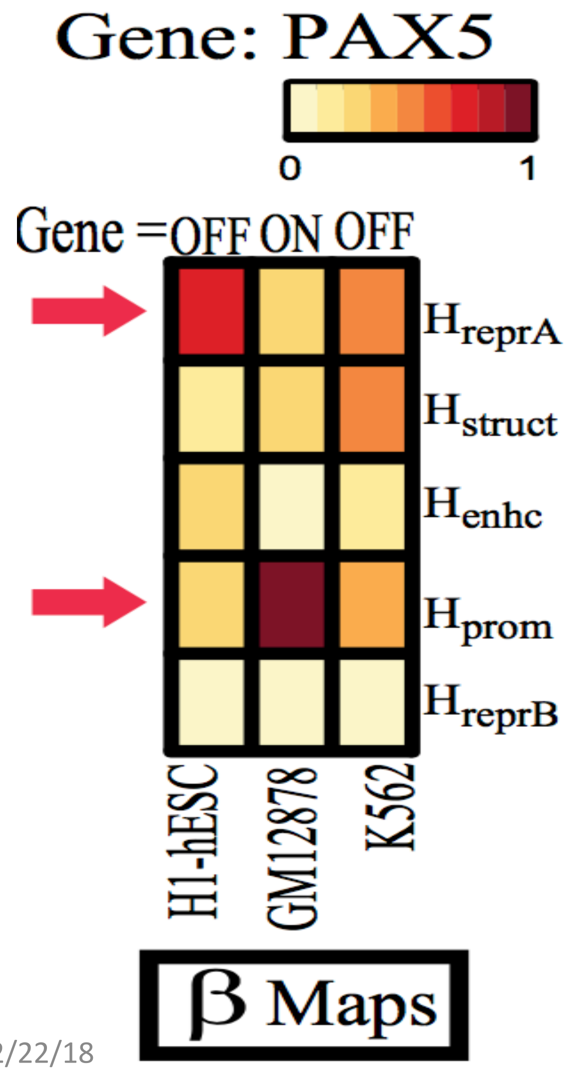
Results: Local level attention

CELL TYPE: GM12878 (Blood Cell)



(1) What positions are important?

Results: Global level attention



- An important differentially regulated gene (PAX5) across three blood lineage cell types:
  - H1-hESC (stem cell),
  - GM12878 (blood cell),
  - K562 (leukemia cell).
- Trend of its global weights (beta) Verified through the literature.

(2) What HMs are important?

Validation of Attention Weights (using one extra HM signals)

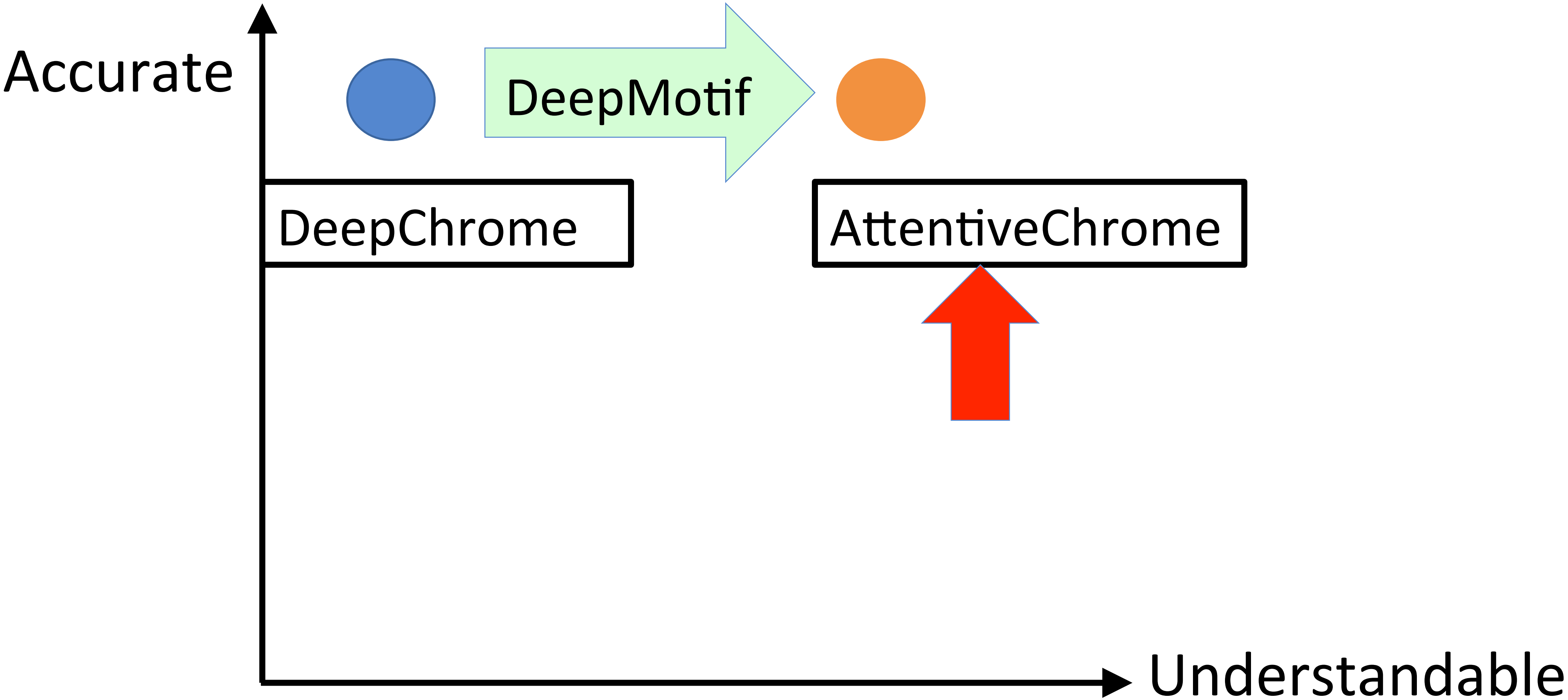
Table 3: Pearson Correlation values between weights assigned for H_{prom} (active HM) by different visualization techniques and H_{active} read coverage (indicating actual activity near "ON" genes) for predicted "ON" genes across three major cell types.

Viz. Methods	H1-hESC	GM12878	K562
α Map (LSTM-α)	0.8523	**0.8827**	**0.9147**
α Map (LSTM-α, β)	**0.8995**	0.8456	0.9027
Class-based Optimization (CNN)	0.0562	0.1741	0.1116
Saliency Map (CNN)	0.1822	-0.1421	0.2238

- Additional signal - H3K27ac (H-Active) from REMC
- Average local attention weights of gene=ON correspond well with H-active
- Indicating AttentiveChrome is focusing on the correct bin positions

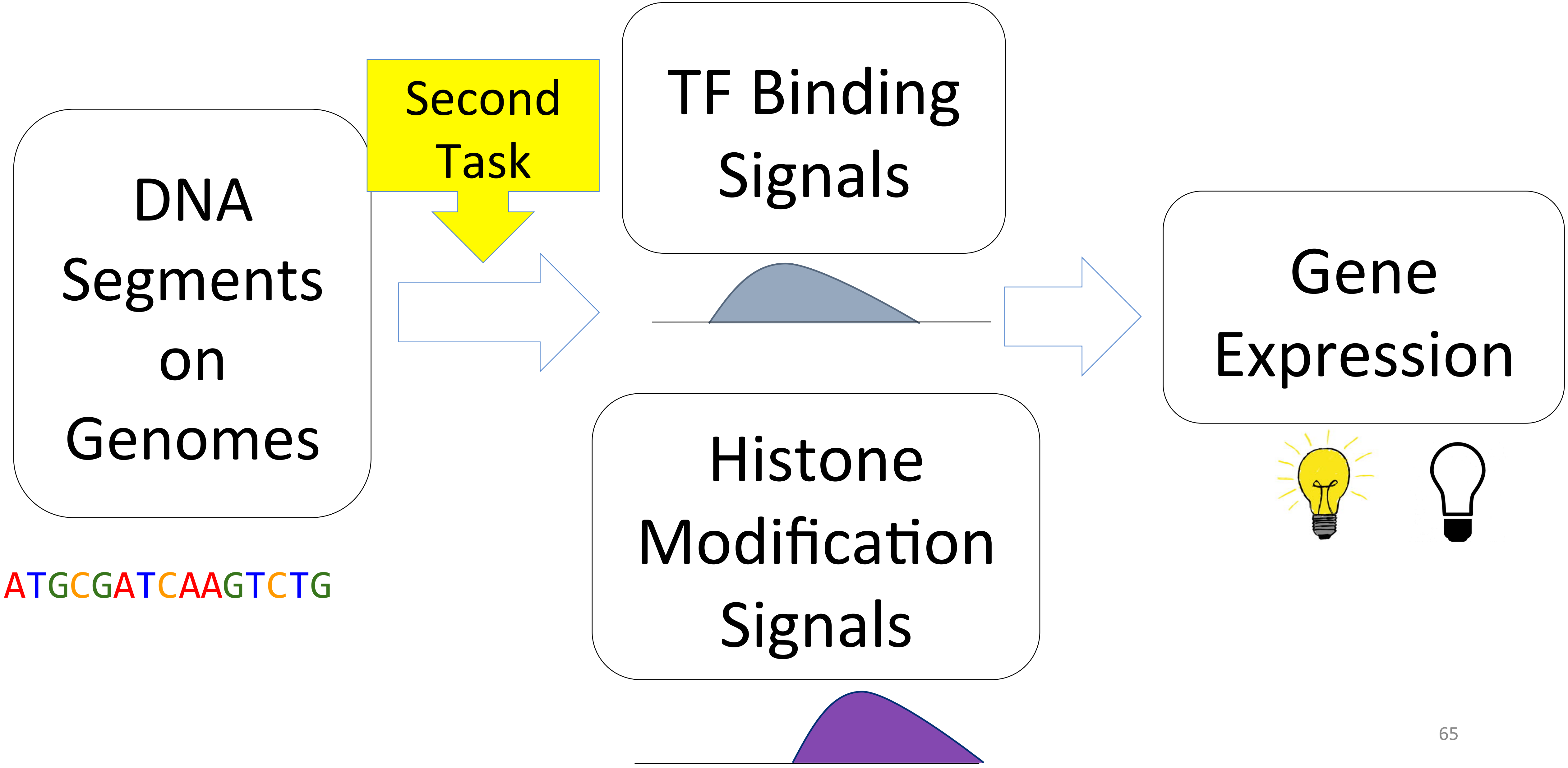
https://www.deepchrome.org

Summary of our tools

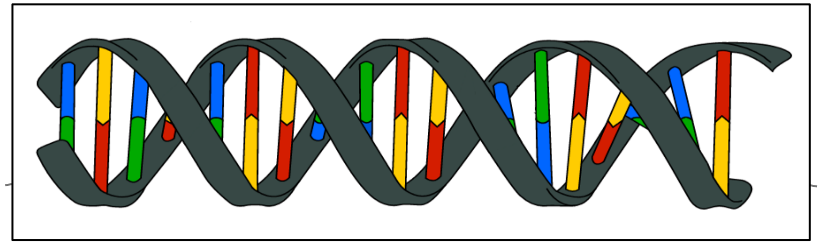


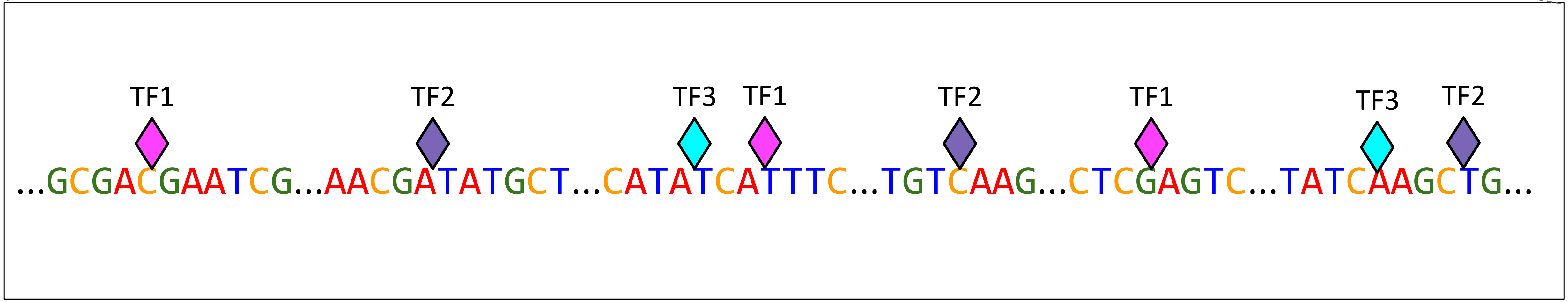
R. Singh, et al. "Attend and Predict: Understanding Gene Regulation by Selective Attention on Chromatin". *NIPS (2017)*

Many Important Data-Driven Computational Tasks



Task: Sequence Based Functional Annotation Tasks



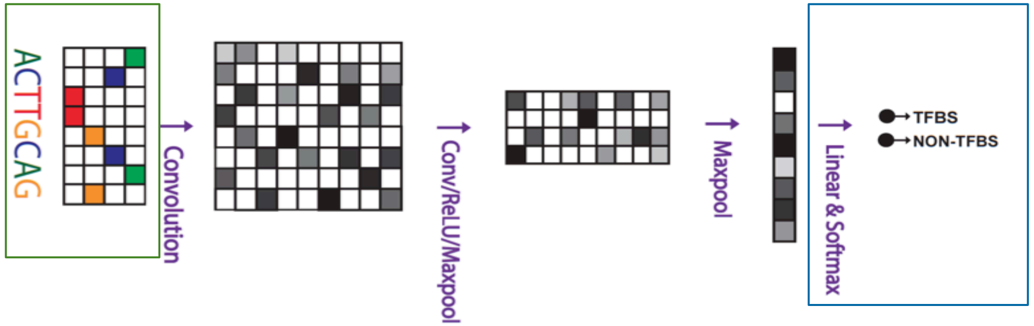


Literature: Various DNN Tools

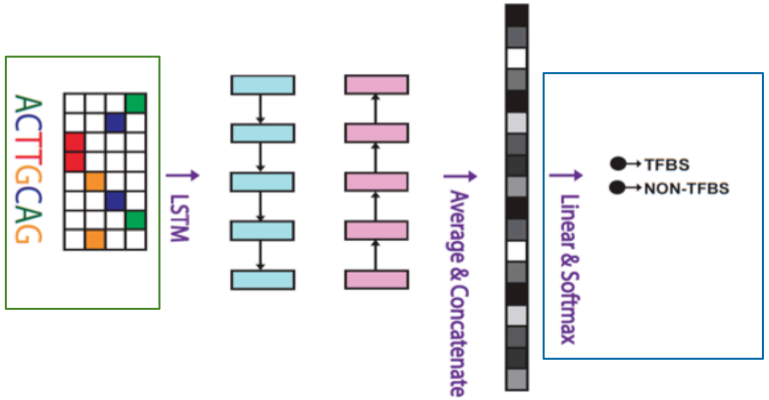
Input Sequence

Probability of Binding Site

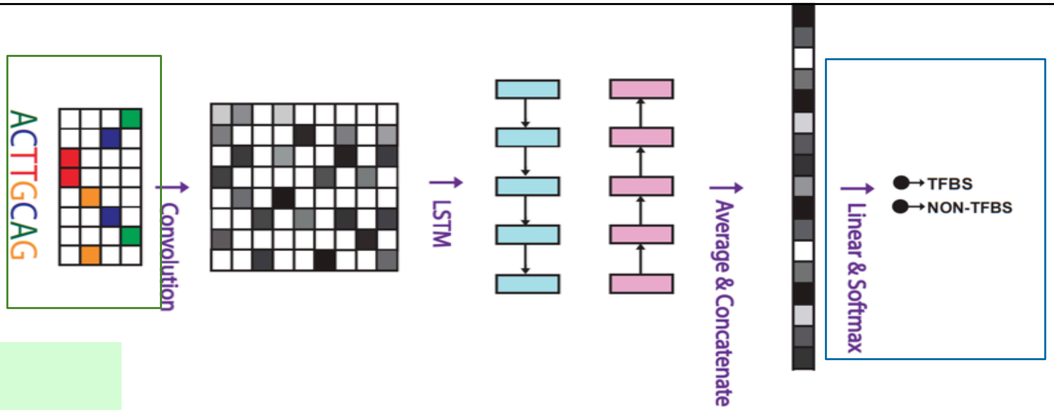
1. **Convolutional (CNN)**



2. **Recurrent (RNN)**



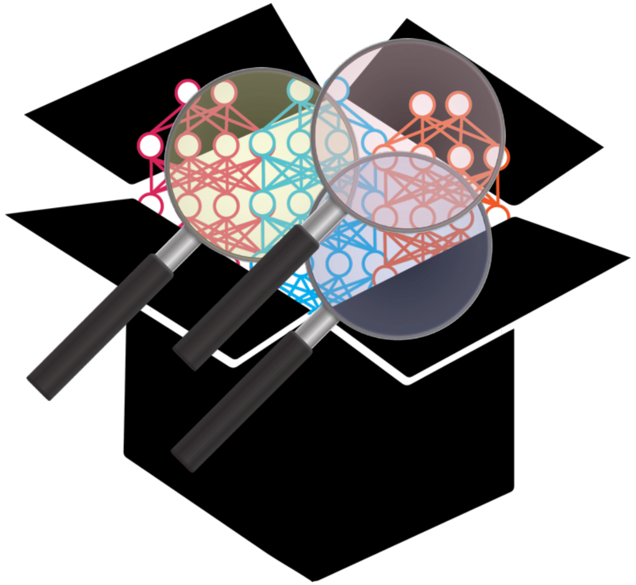
3. **Convolutional-Recurrent (CNN-RNN)**

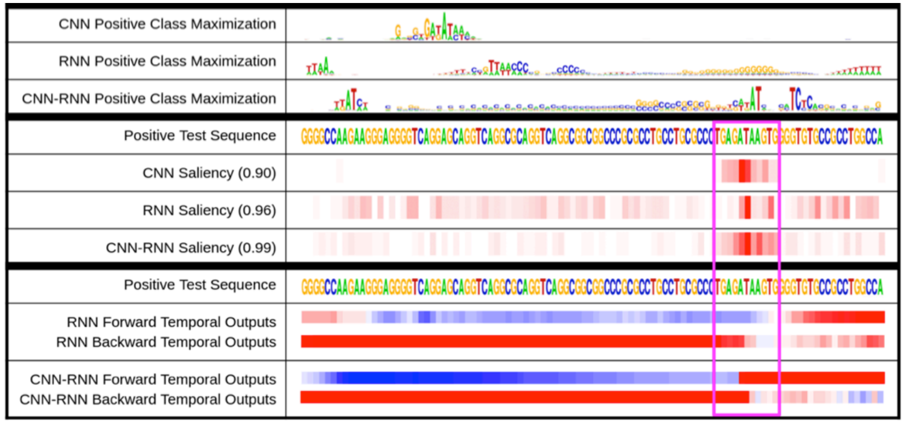


DeepSEA, DeepBind, BASSET, DanQ, ….

Deep Motif Dashboard: Understand DNNs by Post Analysis

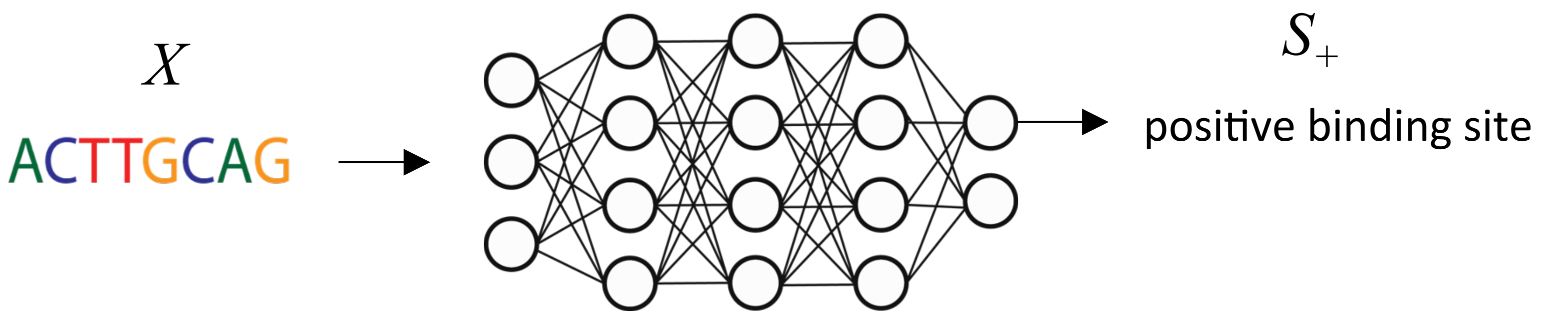
Lanchantin, Singh, Wang & Qi - Pacific Symposium on Biocomputing, 2017





1. Saliency Maps
2. Temporal Output Values
3. Class Optimization

1. Saliency Map

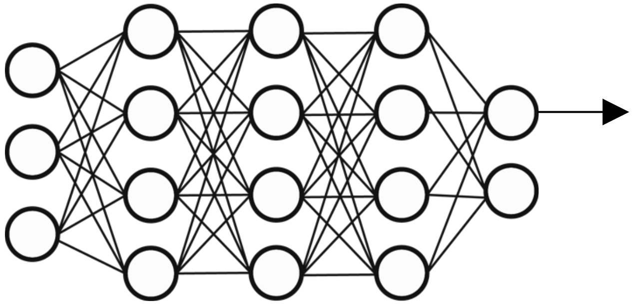


Which nucleotides are most important for my current-sample classification?

1. Saliency Map

X_0

ACTTGCAG $\longrightarrow$



S_+

positive binding site

$$w = \frac{\partial S_+}{\partial X}\bigg|_{X_0} = \text{“}\textit{saliency map}\text{”}$$

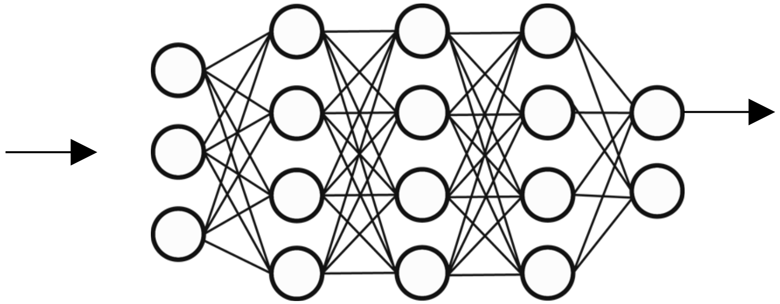
Quiz: What is gradient?

[Deep Inside Convolutional Networks: Visualising Image Classification Models and Saliency Maps](), ICLR 2013

1. Saliency Map

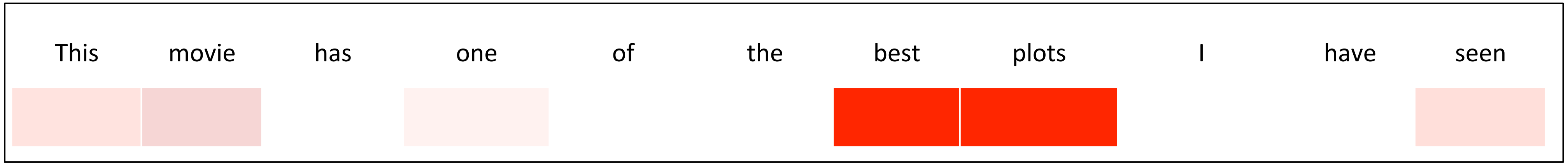
X

This movie has one of the best plots I have seen



S_+

Positive sentiment

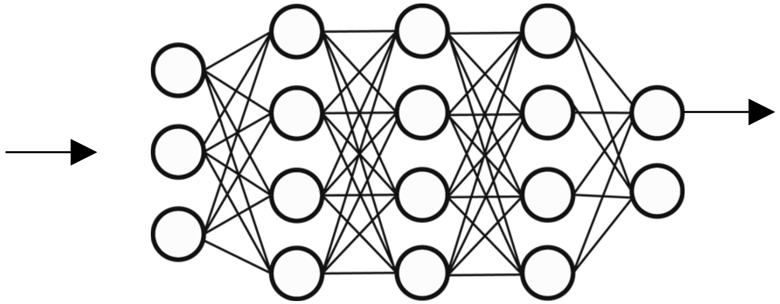


= important for classification

1. Saliency Map

X

ACTTGCAG



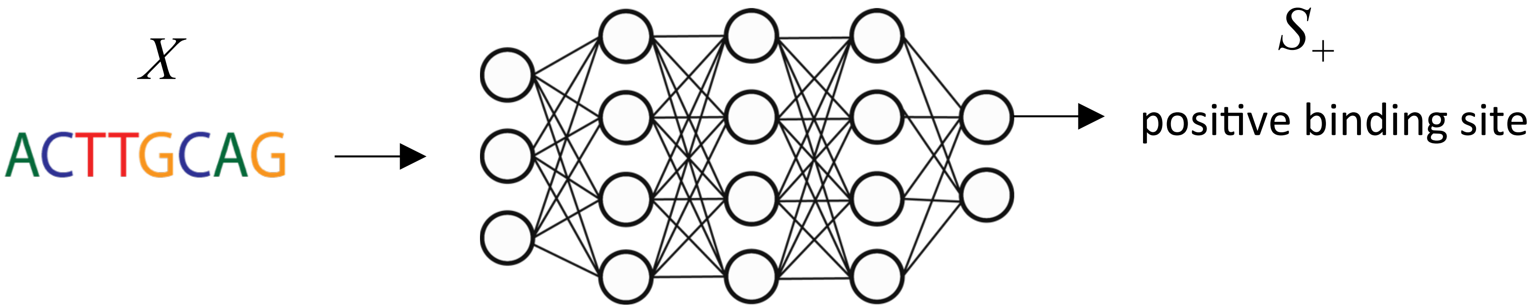
S_+

positive binding site

Positive Test Sequence	TGCTCGCATCCTATTGGCCACGTTAGTCACATGGCCCCACCTGGCTGCAAAGCACGCTGGGAAACGTAGTCTTTCTT
Saliency Map	

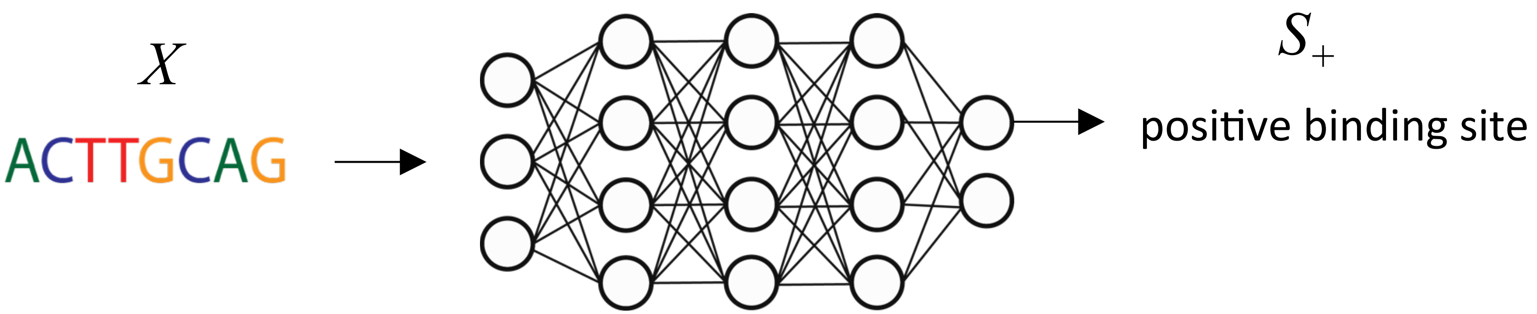
= important nucleotide for prediction

2. Temporal Output Values



What are the model's predictions at each timestep of the DNA sequence?

2. Temporal Output Values

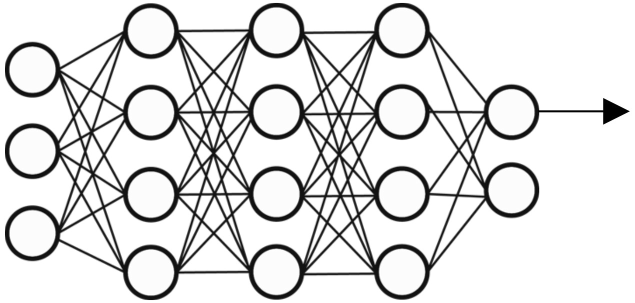


Check the RNN's prediction scores when we vary the input of the RNN starting from the beginning to the end of a sequence.

2. Temporal Output Values

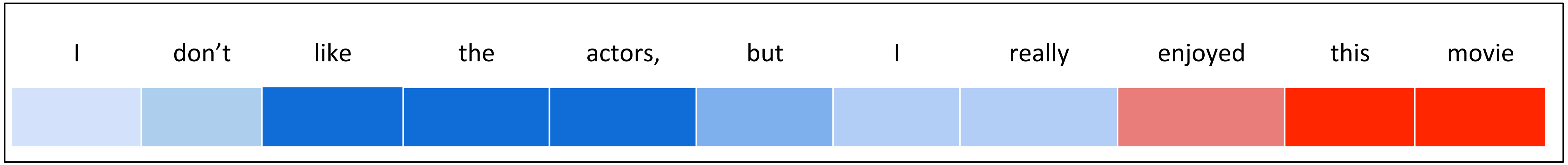
X

I don't like the actors, but I really enjoyed this movie



S_+

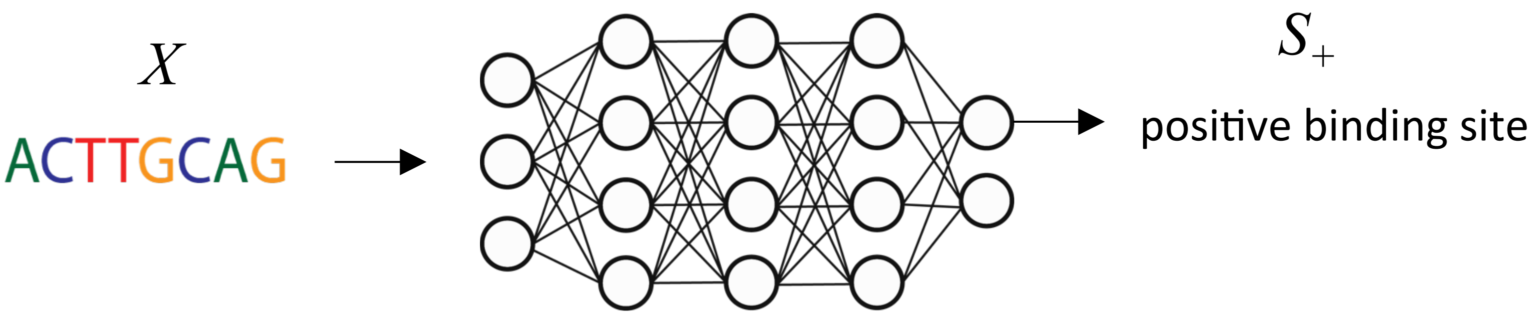
positive sentiment



= negative sentiment

= positive sentiment

2. Temporal Output Values

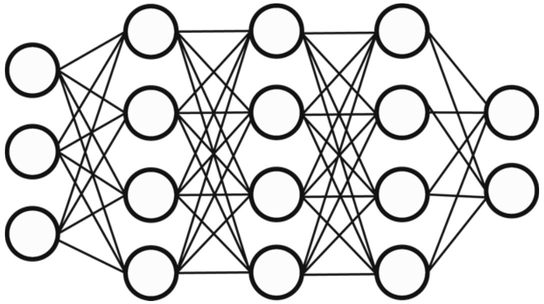


Positive Test Sequence	CTTCTGCTCGCATCCTATTGGCCACGTTAGTCACATGGCCCCACCTGGCTGCAAAGCACGCTGGGAAACGTAGTCTTTCTT
RNN Forward Output	
RNN Backward Output	

= negative binding site prediction   = positive binding site prediction

3. Class Optimization

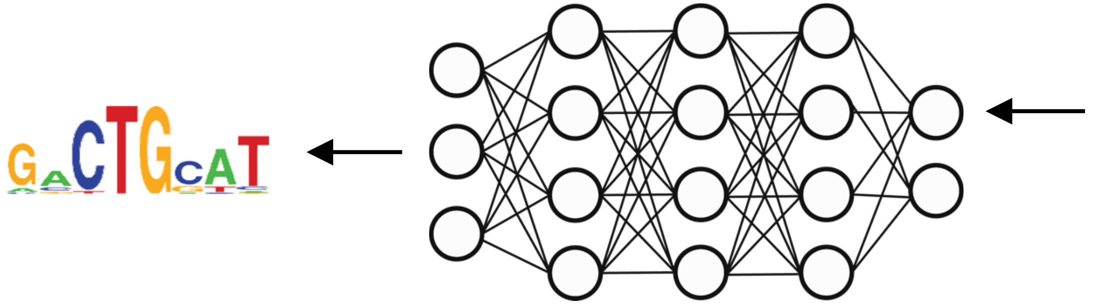
?



positive binding site for TF “CBX3”

For a particular TF, what does the optimal binding site sequence look like?

3. Class Optimization

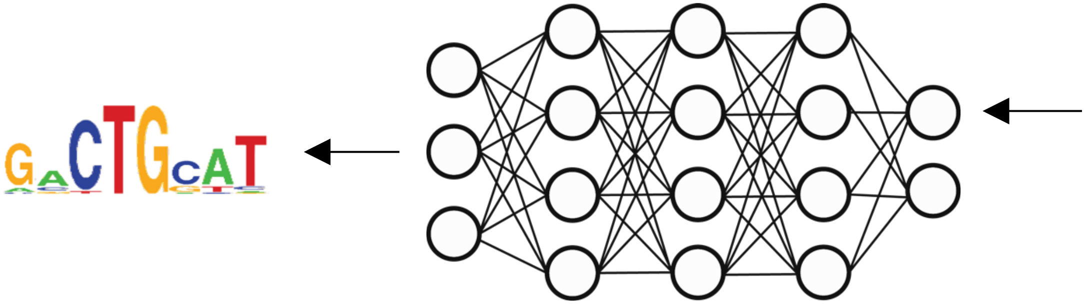


$$\arg\max_{X} S_{+}(X) + \lambda \|X\|_2^2$$

Where X is the input sequence and the score S_+ is probability of sequence X being a positive binding site

[Deep Inside Convolutional Networks: Visualising Image Classification Models and Saliency Maps](), ICLR 2013

3. Class Optimization



positive binding site for TF “CBX3”

Optimal binding site for TF “CBX3”	

Visualization Methods

Sequence Specific

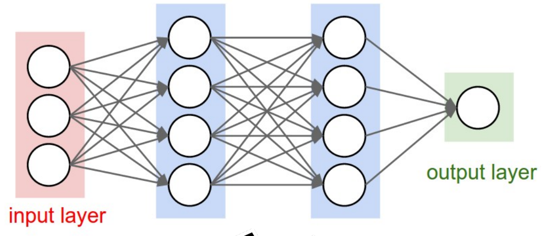
1. Saliency Maps
2. Temporal Output Values

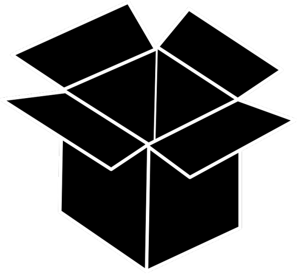
TF Specific

3. Class Optimization

code available at: **deepmotif.org**

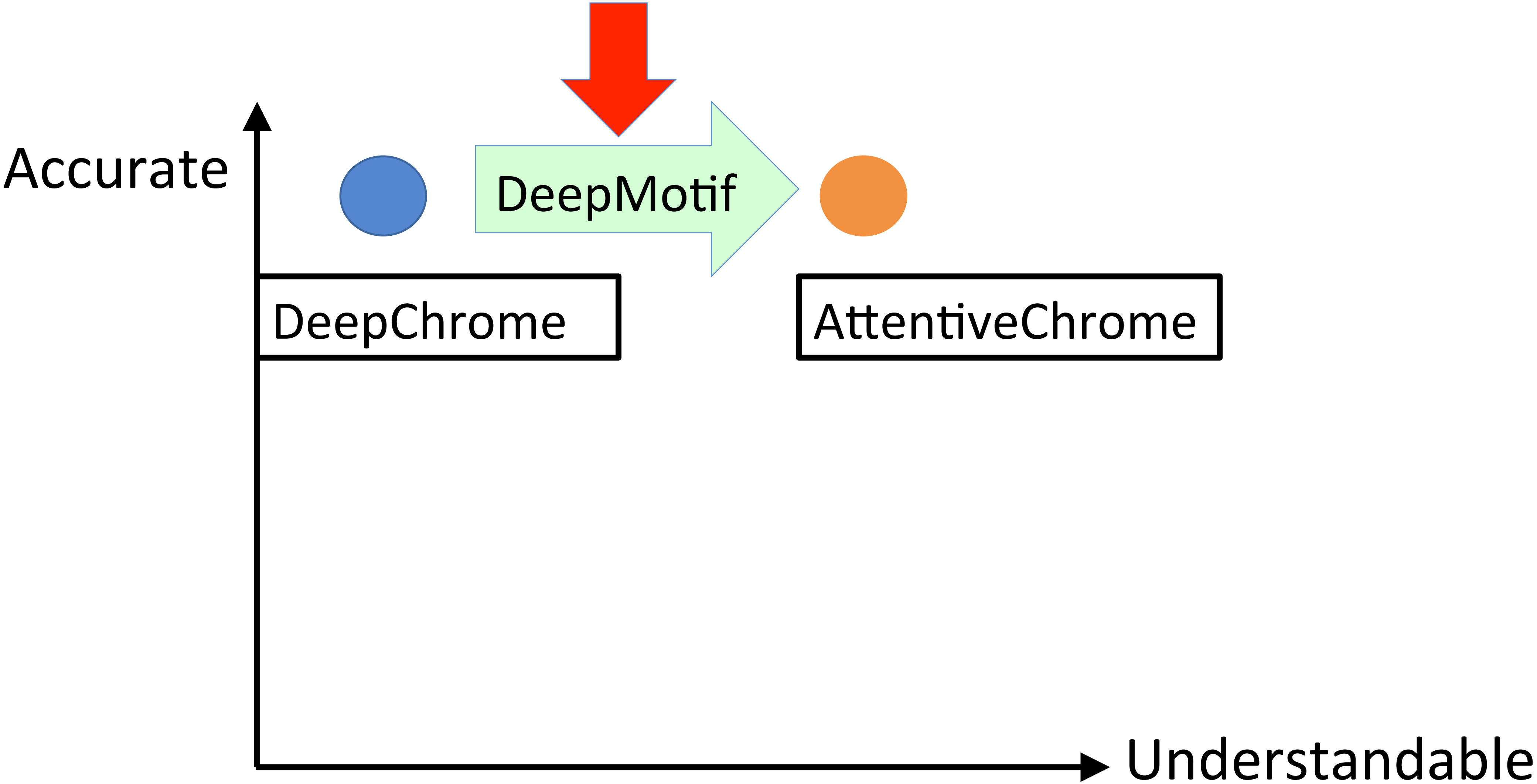
Related Work to Post-Understand DNN



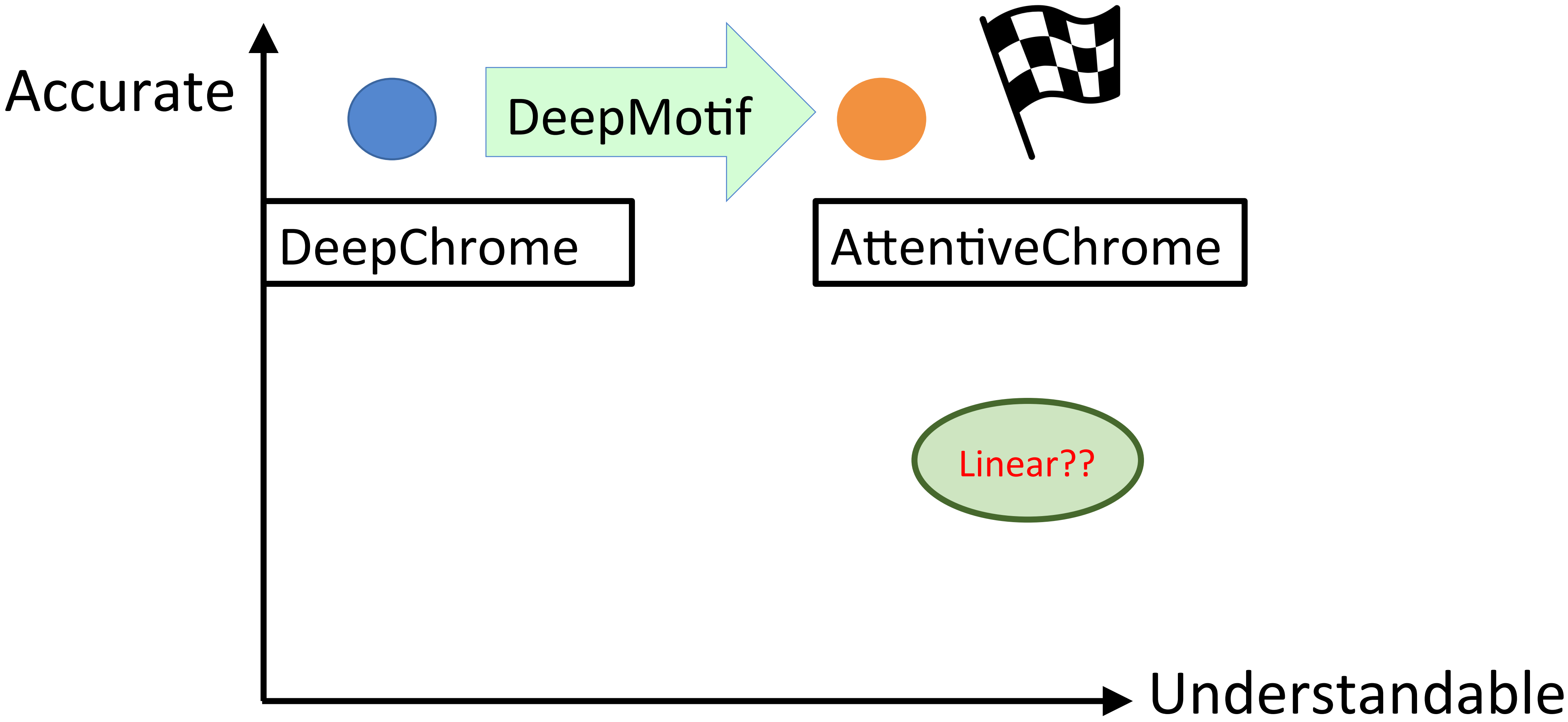


- Deconvolution
- Perturbation-based — Temporal Output Values
- Backpropagation-based — Saliency Map; Class Optimization
- Difference to Reference — DeepLift
- Influence based — Influential Function / ICML27 Best Paper

Summary of our tools



Summary:


Accurate
DeepMotif
DeepChrome
AttentiveChrome
Linear??
Understandable

Acknowledgements

Ritambhara Singh

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Weilin Xu

Arshdeep Sekhon

Beilun Wang

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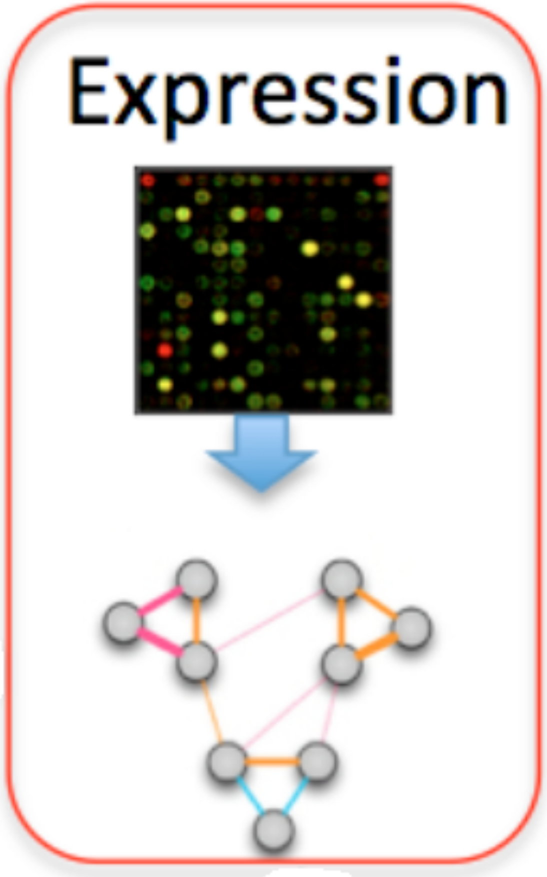
UVA Computer Science Dept. Security Research Group: Prof. David Evans

Thank you

More Tools: learning graphs from data

https://www.jointggm.org

Fast and Scalable Joint Estimators for Learning Sparse Gaussian Graphical Models from Heterogeneous Data

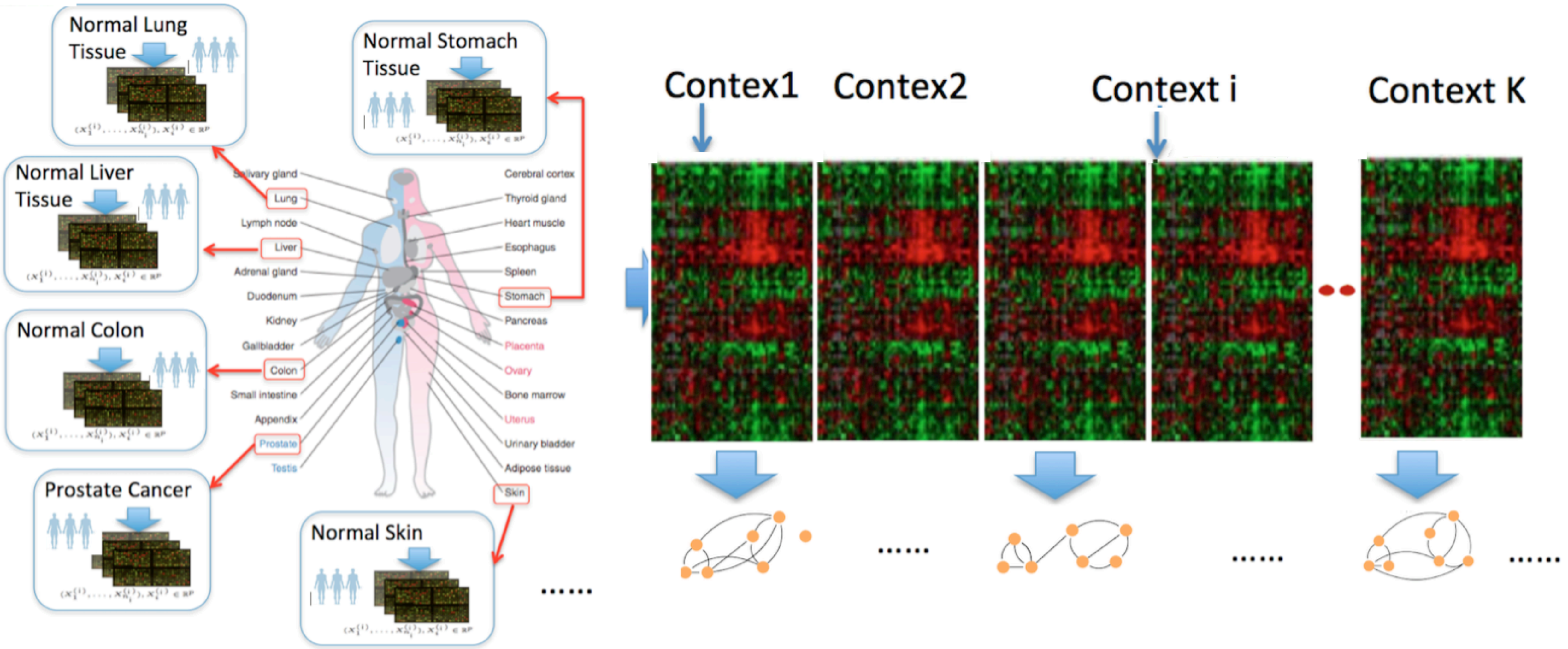


Observational Samples

↓

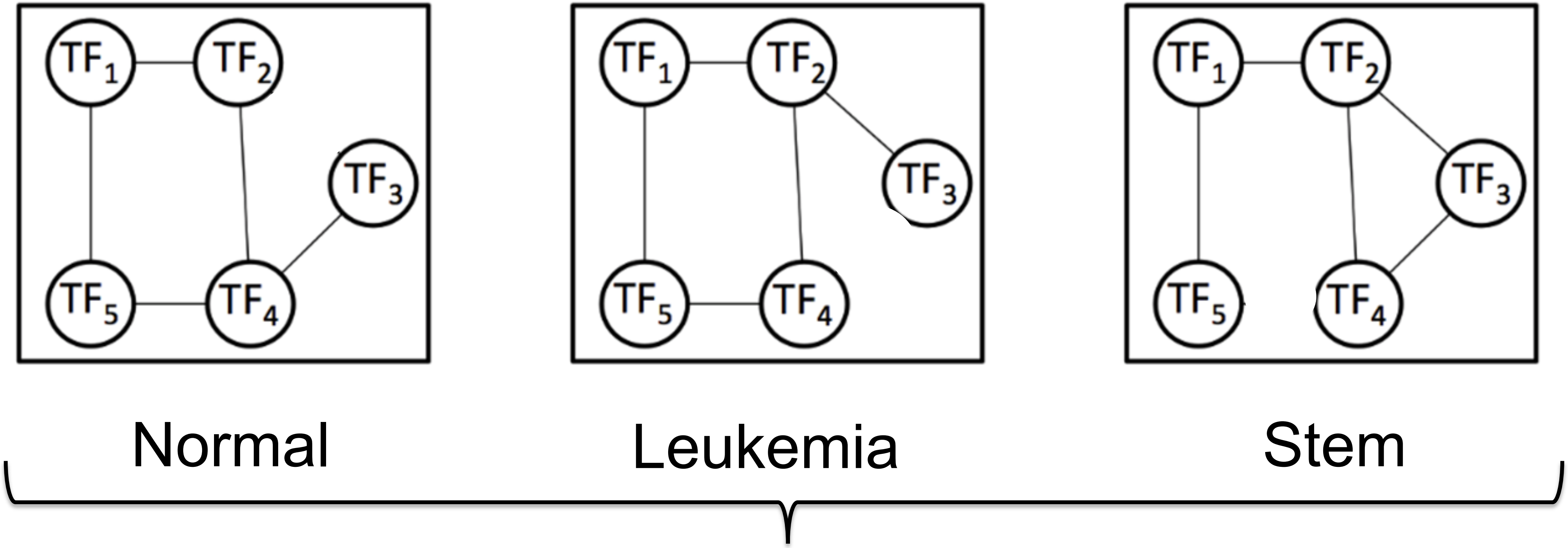
Graphs
(Features as Nodes)

Motivation: Graphs vary across contexts

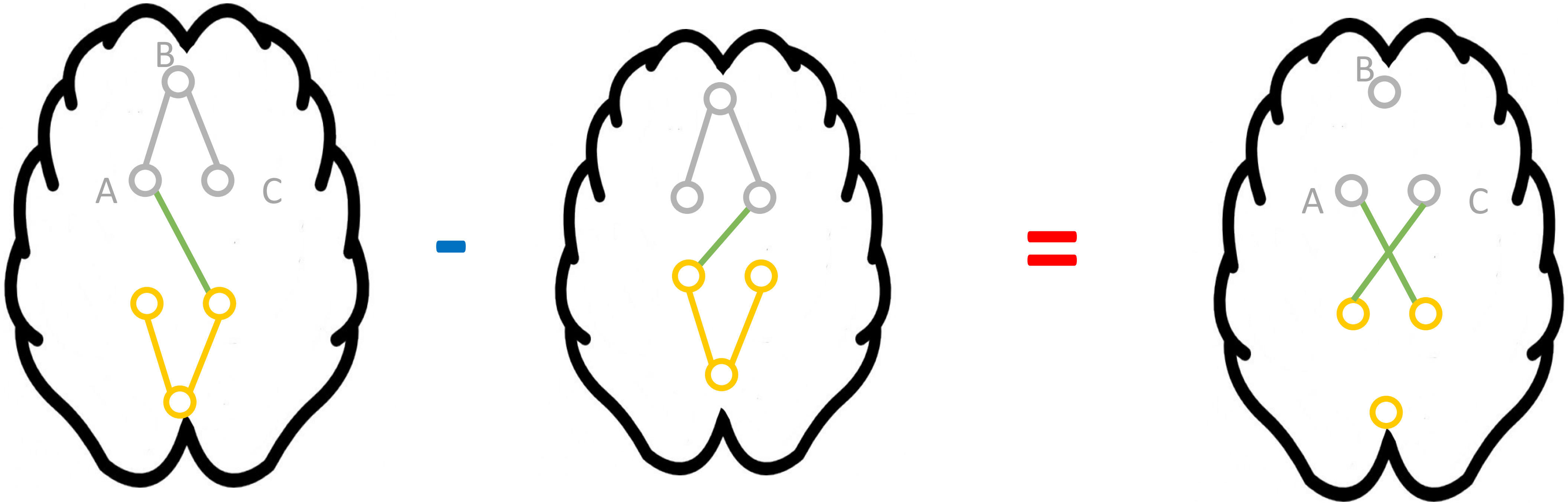


Motivation: Graphs vary across contexts

- Different but related TF co-binding patterns in the form of graphs
- e.g., estimated from Chi-Seq

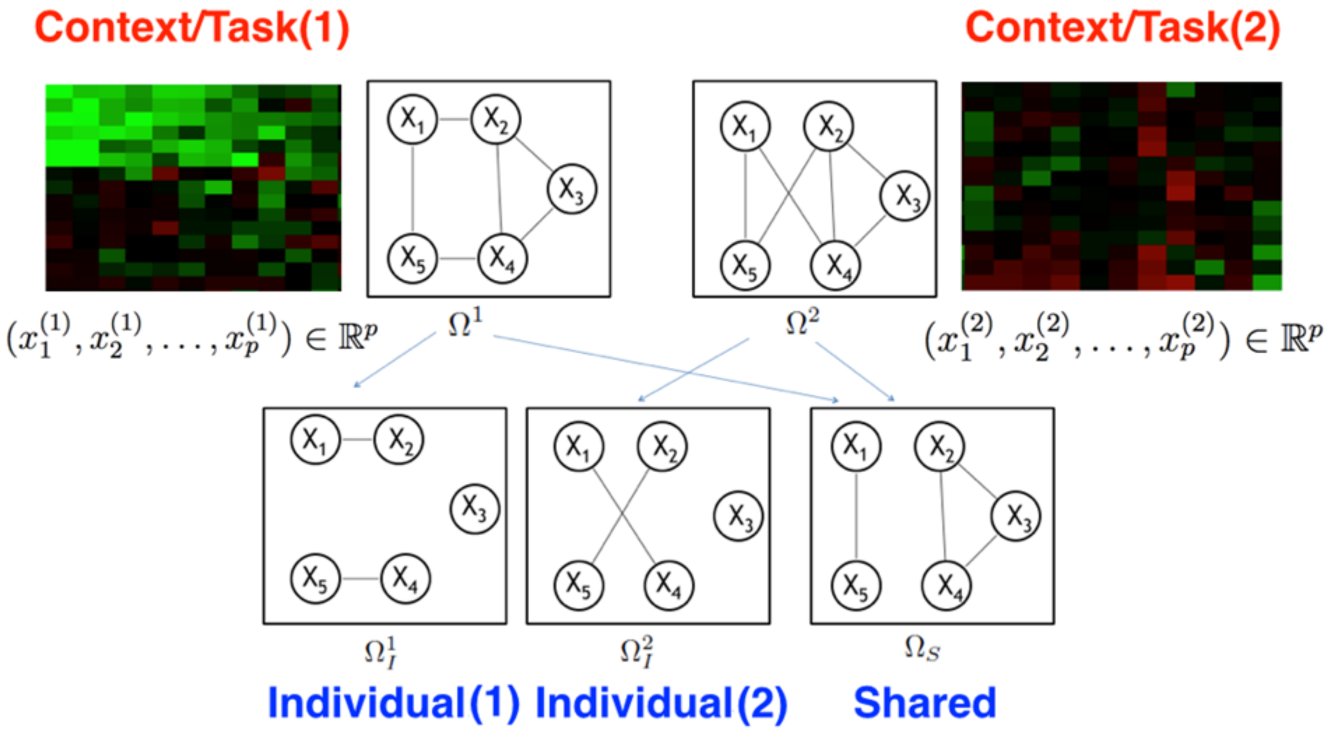


Task I: Learning sparse changes between two graphs



- For example:
  - Find differences in the brains of people with diseases, *e.g.* Autism, Alzheimer's
    - Used for understanding
    - Used for diagnosis

Task II: Learning both shared and context-specific graphs explicitly and simultaneously



- Able to Know both
  - House keeping interactions
  - Context-specific networks

Limitation of Previous Methods : Storage

e.g., calculate the gradient

$$\Sigma = \mathrm{Cov}(X) = \begin{bmatrix} \sigma_{11} & \sigma_{12} & \cdots & \sigma_{1n} \\ \sigma_{21} & \sigma_{22} & \cdots & \sigma_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{n1} & \sigma_{n2} & \cdots & \sigma_{nn} \end{bmatrix}$$

$$\Sigma = \mathrm{Cov}(X) = \begin{bmatrix} \sigma_{11} & \sigma_{12} & \cdots & \sigma_{1n} \\ \sigma_{21} & \sigma_{22} & \cdots & \sigma_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{n1} & \sigma_{n2} & \cdots & \sigma_{nn} \end{bmatrix}$$

$$\Sigma = \mathrm{Cov}(X) = \begin{bmatrix} \sigma_{11} & \sigma_{12} & \cdots & \sigma_{1n} \\ \sigma_{21} & \sigma_{22} & \cdots & \sigma_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{n1} & \sigma_{n2} & \cdots & \sigma_{nn} \end{bmatrix}$$

When K contexts= 91, p nodes= 30K

$O(Kp^2)$ in memory

Double type: 65 TB

Limitation of Previous Methods: Speed

Suppose they have same iteration number T

K = 91, p= 30K

Traditional Optimization Method

---- Block Coordinate Descent : $O(K^3p^4)$ / Itera

more than 2 billion years

Current Optimization:

---- Still needs SVD for each covariance matrix

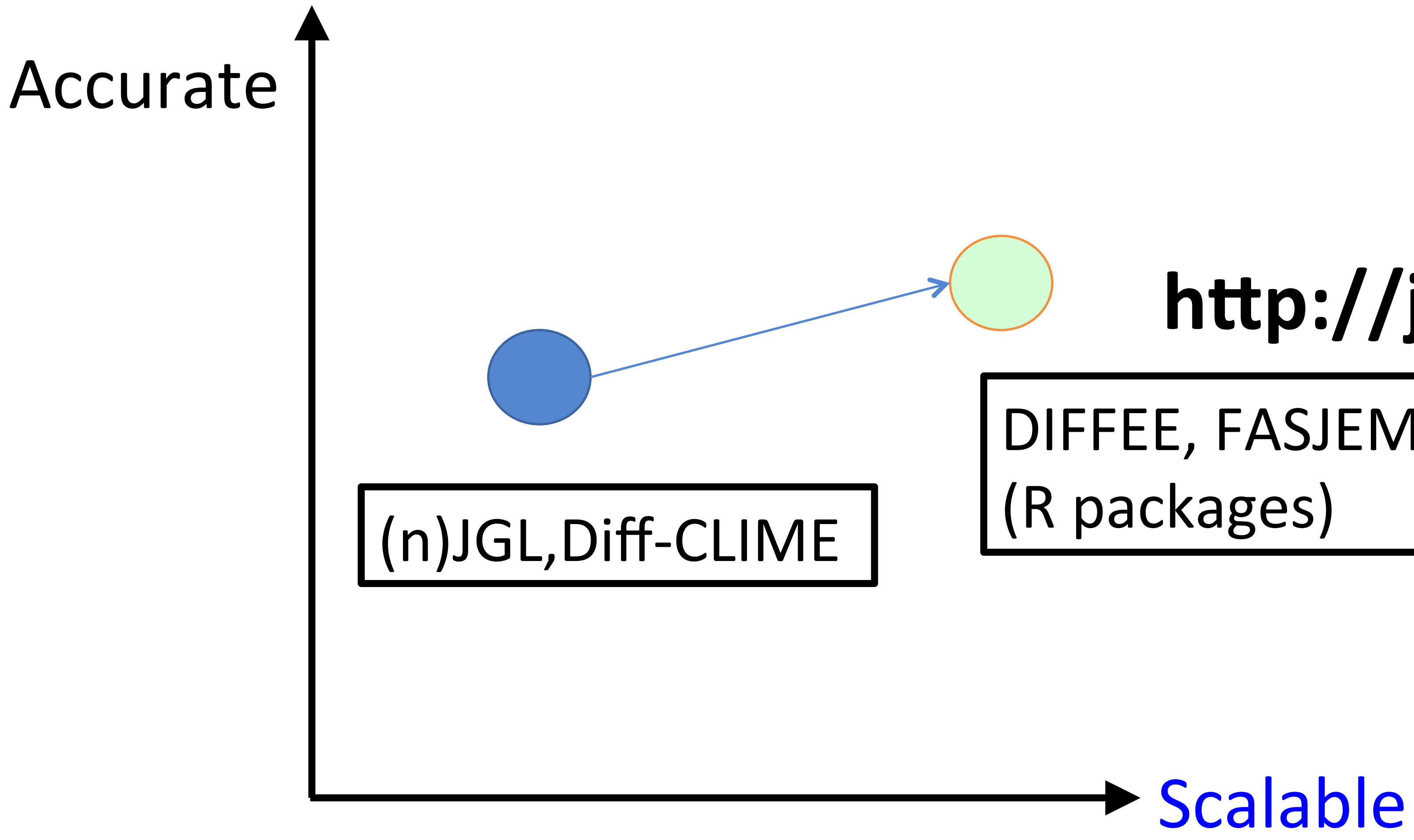
SVD for the matrices needs $O(Kp^3)$ / Itera $\longrightarrow$ 3.5 days

Our Tools

- Fast and scalable estimators for joint graph discovery from heterogeneous samples
- Parallelizable algorithms
- Sharp convergence rate (sharp error bounds)

More details at: http://www.jointggm.org/

Summary

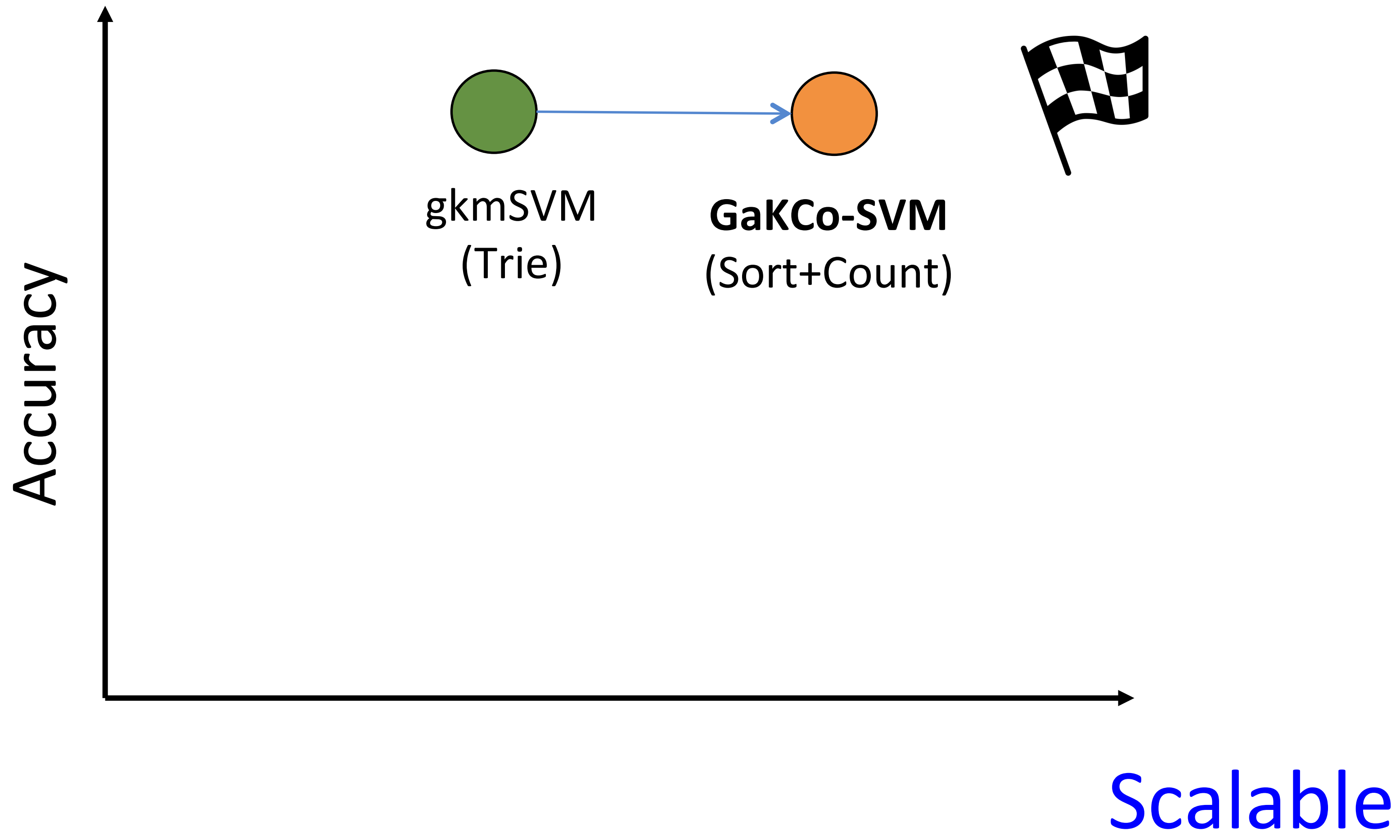


http://jointggm.org/

More Tools: A Scalable Tool to Classify Strings

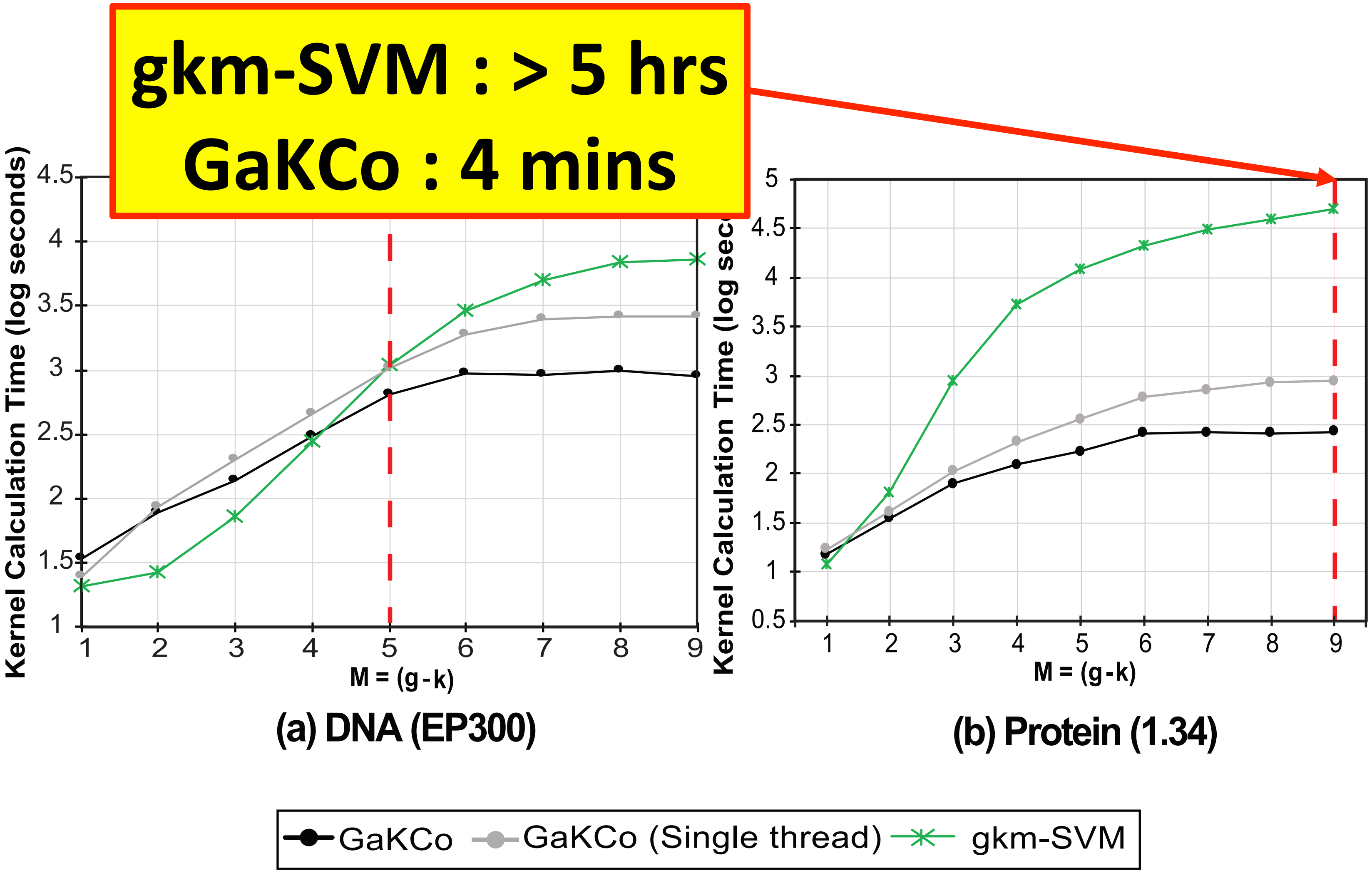
https://www.jointggm.org

One more scalable tool: GaKCo-SVM for sequence classification



R. Singh, et al. "Gakco: a fast gapped k-mer string kernel using counting." *Joint European Conference on Machine Learning and Knowledge Discovery in Databases*. Springer. (2017)

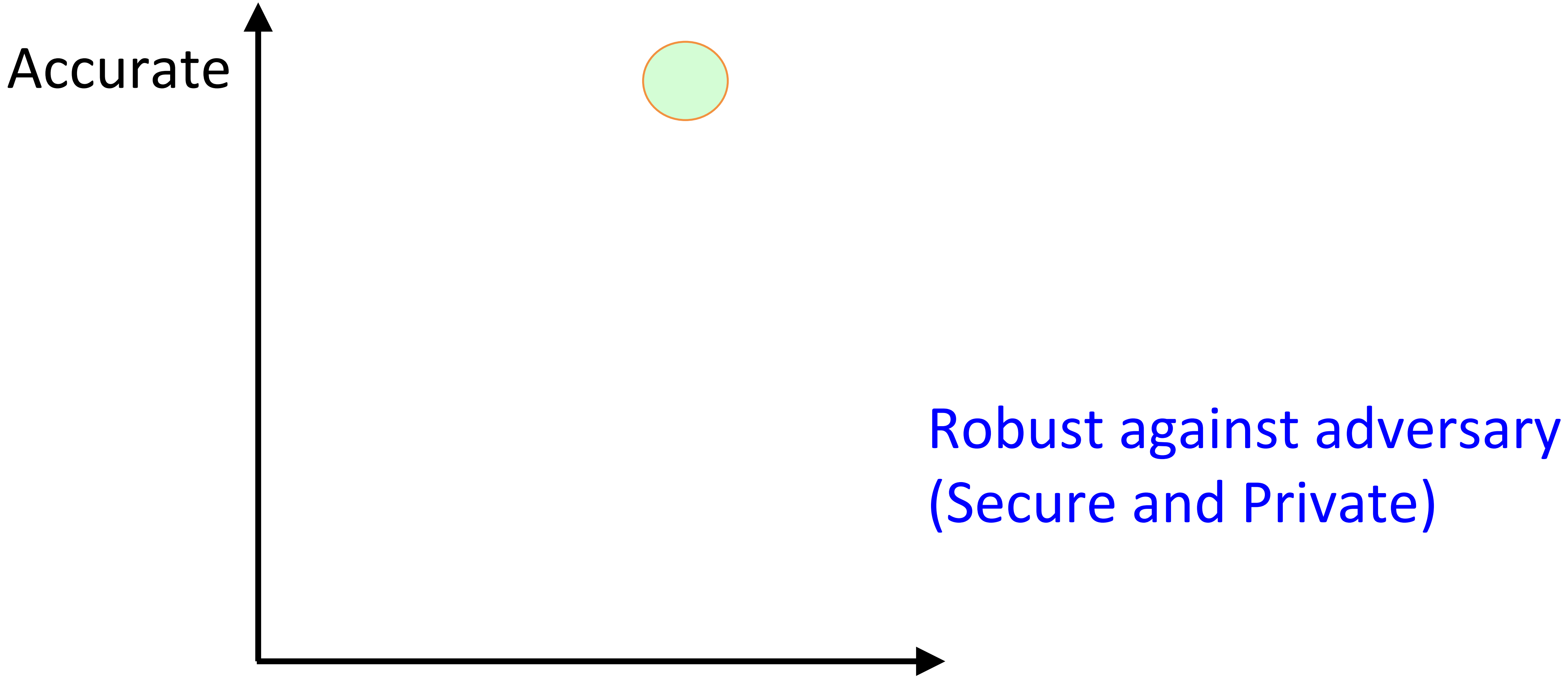
Scales well with increasing ∑ and m



More Tools: Making Machine Learning Robust against Adversaries

Details at:
securemachinelearning.org/

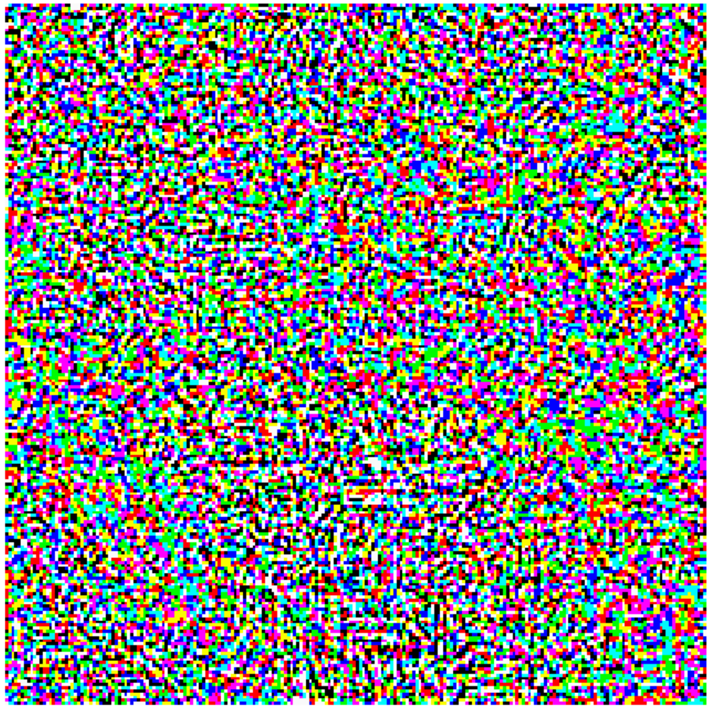
Tools for Robustness of Machine Learning



Adversarial Examples to Fool DNN Models

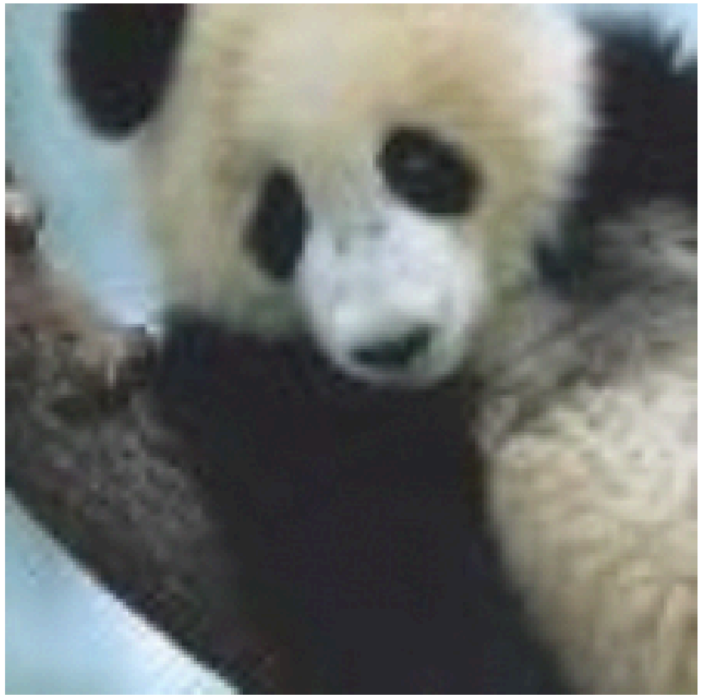
"panda"

$+$



$0.007 \times [noise]$

$=$

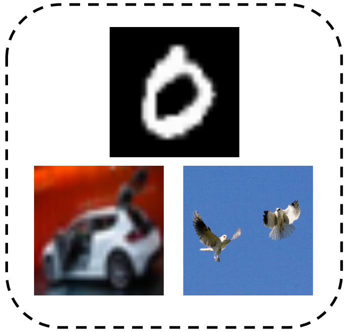


"gibbon"

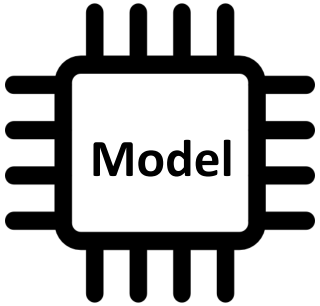
Example from: Ian J. Goodfellow, Jonathon Shlens, Christian Szegedy. *Explaining and Harnessing Adversarial Examples*. ICLR 2015.

More available at: **securemachinelearning.org/**

EvadeML-Zoo: a benchmark toolbox



- MNIST
- CIFAR-10
- ImageNet



- CNN
- DenseNet
- MobileNets

- FGSM, BIM,
- JSMA, DeepFool,
- CW_2, CW_i, CW_0

- Feature Squeezing

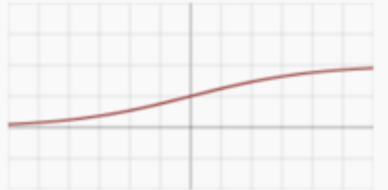
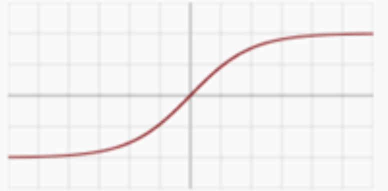
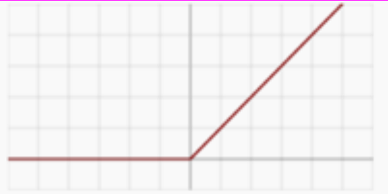
Backup

When to use Machine Learning ?

- 1. Extract knowledge from data
  - Relationships and correlations can be hidden within large amounts of data
  - The amount of knowledge available about certain tasks is simply too large for explicit encoding (e.g. rules) by humans
- 2. Learn tasks that are difficult to formalise
  - Hard to be defined well, except by examples (e.g. face recognition)
- 3. Create software that improves over time
  - New knowledge is constantly being discovered.
  - Rule or human encoding-based system is difficult to continuously re-design "by hand".

Nonlinearity Functions

(aka transfer or activation functions)

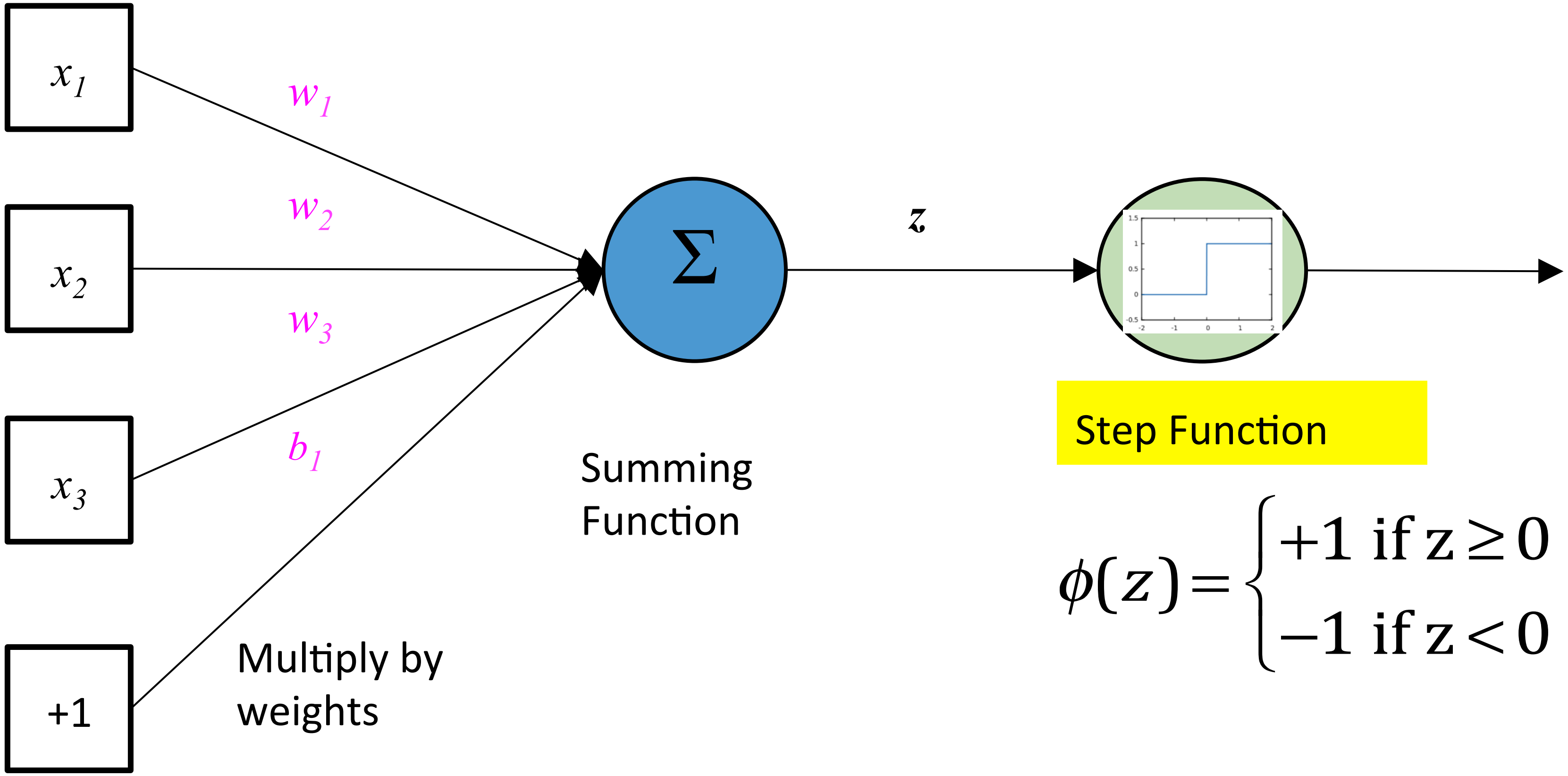
Name	Plot	Equation	Derivative (w.r.t x)
Binary step		$f(x) = \begin{cases} 0 & \text{for} \quad x < 0 \\ 1 & \text{for} \quad x \geq 0 \end{cases}$	$f'(x) = \begin{cases} 0 & \text{for} \quad x \neq 0 \\ ? & \text{for} \quad x = 0 \end{cases}$
Logistic (a.k.a Soft step)		$f(x) = \frac{1}{1+e^{-x}}$	$f'(x) = f(x)(1 - f(x))$
TanH		$f(x) = \tanh(x) = \frac{2}{1+e^{-2x}} - 1$	$f'(x) = 1 - f(x)^2$
Rectifier (ReLU)[9]		$f(x) = \begin{cases} 0 & \text{for} \quad x < 0 \\ x & \text{for} \quad x \geq 0 \end{cases}$	$f'(x) = \begin{cases} 0 & \text{for} \quad x < 0 \\ 1 & \text{for} \quad x \geq 0 \end{cases}$

usually works best in practice

https://en.wikipedia.org/wiki/Activation_function#Comparison_of_activation_functions

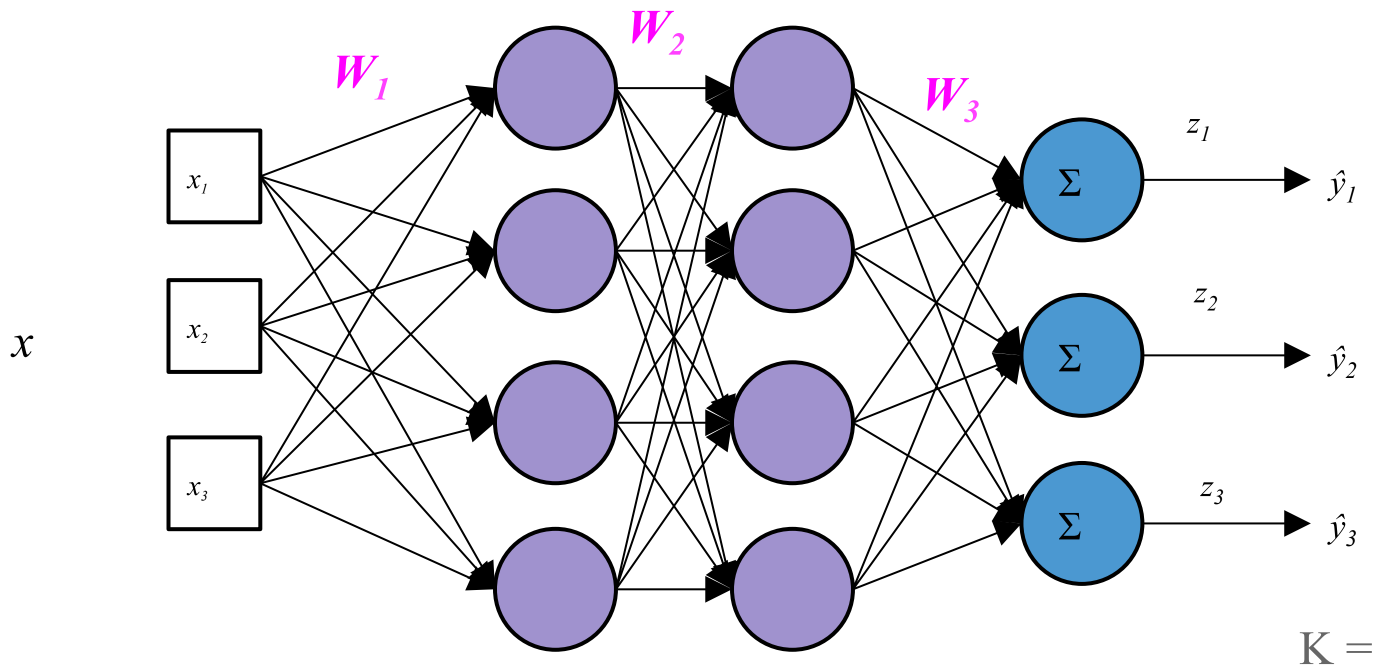
History ➔ Perceptron: 1-Neuron Unit with Step

- First proposed by Rosenblatt (1958)
- A simple neuron that is used to classify its input into one of two categories.
- A perceptron uses a **step function**



$$\phi(z) = \begin{cases} +1 \text{ if } z \geq 0 \\ -1 \text{ if } z < 0 \end{cases}$$

When for Multi-Class Classification

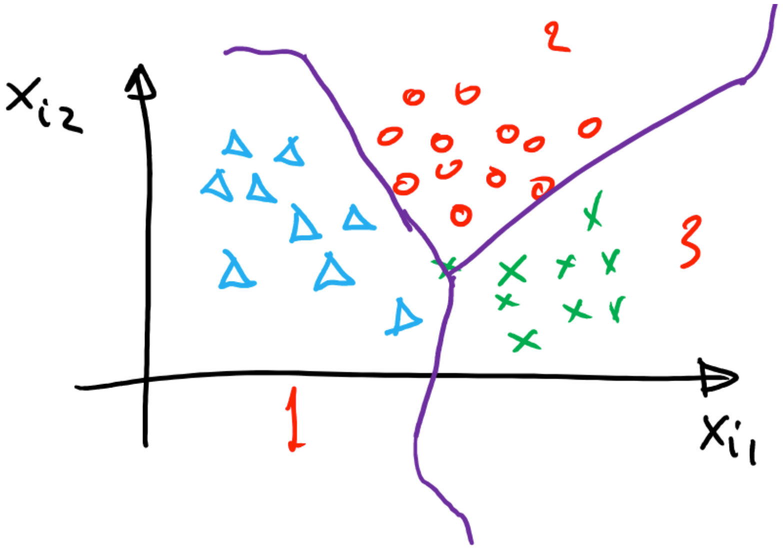


K = 3

$$\hat{y}_i = \frac{e^{z_i}}{\sum_j e^{z_j}} = P(\hat{y}_i = 1 \mid \boldsymbol{x})$$

"Softmax" function. Normalizing function which converts each class output to a probability.

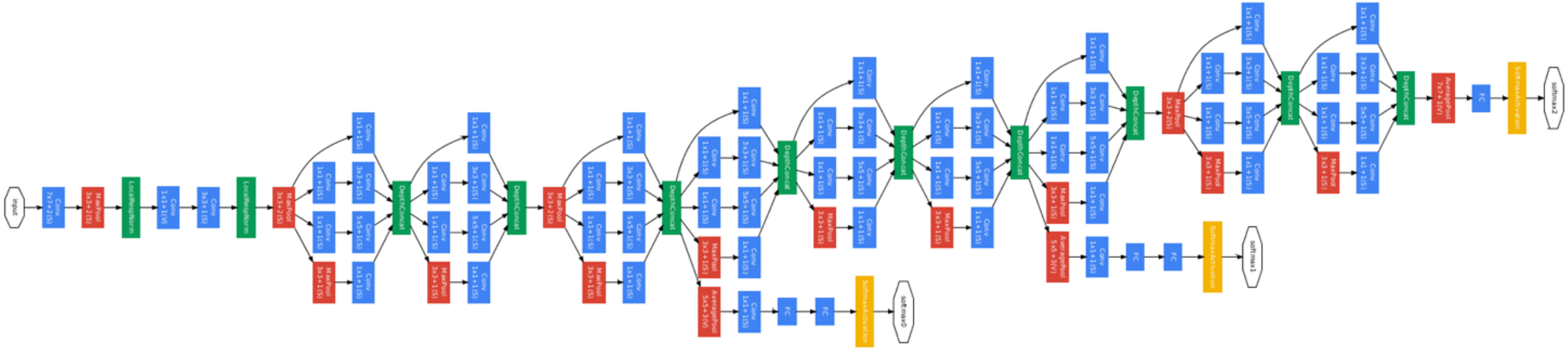
Y_{i1}	Y_{i2}	Y_{i3}	
0	1	0	Class 2
1	0	0	Class 1
0	0	1	Class 3



$$E(\hat{y}, y) = \text{loss} = -\sum_{j=1...K} y_j \ln \hat{y}_j$$

Cross-entropy loss

Building Deep Neural Nets



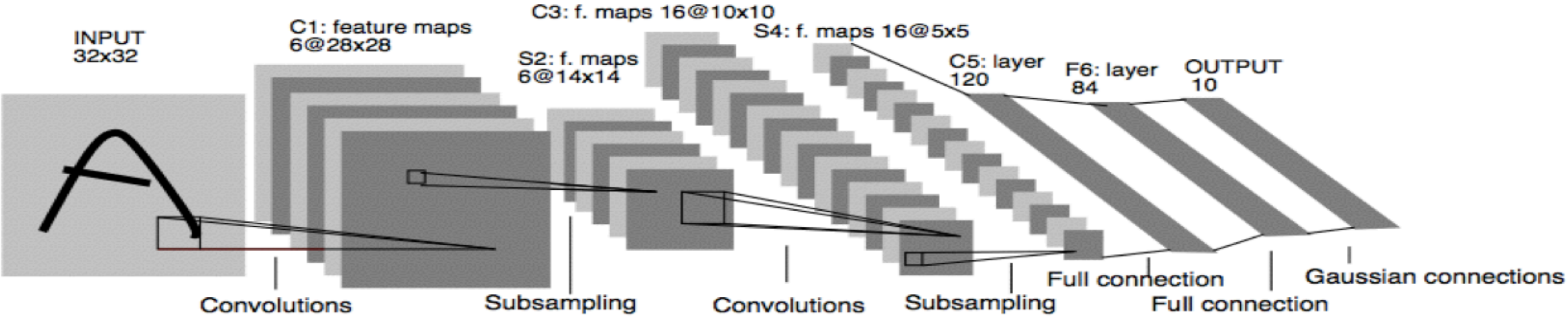
"GoogLeNet" for Object Classification

Many classification models invented since late 80's

- Neural networks
- Boosting
- Support Vector Machine
- Maximum Entropy
- Random Forest
- ……

Deep Learning (CNN) in the 90's

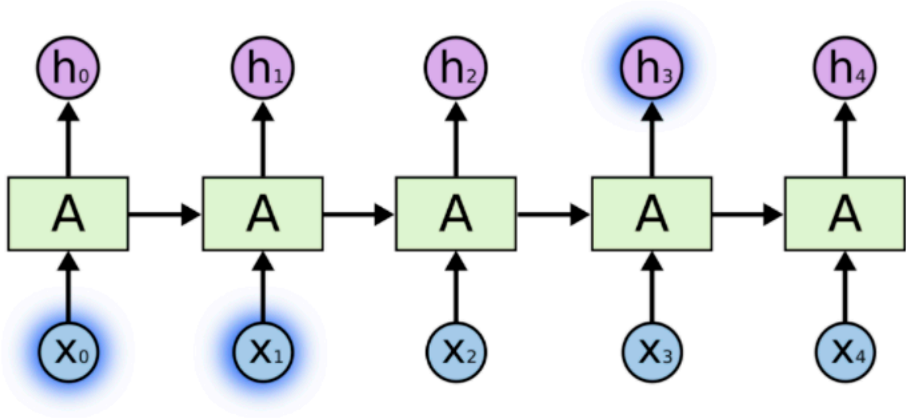
- Prof. Yann LeCun invented Convolutional Neural Networks (CNN) in 1998
- First NN successfully trained with many layers

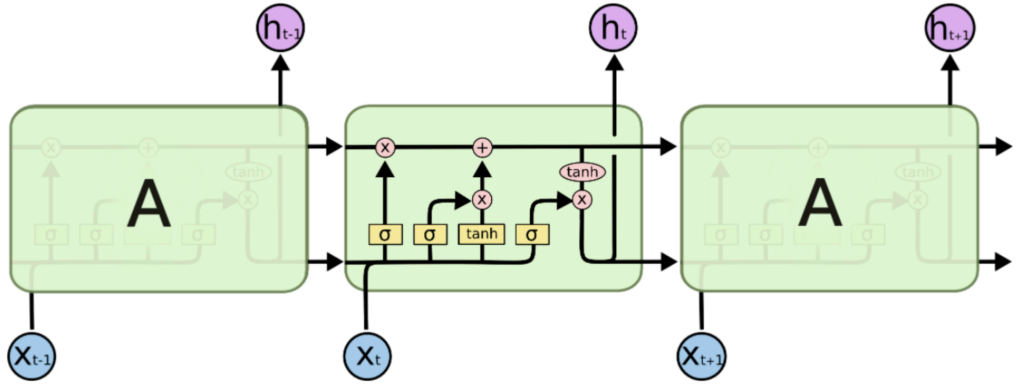


Y. LeCun, L. Bottou, Y. Bengio, and P. Haffner, Gradient-based learning applied to document recognition, Proceedings of the IEEE 86(11): 2278–2324, 1998.

Deep Learning (RNN) in the 90's

- Prof. Schmidhuber invented "Long short-term memory" – Recurrent NN (LSTM-RNN) model in 1997





The repeating module in an LSTM contains four interacting layers.

Sepp Hochreiter; Jürgen Schmidhuber (1997). "Long short-term memory". Neural Computation. 9 (8): 1735–1780.

Image Credits from Christopher Olah

Between ~2000 to ~2011 Machine Learning Field Interest

- Learning with Structures ! + Convex Formulation!
  - Kernel learning
  - Manifold Learning
  - Sparse Learning
  - Structured input-output learning …
  - Graphical model
  - Transfer Learning
  - Semi-supervised
  - Matrix factorization
  - ……

“Winter of Neural Networks” Since 90’s to ~2011

- Non-convex

- Need a lot of tricks to play with
  - How many layers ?
  - How many hidden units per layer ?
  - What topology among layers ? …….

- Hard to perform theoretical analysis

Breakthrough in 2012 Large-Scale Visual Recognition Challenge (ImageNet)

10% improve with deepCNN

72%, 2010

74%, 2011

85%, 2012

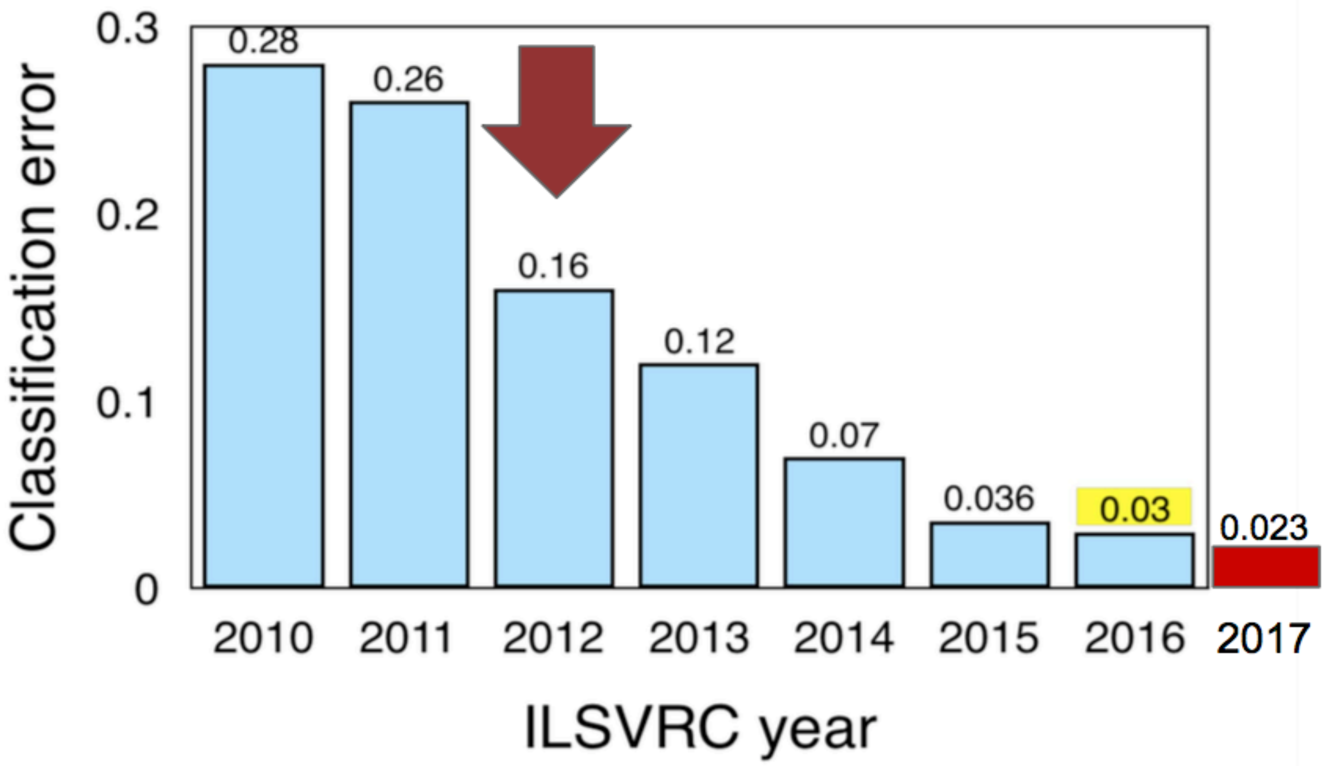
In one “very large-scale” benchmark competition

(1.2 million images [X] vs.1000 different word labels [Y])

ImageNet Challenge

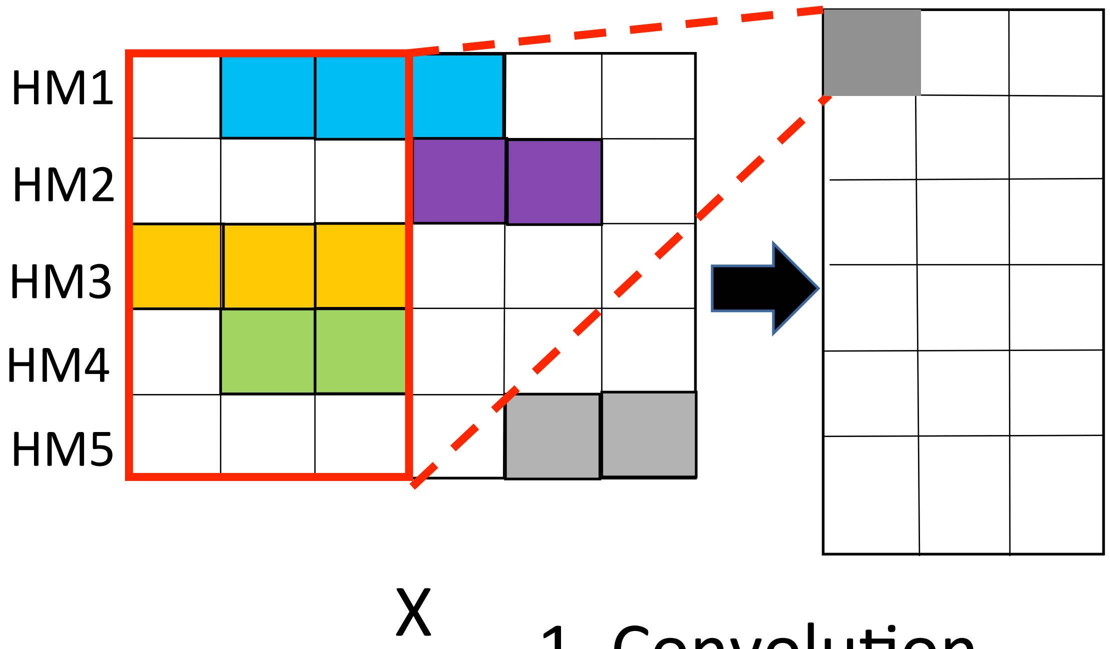
Arch

- 2010-11: hand-crafted computer vision pipelines
- 2012-2016: ConvNets
  - 2012: AlexNet
    - major deep learning success
  - 2013: ZFNet
    - improvements over AlexNet
  - 2014
    - VGGNet: deeper, simpler
    - InceptionNet: deeper, faster
  - 2015
    - ResNet: even deeper
  - 2016
    - ensembled networks
  - 2017
    - Squeeze and Excitation Network



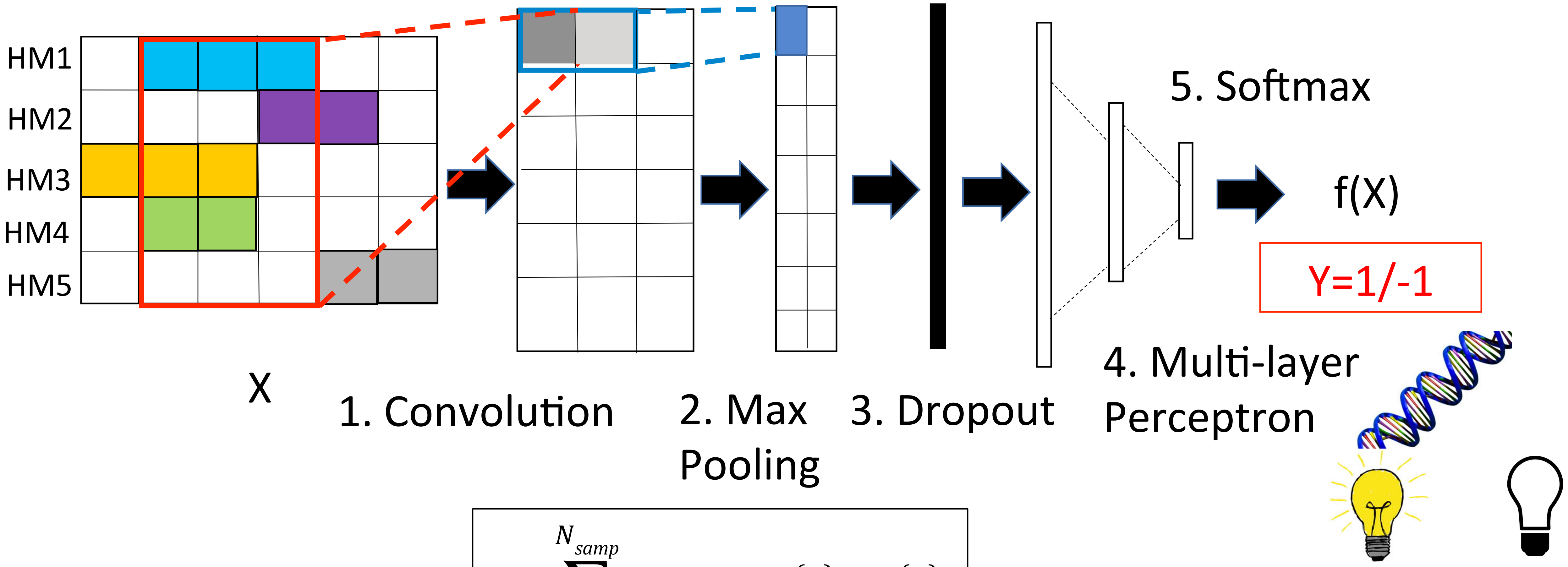
Adapt from From NIPS 2017 DL Trend Tutorial

DeepChrome: Convolutional Neural Network (CNN)



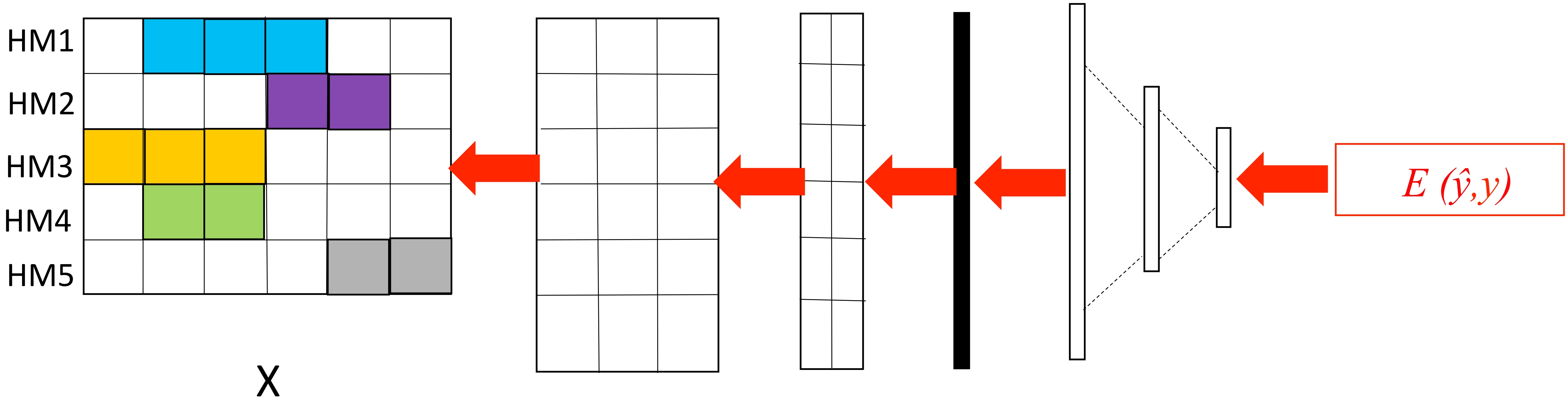
1. Convolution

DeepChrome: Convolutional Neural Network (CNN)



$$E = \sum_{n=1}^{N_{samp}} loss(f(X^{(n)}), y^{(n)})$$

DeepChrome: Convolutional Neural Network (CNN)



Back-propagation: $\Theta \leftarrow \Theta - \eta \dfrac{\partial E}{\partial \Theta}$