

KSBi-BIML 2023

Bioinformatics & Machine Learning(BIML)
Workshop for Life Scientists, Data Scientists,
and Bioinformaticians

생물정보학 & 머신러닝 워크샵 (온라인)

Dimensionality Reduction

이제근 _ 숭실대학교



본 강의 자료는 한국생명정보학회가 주관하는 BIML 2023 워크샵 온라인 수업을 목적으로 제작된 것으로 해당 목적 이외의 다른 용도로 사용할 수 없음을 분명하게 알립니다.

이를 다른 사람과 공유하거나 복제, 배포, 전송할 수 없으며 만약 이러한 사항을 위반할 경우 발생하는 **모든 법적 책임은 전적으로 불법 행위자 본인에게 있음을 경고**합니다.

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안녕하십니까?

한국생명정보학회가 개최하는 동계 교육 워크숍인 BIML-2023에 여러분을 초대합니다. 생명정보학 분야의 연구자들에게 최신 동향의 데이터 분석기술을 이론과 실습을 겸비해 전달하고자 도입한 전문 교육 프로그램인 BIML 워크숍은 2015년에 시작하여 올해로 9차를 맞이하게 되었습니다. 지난 2년간은 심각한 코로나 대유행으로 인해 아쉽게도 모든 강의가 온라인으로 진행되어 현장 강의에서만 가능한 강의자와 수강생 사이에 다양한 소통의 기회가 없음에 대한 아쉬움이 있었습니다. 다행히도 최근 사회적 거리두기 완화로 현장 강의를 가능해져 올해는 현장 강의를 재개함으로써 온라인과 현장 강의의 장점을 모두 갖춘 프로그램을 구성할 수 있게 되었습니다.

BIML 워크숍은 전통적으로 크게 인공지능과 생명정보분석 두 개의 분야로 구성되었습니다. 올해 AI 분야에서는 최근 생명정보 분석에서도 응용이 확대되고 있는 다양한 심층학습(Deep learning) 기법들에 대한 현장 강의를 진행될 예정이며, 관련하여 심층학습을 이용한 단백질구조예측, 유전체 분석, 신약개발에 대한 이론과 실습 강의를 함께 제공할 예정입니다. 또한 싱글셀오믹스 분석과 메타유전체분석 현장 강의는 많은 연구자의 연구 수월성 확보에 큰 도움을 줄 것으로 기대하고 있습니다. 이외에 다양한 생명정보학 분야에 대하여 30개 이상의 온라인 강좌가 개설되어 제공되며 온라인 강의의 한계를 극복하기 위해서 실시간 Q&A 세션 또한 마련했습니다. 특히 BIML은 각 분야 국내 최고 전문가들의 강의로 구성되어 해당 분야의 기초부터 최신 연구 동향까지 포함하는 수준 높은 내용의 강의를 될 것입니다.

이번 BIML-2023을 준비하기까지 너무나 많은 수고를 해주신 BIML-2023 운영위원회의 남진우, 우현구, 백대현, 정성원, 정인경, 장혜식, 박종은 교수님과 KOBIC 이병욱 박사님께 커다란 감사를 드립니다. 마지막으로 부족한 시간에도 불구하고 강의 부탁을 흔쾌히 허락하시고 훌륭한 현장 강의와 온라인 강의를 준비하시는데 노고를 아끼지 않으신 모든 연사분께 깊은 감사를 드립니다.

2023년 2월

한국생명정보학회장 이 인 석

Dimensionality Reduction

바이오 데이터는 고차원의 데이터로 구성되어 있는 경우가 많다. 일례로 유전자 발현 데이터를 생각하면, 일반적으로 유전자가 변수(feature)가 되기에 인간의 경우 20,000 차원의 이상으로 구성된 데이터라 할 수 있으며 이러한 고차원의 데이터를 이용하여 분석을 진행하는 것은 계산학적으로도 간단한 일이 아니다.

본 강의에서는 이러한 고차원 데이터를 분석할 때 활용할 수 있는 dimensionality reduction (차원 축소) 개념과 대표적인 방법들, 활용 방안에 대해 설명한다. 가장 대표적인 방법인 PCA (principal component analysis)를 비롯하여 ICA (independent component analysis), NMF (non-negative matrix factorization) 등 여러 방법론에 대해 간단히 소개한다. 또한 deep neural networks을 이용하여 dimensionality reduction 목적으로 사용할 수 있는 autoencoder의 개념과 활용에 대해서도 설명한다. 각 방법들에 대한 기본 개념 소개와 함께 실제 데이터를 이용한 활용 예시를 통해 이러한 방법들이 바이오 데이터 분석에 어떻게 활용될 수 있는지 보인다.

본 강의에서는 수학적 부분을 아예 제외할 수는 없으나, 각 방법의 특성을 비롯한 주요 개념 이해를 목적으로 설명한다. 또한 이론 위주의 강의이나 R이나 python을 이용하여 해당 방법들을 어떻게 활용할 수 있는지에 대해서도 간단히 소개한다. 직접적인 R이나 python 실습이 진행되지는 않지만, 강의 중 소개되는 코드 이해를 위해서는 R과 python 기초 문법을 사전에 알고 있으면 도움이 될 수 있다.

* 참고강의교재:

강의 자료

* 교육생준비물:

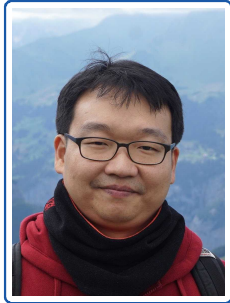
강의 수강을 위한 개인 컴퓨터

* 강의 난이도: 초급

* 강의: 이제근 교수 (숭실대학교 의생명시스템학부)

Curriculum Vitae

Speaker Name: Je-Keun Rhee, Ph.D.



► Personal Info

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Research Interest

Cancer Genomics, Machine Learning

Educational Experience

2004 B.S. in Life Science, Korea University, Korea
2004 B.S. in Computer Science & Engineering, Korea University, Korea (Double Major)
2014 Ph.D. in Bioinformatics, Seoul National University, Korea

Professional Experience

2011 Visiting Scholar, School of Informatics and Computing (SoIC), Indiana University, USA
2014-2018 Research Professor, Cancer Research Institute /
Department of Medical Informatics, The Catholic University of Korea, Korea
2018-2019 Assistant Professor, School of Dentistry, Pusan National University, Korea
2019- Assistant Professor, School of Systems Biomedical Sciences, Soongsil University, Korea

Selected Publications (5 maximum)

1. Bonil Koo, Je-Keun Rhee, Prediction of tumor purity from gene expression data using machine learning, *Briefings in Bioinformatics*, 22(6):bbab163, 2021. (Corresponding author)
2. Yeongjoo Kim, Ji Wan Kang, Junho Kang, Eun Jung Kwon, Mihyang Ha, Yoon Kyoung Kim, Hansong Lee, Je-Keun Rhee, Yun Hak Kim, Novel deep learning-based survival prediction for oral cancer by analyzing tumor-infiltrating lymphocyte profiles through CIBERSORT, *Oncotarget*, 10(1):e1904573, 2021 (Co-corresponding author)
3. Joong Chae Na, Inbok Lee, Je-Keun Rhee, and Soo-Yong Shin, Fast single individual haplotyping method using GPGPU, *Computers in Biology and Medicine*, 113:103421, 2019. (Co-corresponding author)
4. Je-Keun Rhee, Soo-Jin Kim, Byoung-Tak Zhang, Identifying DNA Methylation Modules Associated with a Cancer by Probabilistic Evolutionary Learning, *IEEE Computational Intelligence Magazine*, 13(3): 12-19, 2018. (First author)
5. Joong Chae Na, Jong-Chan Lee, Je-Keun Rhee, and Soo-Yong Shin, PEATH: Single Individual Haplotyping by Probabilistic Evolutionary Algorithm with Toggling, *Bioinformatics*, 34(11): 1801-1807, 2018. (Co-corresponding author)

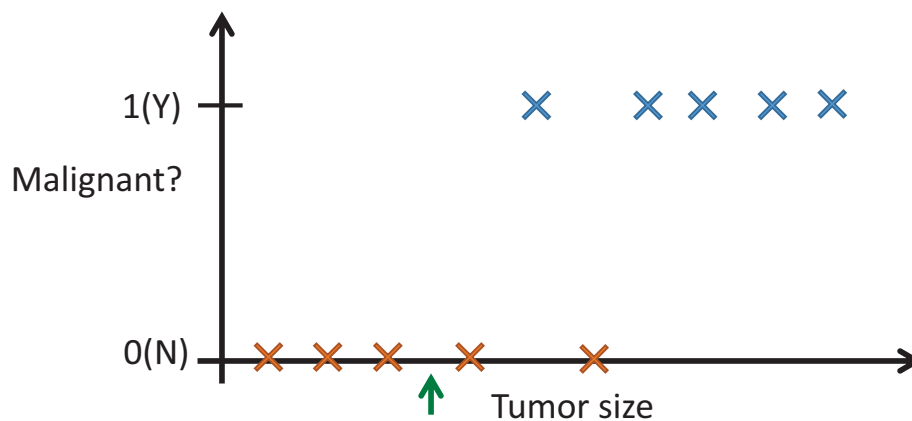
KSBi-BIML

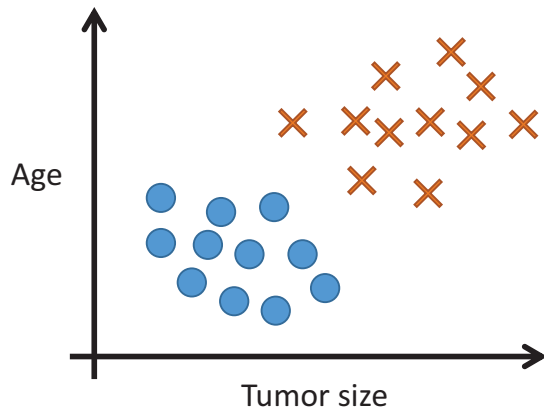
Dimensionality Reduction

Rhee, Je-Keun

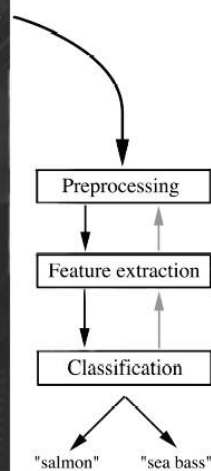
Soongsil University (송실대 이제근)

Cancer (Malignant, Benign)



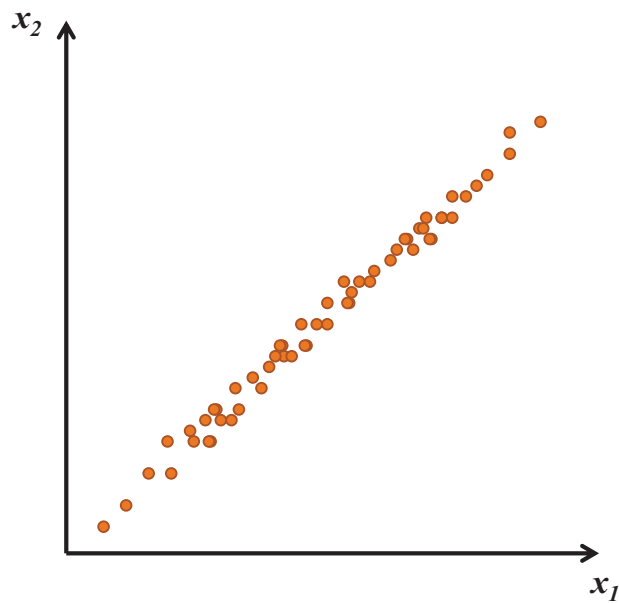


- Clump Thickness
- Uniformity of Cell Size
- Uniformity of Cell Shape
- ...

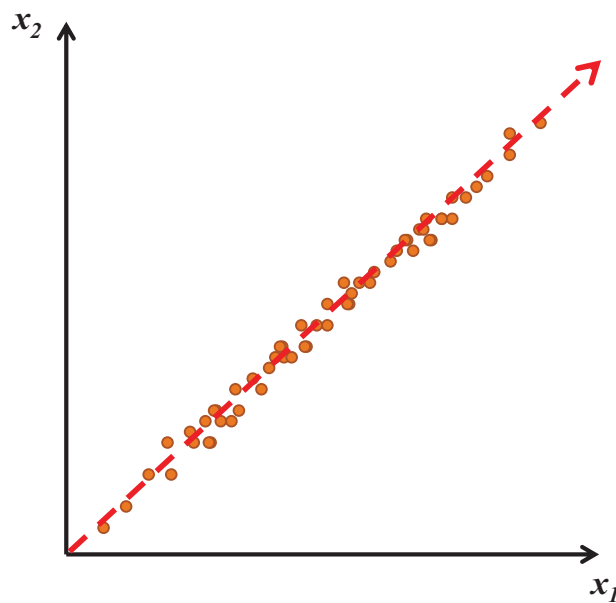


from Pattern Classification (book)

Principal component analysis (PCA)



(0.9, 1.0), (1.3, 1.4), (1.9, 1.8), (2.2, 2.2), (2.4, 2.3),



From k original variables: x_1, x_2, \dots, x_k :

Produce k new variables: y_1, y_2, \dots, y_k :

$$y_1 = a_{11}x_1 + a_{12}x_2 + \dots + a_{1k}x_k$$

$$y_2 = a_{21}x_1 + a_{22}x_2 + \dots + a_{2k}x_k$$

...

$$y_k = a_{k1}x_1 + a_{k2}x_2 + \dots + a_{kk}x_k$$

y_k 's are
Principal Components

such that:

y_k 's are orthogonal

y_1 explains as much as possible of original variance in data set

y_2 explains as much as possible of remaining variance etc.

$\{a_{11}, a_{12}, \dots, a_{1k}\}$ is 1st **Eigenvector** of covariance matrix, and **coefficients** of first principal component

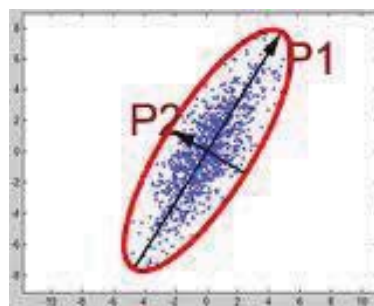
$\{a_{21}, a_{22}, \dots, a_{2k}\}$ is 2nd **Eigenvector** of covariance matrix, and **coefficients** of 2nd principal component

...

$\{a_{k1}, a_{k2}, \dots, a_{kk}\}$ is *k*th **Eigenvector** of covariance matrix, and **coefficients** of *k*th principal component

Computation of PCA

- The direction is given by the eigenvector γ_1 corresponding to the largest eigenvalue of covariance matrix **C**
- The second vector that is orthogonal (uncorrelated) to the first is the one that has the second highest variance which comes to be the eigenvector corresponding to the second eigenvalue
- And so on ...



- The eigenvalues λ_i are found by solving the equation

$$Cx = \lambda x$$

$$\det(C - \lambda I) = 0$$

- Eigenvectors are columns of the matrix A such that

$$C = A D A^T$$

where D is a diagonal matrix

$$D = \begin{pmatrix} \lambda_1 & 0 & \dots & 0 \\ 0 & \lambda_2 & \dots & 0 \\ 0 & & & \\ 0 & \dots & \dots & \lambda_p \end{pmatrix}$$

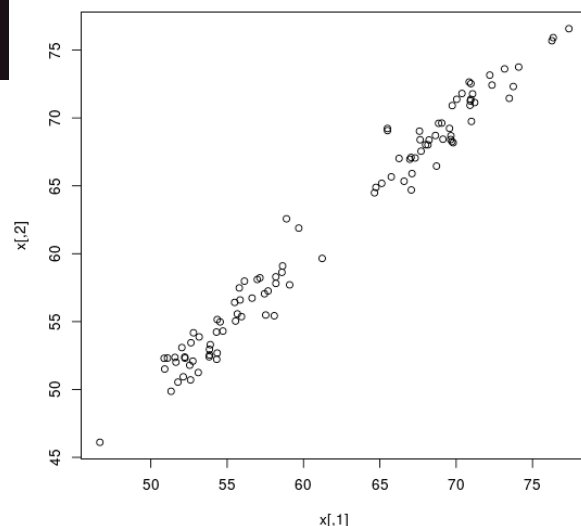
- In practice, the eigenvectors are computed by SVD (singular value decomposition).

```
> X <- matrix(rnorm(32000), 1000, 32)
> dim(X)
[1] 1000 32
> pca_X <- prcomp(X)
> pca_X
Standard deviations (1, .., p=32):
 [1] 1.1611268 1.1515482 1.1477628 1.1316116 1.1165251 1.1021387 1.0869687
 [8] 1.0770949 1.0669926 1.0638087 1.0539471 1.0525123 1.0368192 1.0296589
[15] 1.0204239 1.0106765 1.0014669 0.9868647 0.9819980 0.9618256 0.9587249
[22] 0.9491361 0.9463531 0.9391354 0.9229802 0.9129457 0.9069524 0.8888694
[29] 0.8832288 0.8669869 0.8599976 0.8498946

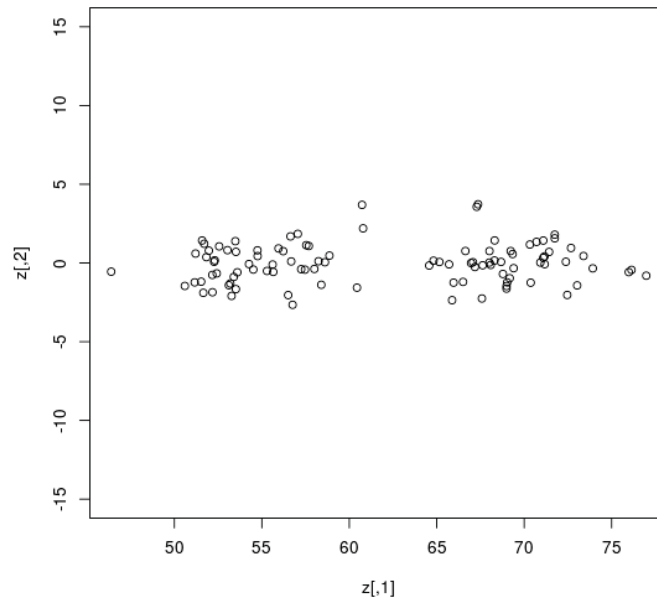
Rotation (n x k) = (32 x 32):
      PC1      PC2      PC3      PC4      PC5
[1,] 0.1273681775 -0.141384568 0.10253371 -0.025551064 0.063805435
[2,] -0.0586362373 -0.097460978 -0.23289460 0.033280613 -0.057664530
[3,] -0.0568348643 -0.145480526 -0.03000443 -0.364971502 -0.165182630
[4,] -0.0267425081 0.217378536 -0.16041250 0.014201023 -0.256952950
[5,] -0.4712193258 -0.166847283 -0.09229190 -0.059443440 -0.046960081
[6,] -0.1614406885 -0.166437088 -0.21686270 0.168164903 -0.242285265
[7,] -0.0014116763 -0.191471560 0.03982241 -0.050303873 -0.003665553
[8,] 0.1099764928 0.400860439 -0.38249763 0.024063732 0.068599711
```

```
> summary(pca_X)
Importance of components:
      PC1      PC2      PC3      PC4      PC5      PC6      PC7
Standard deviation  1.16113  1.15155  1.14776  1.13161  1.11653  1.10214  1.08697
Proportion of Variance  0.04146  0.04078  0.04051  0.03938  0.03834  0.03736  0.03633
Cumulative Proportion  0.04146  0.08224  0.12275  0.16213  0.20047  0.23783  0.27416
      PC8      PC9      PC10     PC11     PC12     PC13     PC14
Standard deviation  1.07709  1.06699  1.0638  1.05395  1.05251  1.03682  1.0297
Proportion of Variance  0.03568  0.03501  0.0348  0.03416  0.03407  0.03306  0.0326
Cumulative Proportion  0.30984  0.34485  0.3796  0.41381  0.44788  0.48094  0.5135
      PC15     PC16     PC17     PC18     PC19     PC20     PC21
Standard deviation  1.02042  1.01068  1.00147  0.98686  0.98200  0.96183  0.95872
Proportion of Variance  0.03202  0.03141  0.03084  0.02995  0.02966  0.02845  0.02827
Cumulative Proportion  0.54557  0.57698  0.60782  0.63777  0.66743  0.69588  0.72414
      PC22     PC23     PC24     PC25     PC26     PC27     PC28
Standard deviation  0.9491  0.94635  0.93914  0.9230  0.91295  0.9070  0.8889
Proportion of Variance  0.0277  0.02754  0.02712  0.0262  0.02563  0.0253  0.0243
Cumulative Proportion  0.7519  0.77939  0.80651  0.8327  0.85834  0.8836  0.9079
      PC29     PC30     PC31     PC32
Standard deviation  0.88323  0.86699  0.86000  0.84989
Proportion of Variance  0.02399  0.02312  0.02274  0.02221
Cumulative Proportion  0.93193  0.95504  0.97779  1.00000
> 
```

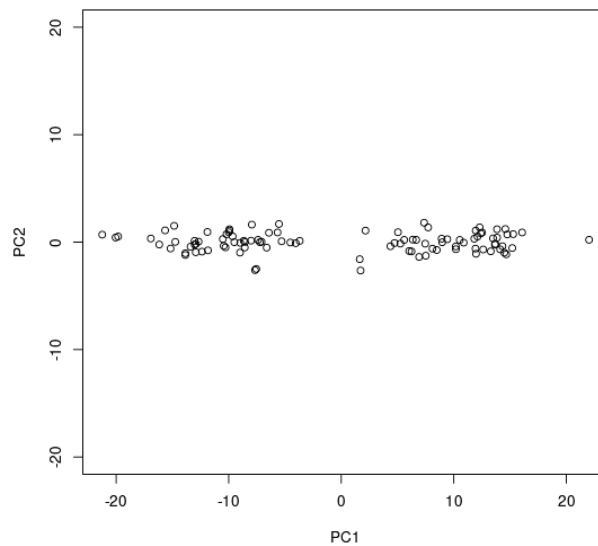
```
> set.seed(1988)
> library(MASS)
> n <- 100
> Sigma <- matrix(c(9, 9 * 0.9, 9 * 0.92, 9 * 1), 2, 2)
> x <- rbind(mvrnorm(n / 2, c(69, 69), Sigma),
+           mvrnorm(n / 2, c(55, 55), Sigma))
>
> dim(x)
[1] 100  2
```



```
> z <- cbind((x[,2] + x[,1])/2, x[,2] - x[,1])
```



```
> summary(prcomp(x))
Importance of components:
              PC1    PC2
Standard deviation  11.357  0.88114
Proportion of Variance  0.994  0.00598
Cumulative Proportion  0.994  1.00000
```



```

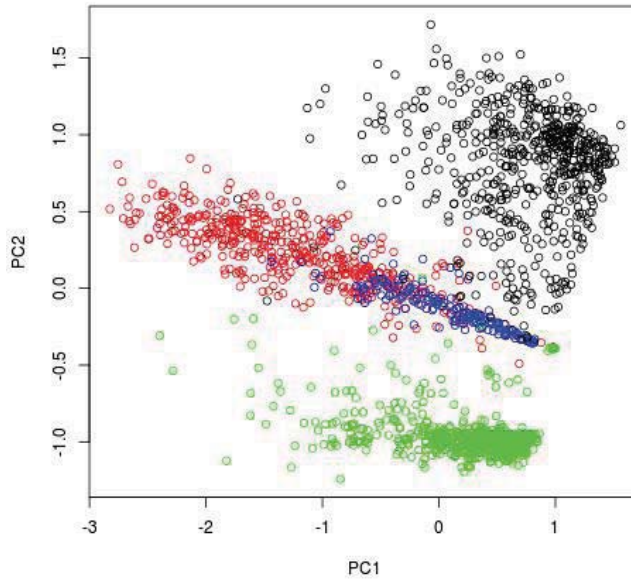
> head(USArrests)
      Murder Assault UrbanPop Rape
Alabama   13.2    236      58 21.2
Alaska   10.0    263      48 44.5
Arizona   8.1    294      80 31.0
Arkansas  8.8    190      50 19.5
California 9.0    276      91 40.6
Colorado  7.9    204      78 38.7
>
> pca_usarrests <- prcomp(USArrests)
> summary(pca_usarrests)
Importance of components:
                PC1      PC2      PC3      PC4
Standard deviation  83.7324 14.21240 6.4894 2.48279
Proportion of Variance 0.9655 0.02782 0.0058 0.00085
Cumulative Proportion 0.9655 0.99335 0.9991 1.00000
>
> pca_usarrests$rotation
      PC1      PC2      PC3      PC4
Murder  0.04170432 -0.04482166 0.07989066 -0.99492173
Assault 0.99522128 -0.05876003 -0.06756974 0.03893830
UrbanPop 0.04633575 0.97685748 -0.20054629 -0.05816914
Rape    0.07515550 0.20071807 0.97408059 0.07232502
  
```

sklearn.decomposition.PCA

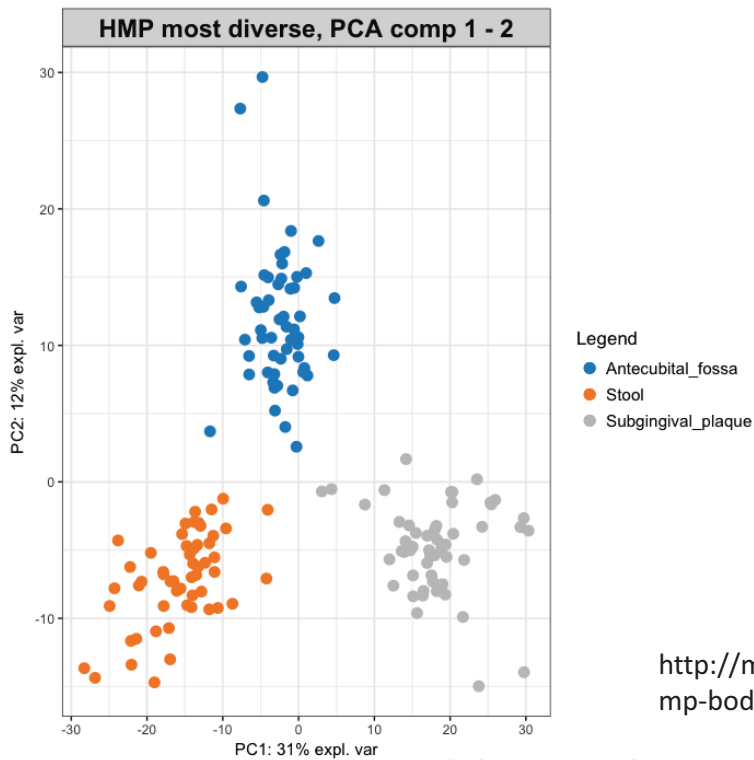
```
class sklearn.decomposition.PCA(n_components=None, *, copy=True, whiten=False, svd_solver='auto', tol=0.0,
iterated_power='auto', random_state=None)
```

[\[source\]](#)

<https://scikit-learn.org/stable/modules/generated/sklearn.decomposition.PCA.html>



Red: COADREAD
 Blue: GBM
 Black: HNSC
 Green: PRAD



<http://mixomics.org/mixmc/case-study-hmp-bodysites-repeated-measures/>

Independent Component Analysis (ICA)

ICA

- Independent component analysis (ICA) is a method for finding underlying factors or components from multivariate (multi-dimensional) statistical data.
- It looks for components that are both *statistically independent*, and *nonGaussian*.
- The two broadest definitions of independence for ICA are
 - 1) Minimization of Mutual Information
 - 2) Maximization of non-Gaussianity

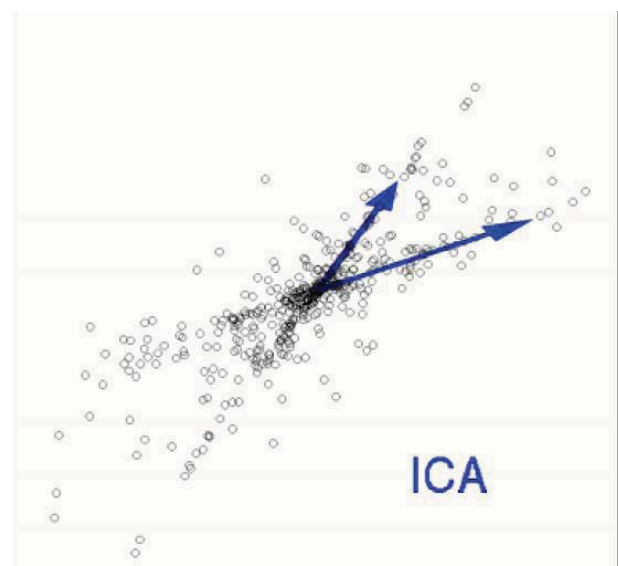
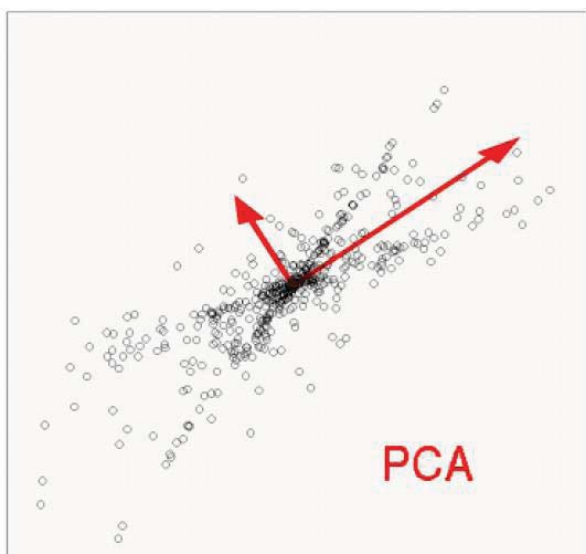
- For example, given two-dimensional vector , $\mathbf{x} = [x_1 \ x_2]^T$, ICA aims at finding the following decomposition

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} a_{11} \\ a_{21} \end{bmatrix} s_1 + \begin{bmatrix} a_{12} \\ a_{22} \end{bmatrix} s_2$$

$$\mathbf{x} = \mathbf{a}_1 s_1 + \mathbf{a}_2 s_2$$

where $\mathbf{a}_1, \mathbf{a}_2$ are **basis vectors** and s_1, s_2 are **basis coefficients**.

- Constraint: Basis coefficients s_1 and s_2 are statistically independent



sklearn.decomposition.FastICA

```
class sklearn.decomposition.FastICA(n_components=None, *, algorithm='parallel', whiten=True, fun='logcosh',  
fun_args=None, max_iter=200, tol=0.0001, w_init=None, random_state=None)
```

[\[source\]](#)

FastICA: a fast algorithm for Independent Component Analysis.

<https://scikit-learn.org/stable/modules/generated/sklearn.decomposition.FastICA.html>

Non-negative Matrix Factorization (NMF)



Letter | Published: 21 October 1999

Learning the parts of objects by non-negative matrix factorization

Daniel D. Lee & H. Sebastian Seung

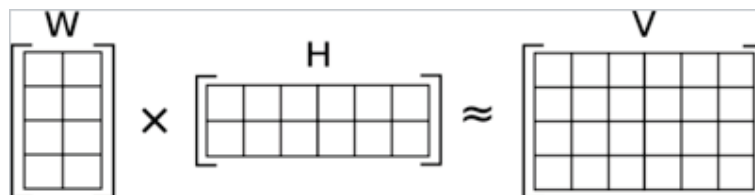
Nature 401, 788–791 (1999) | [Download Citation](#)

Algorithms for Non-negative Matrix Factorization

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NMF

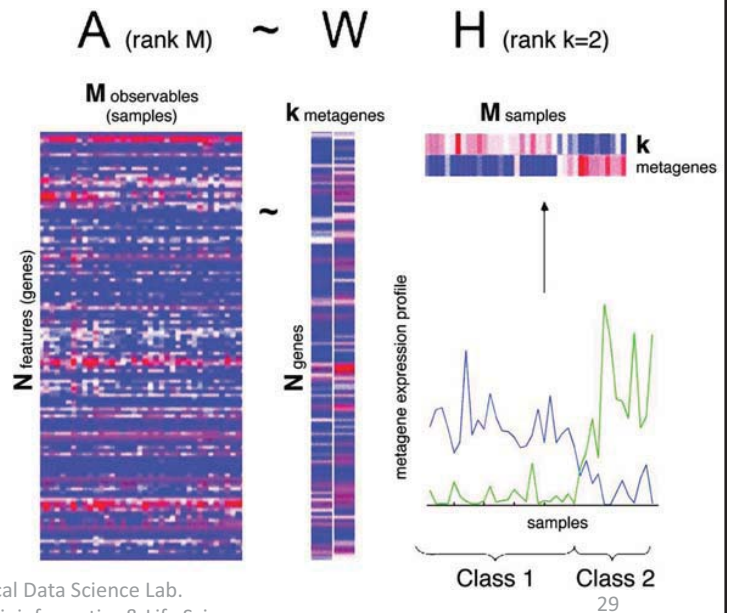


From Wikipedia

- **Non-negative matrix factorization (NMF or NNMF)**, also **non-negative matrix approximation** is a group of algorithms in multivariate analysis and linear algebra where a matrix **V** is factorized into (usually) two matrices **W** and **H**, with the property that all three matrices have no negative elements.
- The matrix **V** is represented by the two smaller matrices **W** and **H**, which, when multiplied, approximately reconstruct **V**.

Metagenes and molecular pattern discovery using matrix factorization

Jean-Philippe Brunet, Pablo Tamayo, Todd R. Golub, and Jill P. Mesirov
 PNAS March 23, 2004 101 (12) 4164-4169; https://doi.org/10.1073/pnas.0308531101



NATURE | ARTICLE



日本語要約

Signatures of mutational processes in human cancer

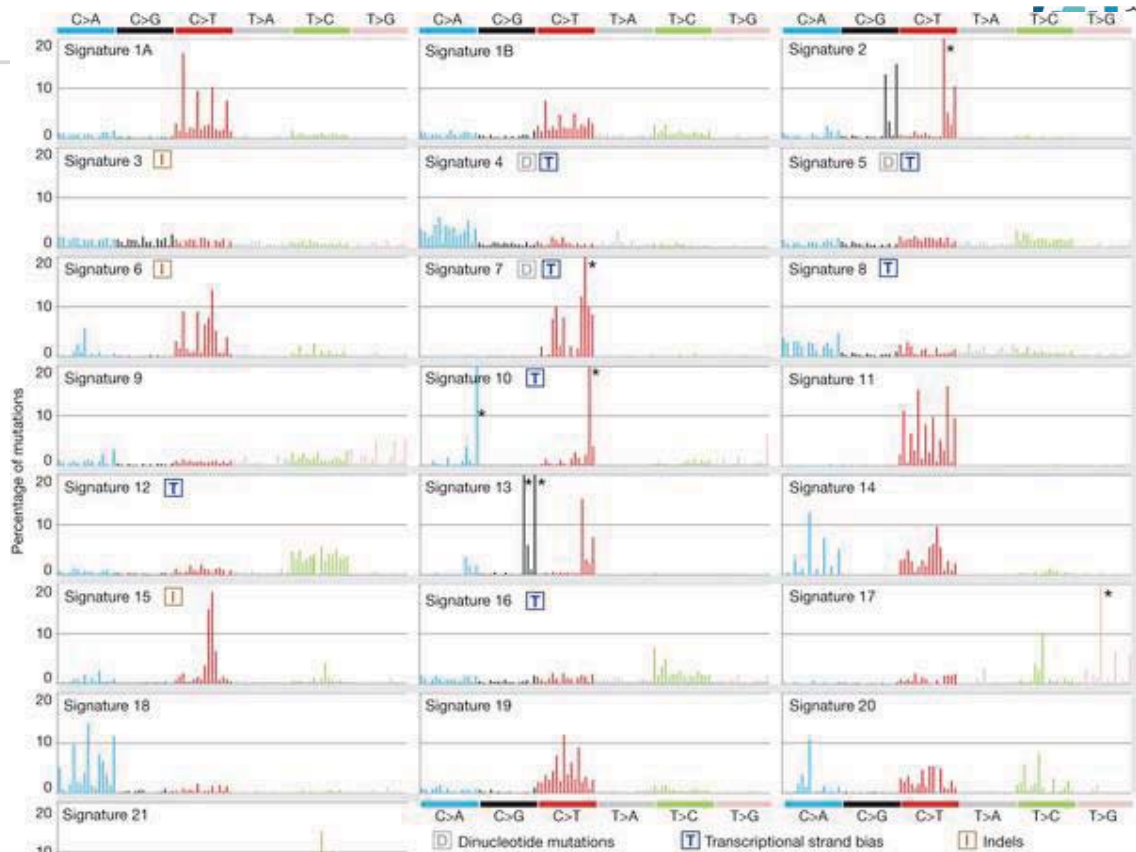
Ludmil B. Alexandrov, Serena Nik-Zainal, David C. Wedge, Samuel A. J. R. Aparicio, Sam Behjati, Andrew V. Biankin, Graham R. Bignell, Niccolò Bolli, Ake Borg, Anne-Lise Børresen-Dale, Sandrine Boyault, Birgit Burkhardt, Adam P. Butler, Carlos Caldas, Helen R. Davies, Christine Desmedt, Roland Eils, Jörunn Eira Eyfjörd, John A. Foekens, Mel Greaves, Fumie Hosoda, Barbara Hutter, Tomislav Illicic, Sandrine Imbeaud, Marcin Imielinski + et al.

Affiliations | Contributions | Corresponding author

Nature 500, 415–421 (22 August 2013) | doi:10.1038/nature12477



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COSMIC
Catalogue of somatic mutations in cancer

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Signatures in Human Cancer

Somatic mutations are mutations that occur in the DNA of somatic cells of the human body and occur throughout life. They are the consequence of multiple processes including the intrinsic slight infidelity of the DNA replication machinery, environmental exposures, enzymatic modification of DNA and defective DNA repair. Different combinations of mutation types, termed "Mutational Signatures".

In the past few years, large-scale genomic studies have revealed many mutational signatures across the spectrum of human cancer (Alexandrov L.B. et al., Cell Reports (2013); Alexandrov L.B. et al., Nature (2013); Alexandrov L.B. and Stratton M.R., Curr Opin Genet Dev (2014)). However, as the number of cancer types and the amount of genomic data has increased, the need for a curated census of signatures has become apparent. Here, we deliver such additional information about, known mutational signatures.

The current COSMIC census is based on an analysis of 10,952 exomes and 1,048 whole-genomes across 40 distinct cancer types. The data were generated by The Cancer Genome Atlas (TCGA), the International Cancer Genome Consortium (ICGC), and a large set of freely available somatic mutations published in peer-reviewed journals. The data sources will be provided in future releases of COSMIC.

The profile of each signature is based on the six substitution subtypes: C>A, C>G, C>T, T>A, T>C, and T>G (all substitutions are relative to the mutated Watson-Crick base pair). Further, each of the substitutions is examined by incorporating information on the bases immediately 5' and 3' to each mutated base generating 96 possible mutation types (6 types of substitution × 4 types of 5' base × 4 types of 3' base). Mutational signatures are displayed and reported based on the observed trinucleotide frequency of the human genome, i.e., representing the relative proportions of mutations generated by each signature based on the actual trinucleotide frequencies of the reference human genome version GRCh37. Note that only validated mutational signatures have been included in the curated census of mutational signatures.

Additional information is provided for each signature, including the cancer types in which the signature has been found, proposed aetiology for the mutational processes underlying the signature, other mutational features that are associated with each signature and information that may be relevant for better understanding of a particular mutational signature.

Mutational signatures across human cancer

Patterns of mutational signatures (Download signatures)

```
# Install
install.packages('NMF')
# Load
library(NMF)
```

```
mat <- matrix(runif(n= 200, min= 0, max=
100), nrow= 30, ncol= 10)

res<- nmf(mat, rank= 2)
w<- basis(res)
h<- coef(res)

w %*% h # ~ mat
dim(w) # 30 2
```


sklearn.decomposition.NMF

```
class sklearn.decomposition.NMF(n_components=None, *, init='warn', solver='cd', beta_loss='frobenius', tol=0.0001,
max_iter=200, random_state=None, alpha=0.0, l1_ratio=0.0, verbose=0, shuffle=False, regularization='both') \[source\]
```

Non-Negative Matrix Factorization (NMF).

Examples

```
>>> import numpy as np
>>> X = np.array([[1, 1], [2, 1], [3, 1.2], [4, 1], [5, 0.8], [6, 1]])
>>> from sklearn.decomposition import NMF
>>> model = NMF(n_components=2, init='random', random_state=0)
>>> W = model.fit_transform(X)
>>> H = model.components_
```

Methods

<code>fit(X[, y])</code>	Learn a NMF model for the data X.
<code>fit_transform(X[, y, W, H])</code>	Learn a NMF model for the data X and returns the transformed data.
<code>get_params([deep])</code>	Get parameters for this estimator.
<code>inverse_transform(W)</code>	Transform data back to its original space.
<code>set_params(**params)</code>	Set the parameters of this estimator.
<code>transform(X)</code>	Transform the data X according to the fitted NMF model.

<https://scikit-learn.org/stable/modules/generated/sklearn.decomposition.NMF.html>

t-SNE

- T-distributed Stochastic Neighbor Embedding (t-SNE) is a machine learning algorithm for visualization developed by Laurens van der Maaten and Geoffrey Hinton.
- It is a nonlinear dimensionality reduction technique well-suited for embedding high-dimensional data for visualization in a low-dimensional space of two or three dimensions.

```
> install.packages("Rtsne")
```

sklearn.manifold.TSNE

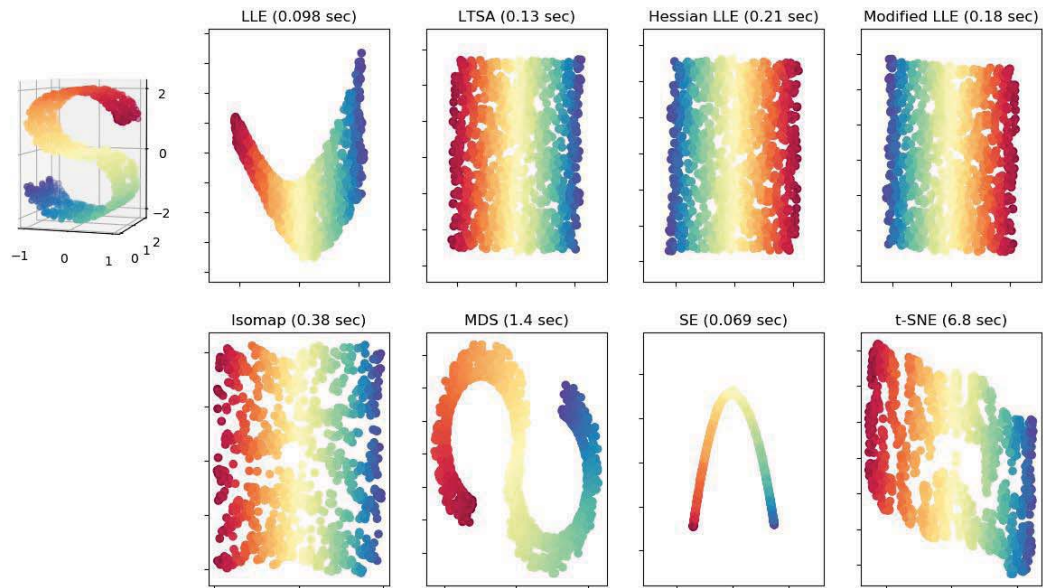
```
class sklearn.manifold.TSNE(n_components=2, *, perplexity=30.0, early_exaggeration=12.0, learning_rate=200.0,  
n_iter=1000, n_iter_without_progress=300, min_grad_norm=1e-07, metric='euclidean', init='random', verbose=0,  
random_state=None, method='barnes_hut', angle=0.5, n_jobs=None, square_distances='legacy')
```

[\[source\]](#)

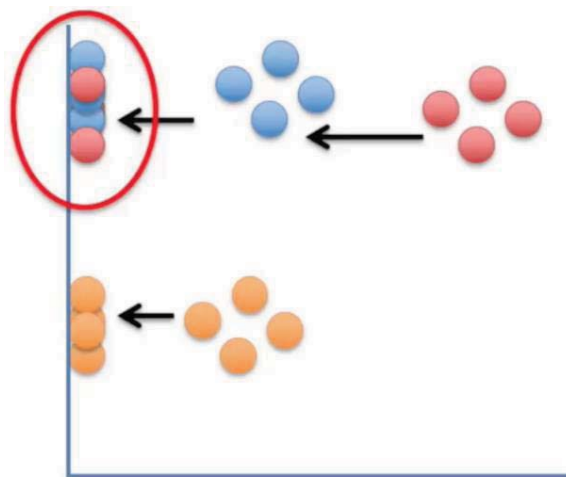
t-distributed Stochastic Neighbor Embedding.

<https://scikit-learn.org/stable/modules/generated/sklearn.manifold.TSNE.html>

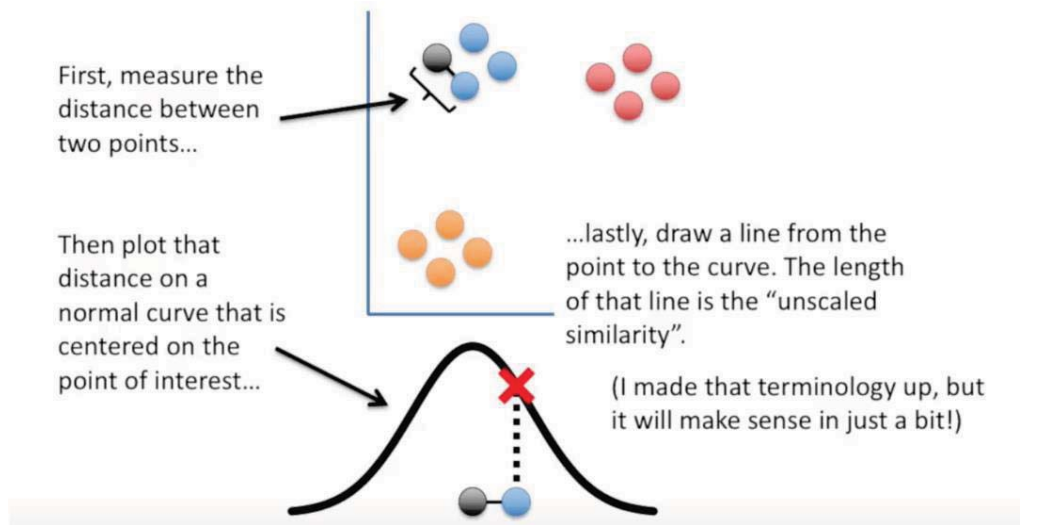
Manifold Learning with 1000 points, 10 neighbors



<https://scikit-learn.org/stable/modules/manifold.html>

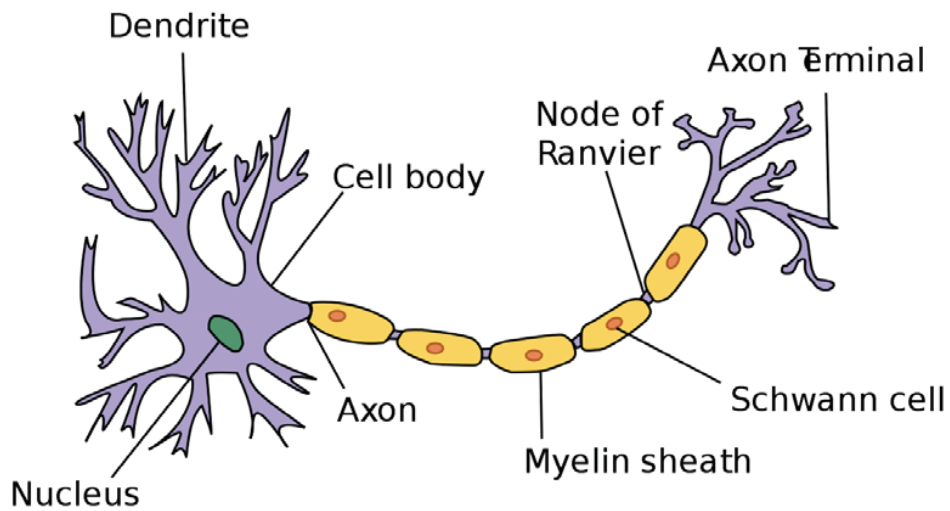


<https://www.youtube.com/watch?v=NEaUSP4YerM>

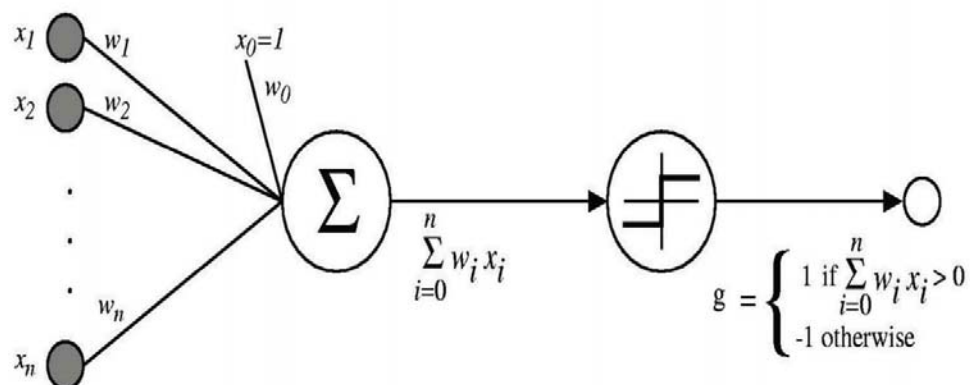


<https://www.youtube.com/watch?v=NEaUSP4YerM>

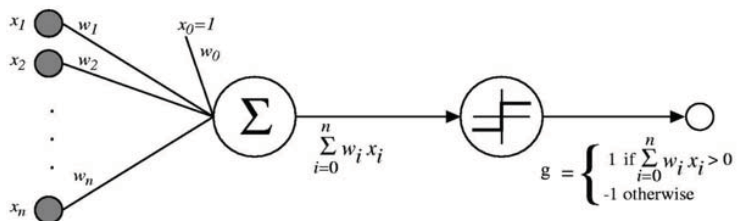
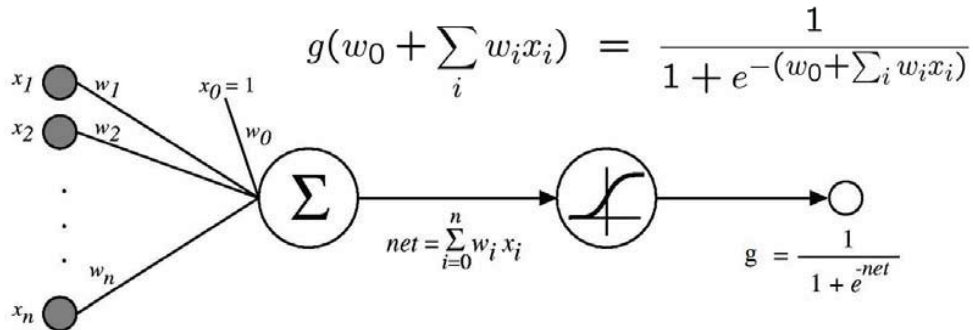
Deep Learning & Autoencoder



Perceptron as a neuron



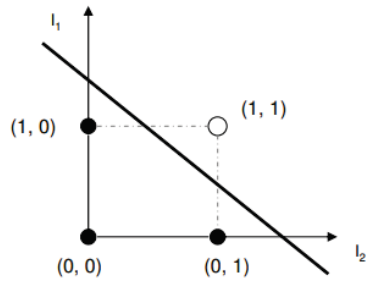
- x_1, x_2, \dots, x_n as inputs
- Sum is passed through **activation function** $g()$



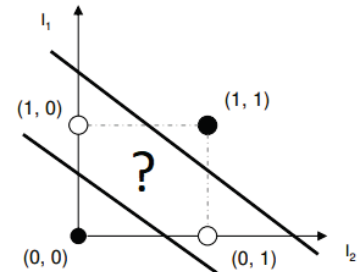
XOR truth table

Input		Output
A	B	
0	0	0
0	1	1
1	0	1
1	1	0

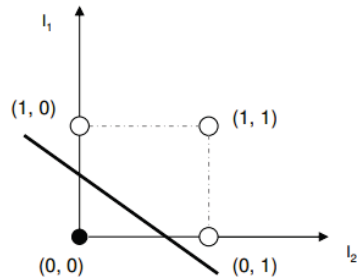
AND		
I_1	I_2	out
0	0	0
0	1	0
1	0	0
1	1	1



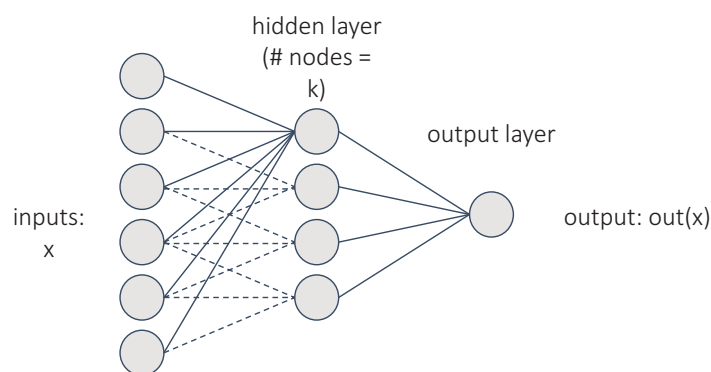
XOR		
I_1	I_2	out
0	0	0
0	1	1
1	0	1
1	1	0



OR		
I_1	I_2	out
0	0	0
0	1	1
1	0	1
1	1	1

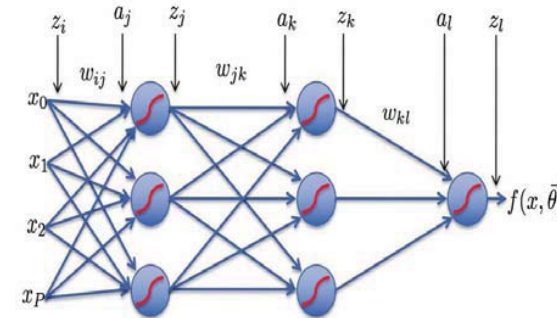


Multilayer perceptron



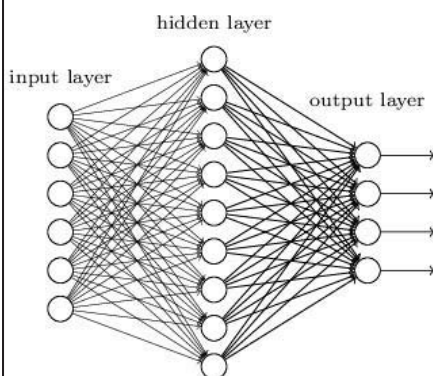
$$out(x) = g(w_0 + \sum w_k g(\sum w_i^k x_i))$$

Backpropagation of errors

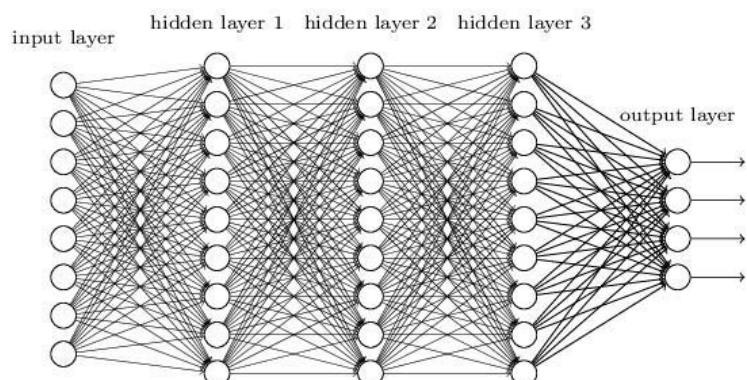
$$\begin{aligned}
 R(\theta) &= \frac{1}{N} \sum_{n=0}^N L(y_n - f(x_n)) && \text{Empirical Risk Function} \\
 &= \frac{1}{N} \sum_{n=0}^N \frac{1}{2} (y_n - f(x_n))^2 \\
 &= \frac{1}{N} \sum_{n=0}^N \frac{1}{2} \left(y_n - g \left(\sum_k w_{kl} g \left(\sum_j w_{jk} g \left(\sum_i w_{ij} x_{n,i} \right) \right) \right) \right)^2
 \end{aligned}$$


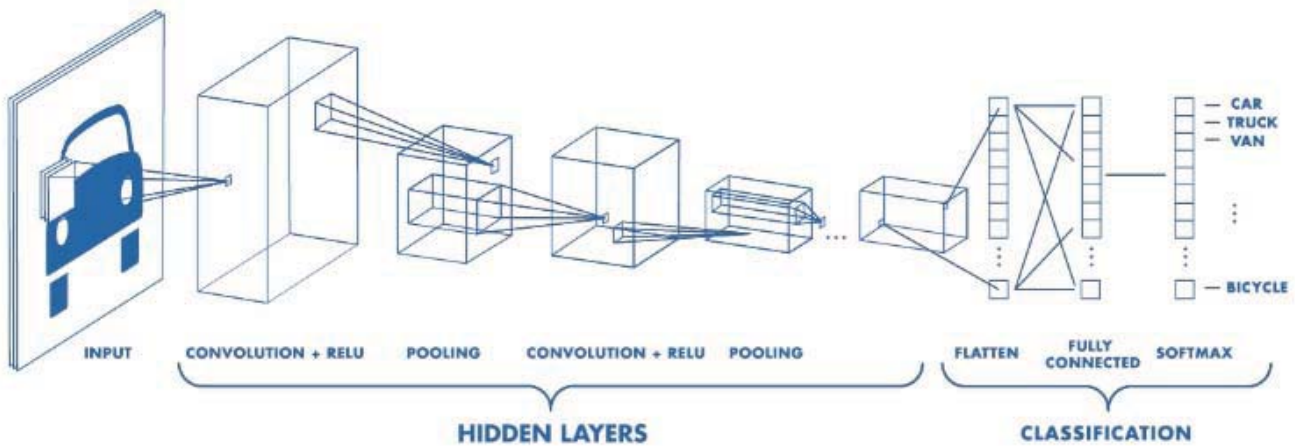
Deep neural networks

"Non-deep" feedforward neural network



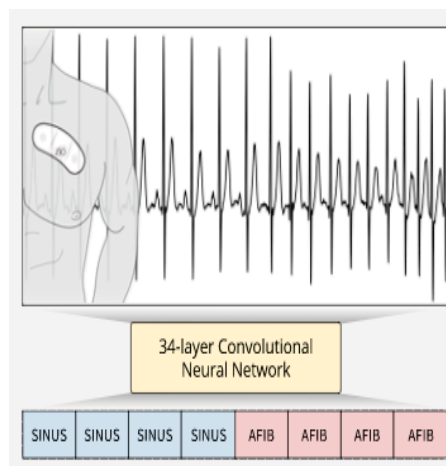
Deep neural network



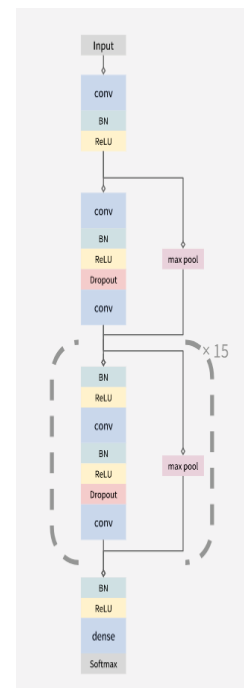


Cardiologist-Level Arrhythmia Detection With Convolutional Neural Networks

- They have a dataset of 64,121 ECG records from 29,163 patients.
- The model outperforms the cardiologist average on both the Sequence and Set F1 metrics



<https://stanfordmlgroup.github.io/projects/ecg/>



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NATURE | LETTER



日本語要約

Dermatologist-level classification of skin cancer with deep neural networks

[Andre Esteva](#), [Brett Kuprel](#), [Roberto A. Novoa](#), [Justin Ko](#), [Susan M. Swetter](#), [Helen M. Blau](#) & [Sebastian Thrun](#)

[Affiliations](#) | [Contributions](#) | [Corresponding authors](#)

Nature **542**, 115–118 (02 February 2017) | doi:10.1038/nature21056

- 5.4 million new cases of skin cancer in USA every year.
- Melanomas represent fewer than 5% but they account for 75% of all skin cancer deaths
- Early detection is critical (survival rate would be 99% at early stage, but 14% at latest stage)

MENU ▾

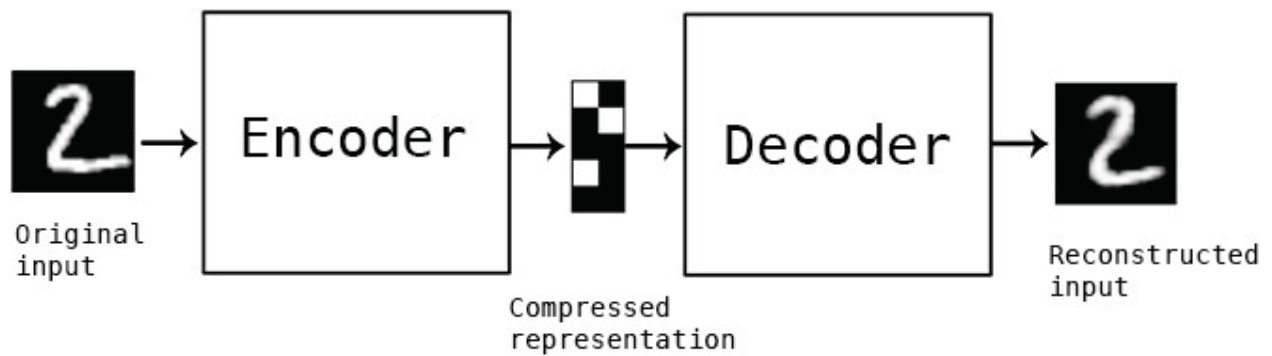
nature
biotechnology

Brief Communication | Published: 29 January 2018

Deep learning improves prediction of CRISPR–Cpf1 guide RNA activity

[Hui Kwon Kim](#), [Seonwoo Min](#), [Myungjae Song](#), [Soobin Jung](#), [Jae Woo Choi](#), [Younggwang Kim](#), [Sangeun Lee](#), [Sunghroh Yoon](#) ✉ & [Hyongbum \(Henry\) Kim](#) ✉

Nature Biotechnology **36**, 239–241 (2018) | [Download Citation](#) ↓



Keras example

```
from keras import layers

# This is the size of our encoded representations
encoding_dim = 32

# This is our input image
input_img = keras.Input(shape=(784,))

# "encoded" is the encoded representation of the input
encoded = layers.Dense(encoding_dim, activation='relu')(input_img)

# "decoded" is the lossy reconstruction of the input
decoded = layers.Dense(784, activation='sigmoid')(encoded)

# This model maps an input to its reconstruction
autoencoder = keras.Model(input_img, decoded)
```


Deep autoencoder

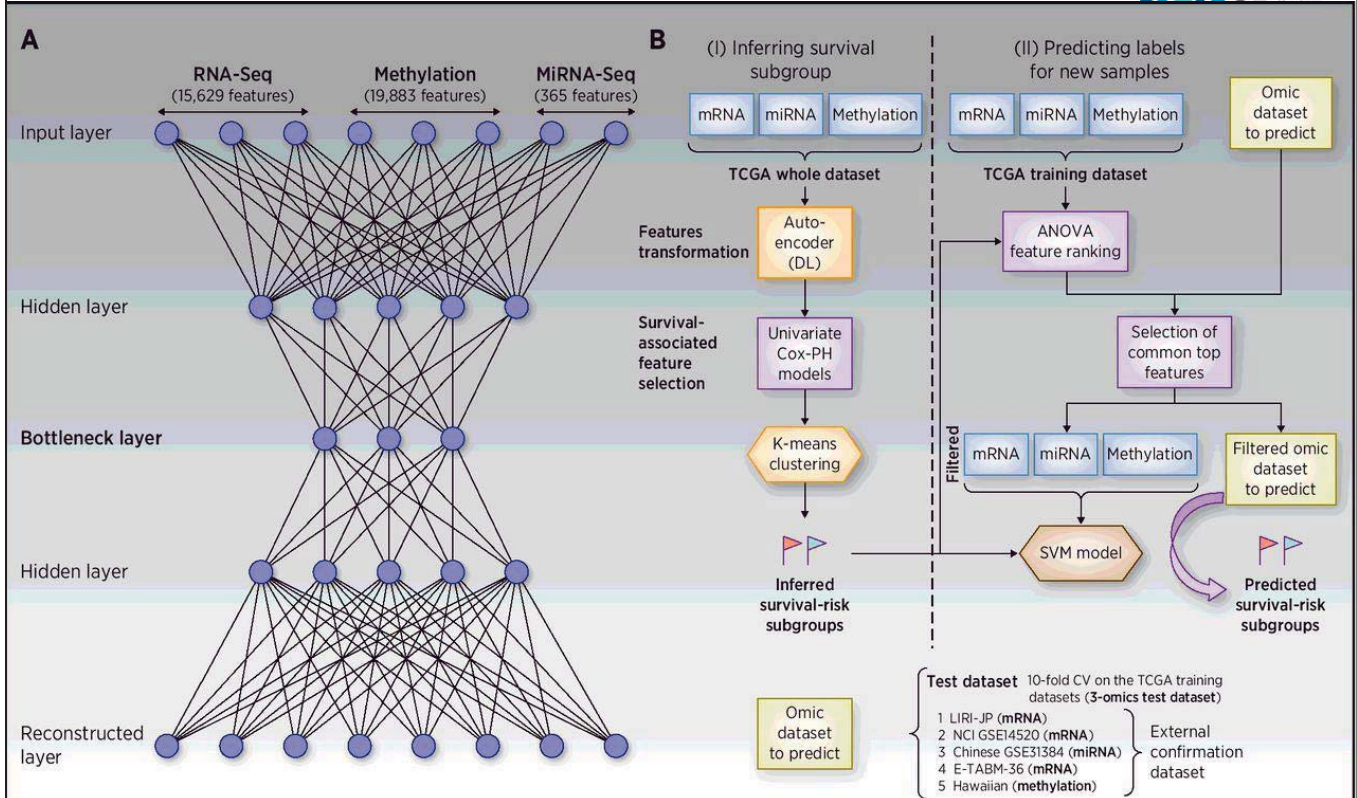
```

input_img = keras.Input(shape=(784,))
encoded = layers.Dense(128, activation='relu')(input_img)
encoded = layers.Dense(64, activation='relu')(encoded)
encoded = layers.Dense(32, activation='relu')(encoded)

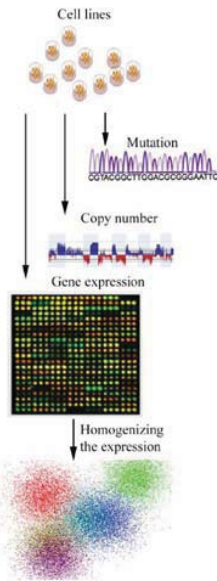
decoded = layers.Dense(64, activation='relu')(encoded)
decoded = layers.Dense(128, activation='relu')(decoded)
decoded = layers.Dense(784, activation='sigmoid')(decoded)

autoencoder = keras.Model(input_img, decoded)
autoencoder.compile(optimizer='adam', loss='binary_crossentropy')

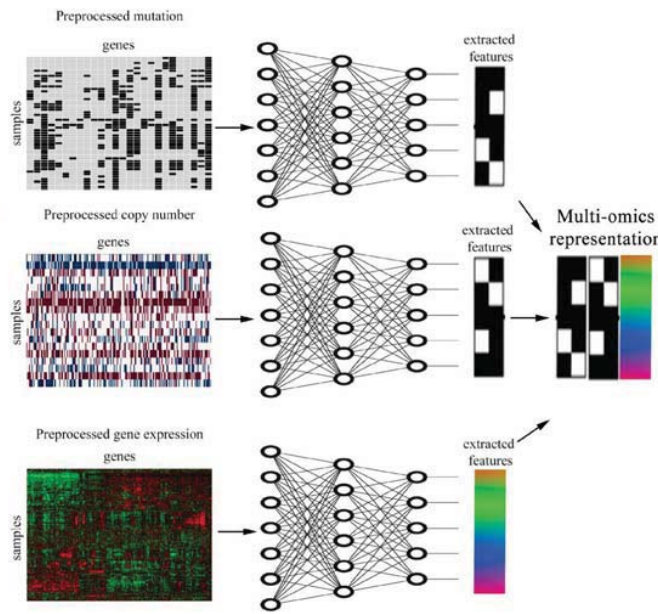
autoencoder.fit(x_train, x_train,
                epochs=100,
                batch_size=256,
                shuffle=True,
                validation_data=(x_test, x_test))
    
```



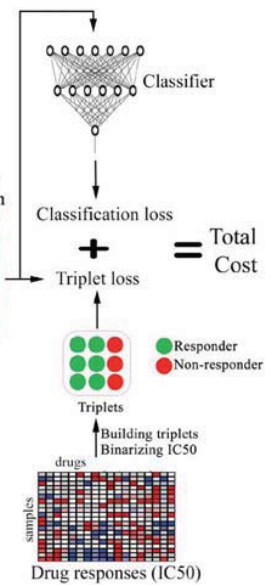
A Preprocessing the input data



B Encoding subnetworks



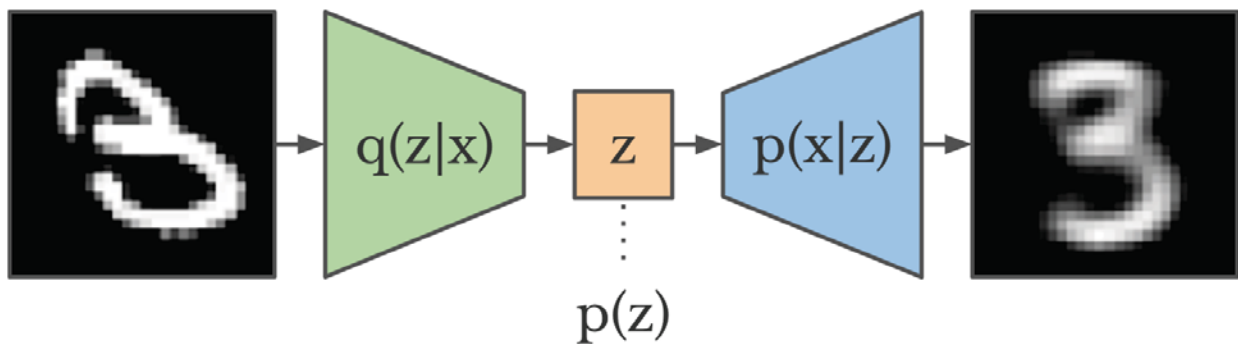
C Optimization of features



<https://academic.oup.com/bioinformatics/article/35/14/i501/5529255>

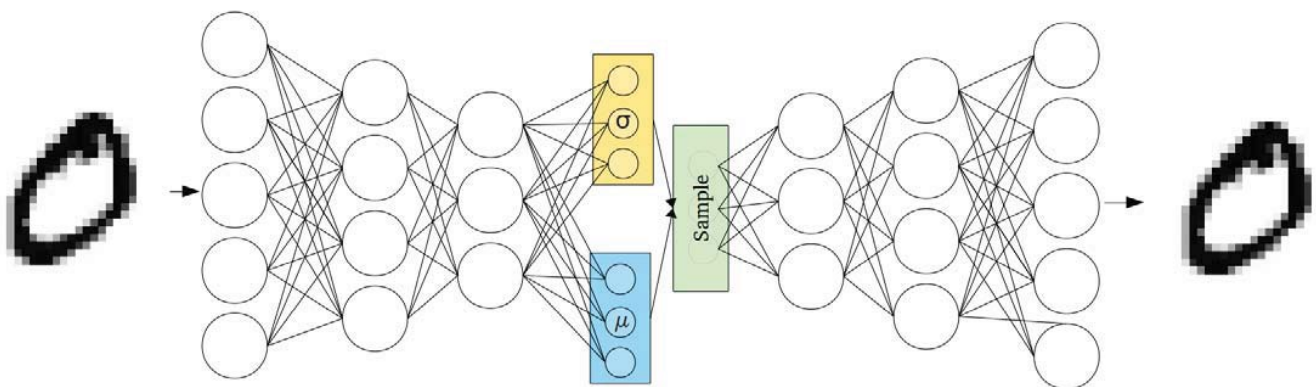
Variational Autoencoder

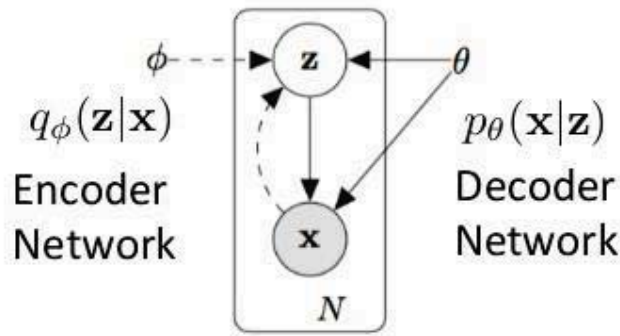
A VAE consist of three components: an encoder $q(z|x)$, a prior $p(z)$, and a decoder $p(x|z)$.



<https://danijar.com/building-variational-auto-encoders-in-tensorflow/>

- Autoencoders learn a “compressed representation” of input (*could be image, text sequence etc.*) automatically by first compressing the input (*encoder*) and decompressing it back (*decoder*) to match the original input.
- Variational autoencoders learn the parameters of a probability distribution representing the data. Since it learns to model the data, we can sample from the distribution and generate new input data samples.



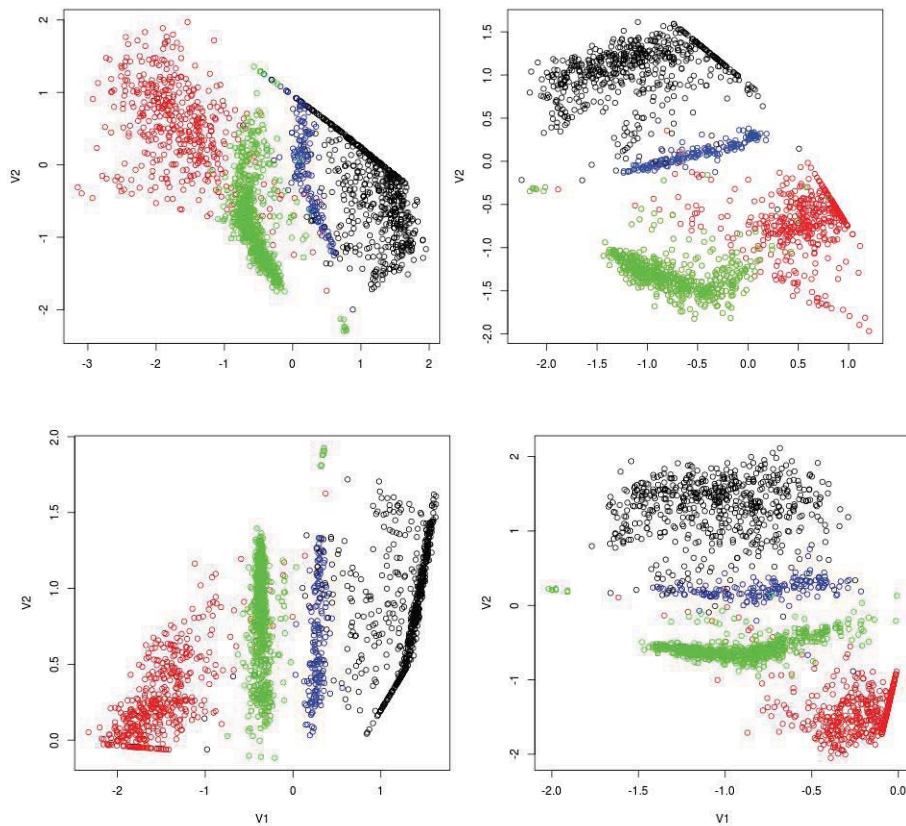


Minimize: $D_{KL}[q_{\phi}(\mathbf{z}|\mathbf{x})||p_{\theta}(\mathbf{z}|\mathbf{x})]$

Intractable: $p_{\theta}(\mathbf{z}|\mathbf{x}) = \frac{p_{\theta}(\mathbf{x}|\mathbf{z})p_{\theta}(\mathbf{z})}{p_{\theta}(\mathbf{x})}$

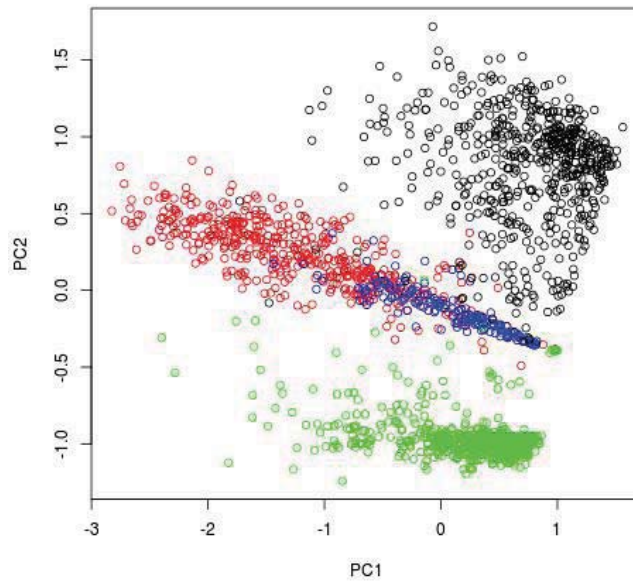
<https://www.slideshare.net/ckmarkohchang/variational-autoencoder>

VAE – TCGA expression



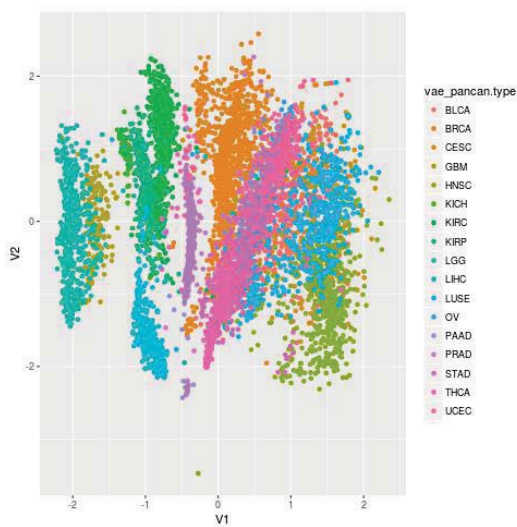
Red: COADREAD
Blue: GBM
Black: HNSC
Green: PRAD

PCA

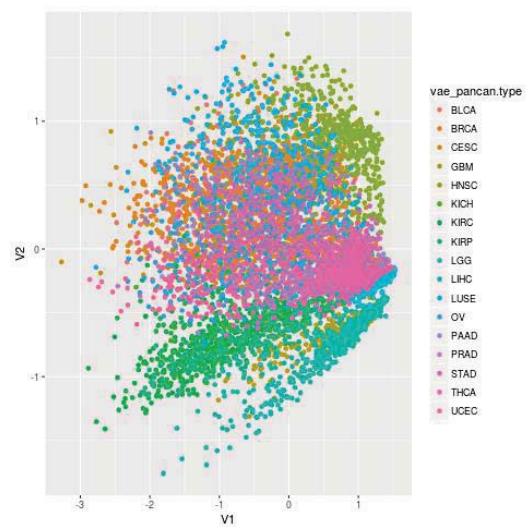


Red: COADREAD
Blue: GBM
Black: HNSC
Green: PRAD

VAE



PCA



Thank you