Artificial Intelligence in Medicine

Real-life data

Nir Friedman and Tommy Kaplan 2/1/23

האוניברסיטה
העברית
בירושלים
THE HEBREW
UNIVERSITY
OF JERUSALEM

Why neural networks?

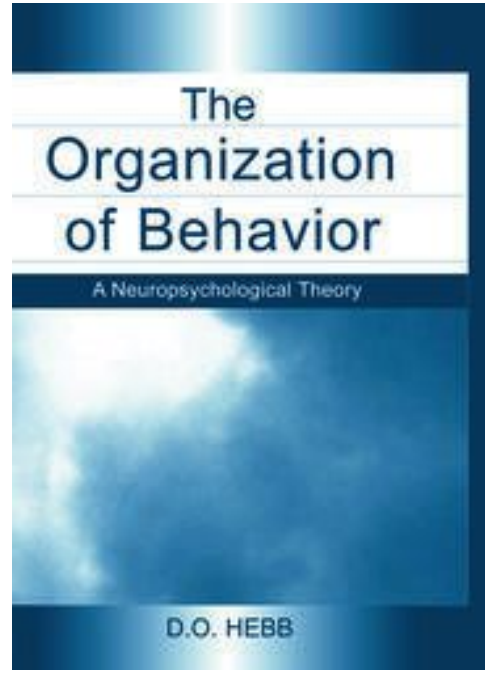
BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 5, 1943

A LOGICAL CALCULUS OF THE
IDEAS IMMANENT IN NERVOUS ACTIVITY

WARREN S. MCCULLOCH AND WALTER PITTS

FROM THE UNIVERSITY OF ILLINOIS, COLLEGE OF MEDICINE,
DEPARTMENT OF PSYCHIATRY AT THE ILLINOIS NEUROPSYCHIATRIC INSTITUTE,
AND THE UNIVERSITY OF CHICAGO

Because of the "all-or-none" character of nervous activity, neural events and the relations among them can be treated by means of propositional logic. It is found that the behavior of every net can be described in these terms, with the addition of more complicated logical means for nets containing circles; and that for any logical expression satisfying certain conditions, one can find a net behaving in the fashion it describes. It is shown that many particular choices among possible neurophysiological assumptions are equivalent, in the sense that for every net behaving under one assumption, there exists another net which behaves under the other and gives the same results, although perhaps not in the same time. Various applications of the calculus are discussed.



1949

J. Physiol. (1959) 148, 574–591

RECEPTIVE FIELDS OF SINGLE NEURONES IN
THE CAT'S STRIATE CORTEX

BY D. H. HUBEL* AND T. N. WIESEL*

*From the Wilmer Institute, The Johns Hopkins Hospital and
University, Baltimore, Maryland, U.S.A.*

J. Physiol. (1962), **160**, *pp.* 106–154

RECEPTIVE FIELDS, BINOCULAR INTERACTION
AND FUNCTIONAL ARCHITECTURE IN
THE CAT'S VISUAL CORTEX

BY D. H. HUBEL AND T. N. WIESEL

*From the Neurophysiology Laboratory, Department of Pharmacology
Harvard Medical School, Boston, Massachusetts, U.S.A.*

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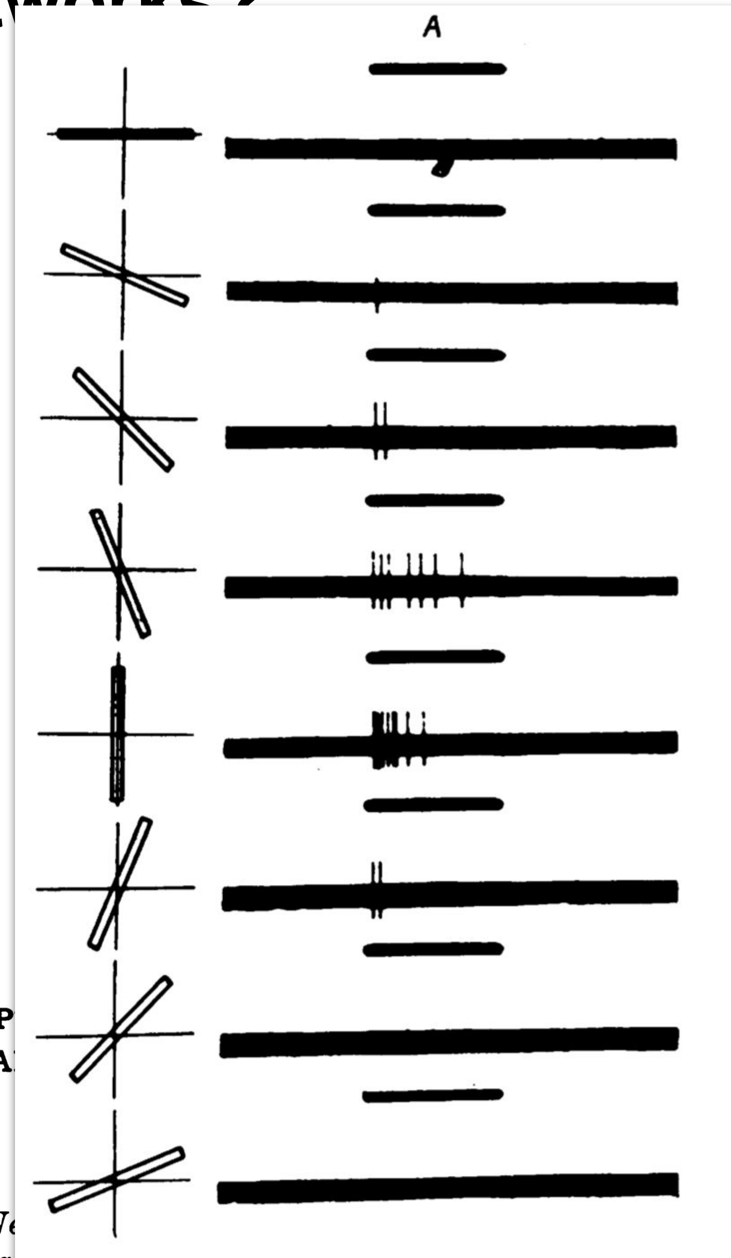
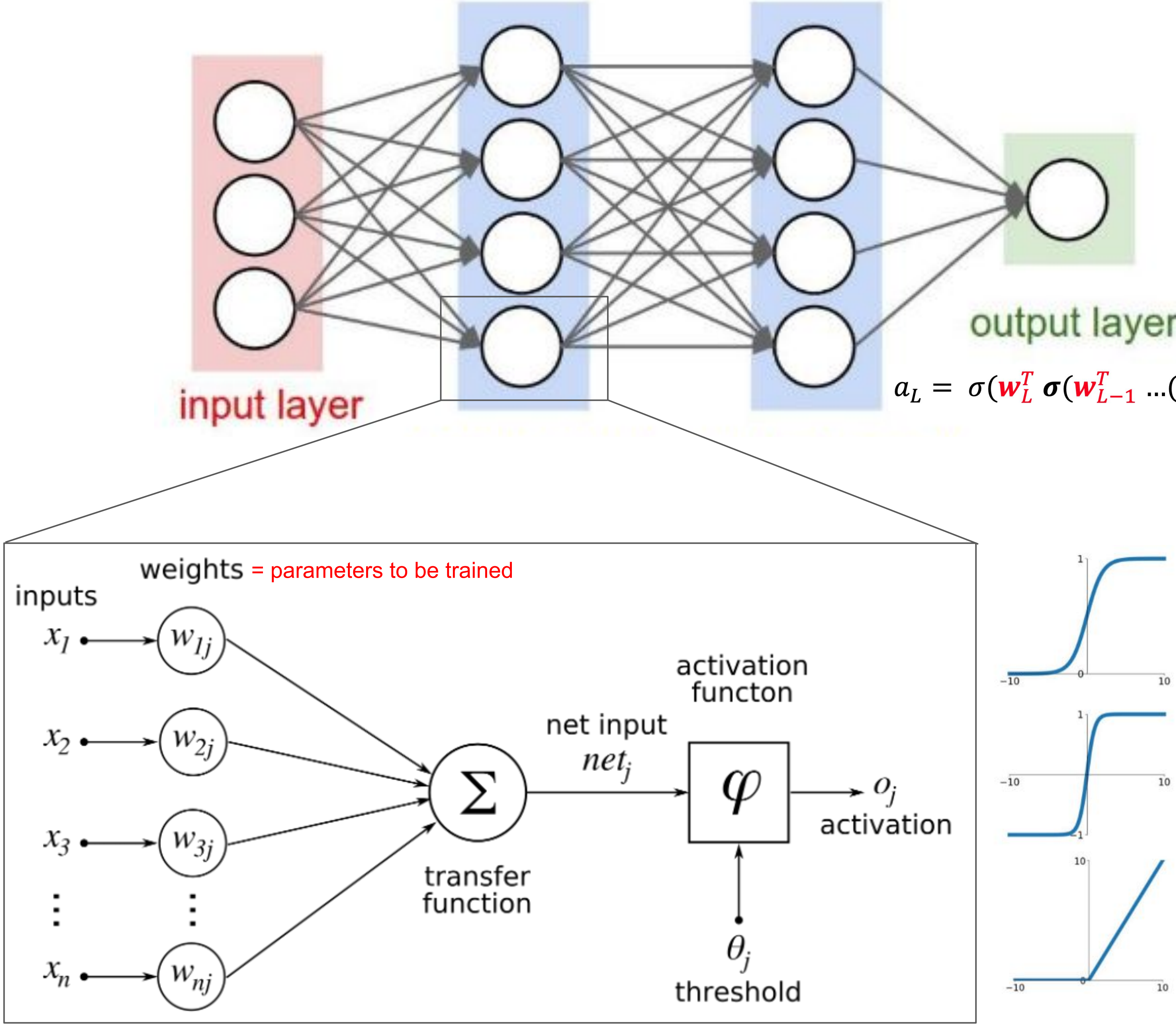


-154

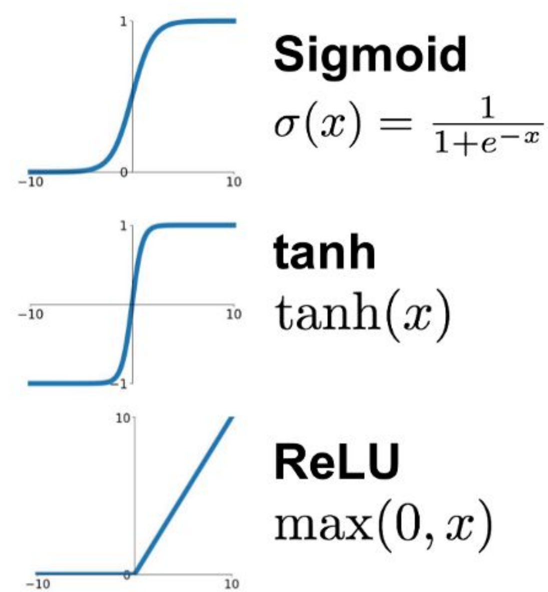
RECEP

A

From the Ne ... gy
Harva...

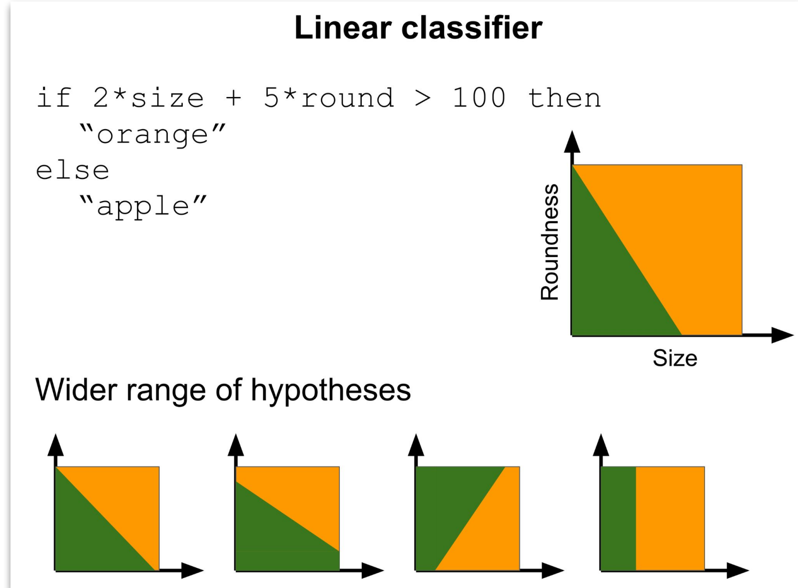


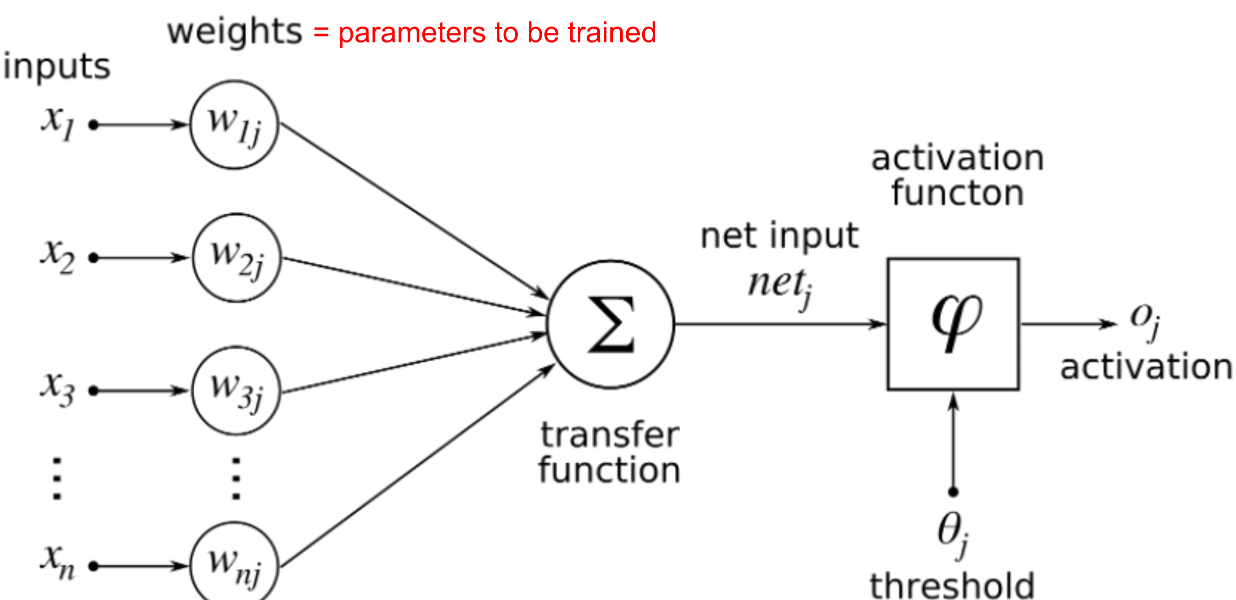
$$a_L = \sigma(\boldsymbol{w}_L^T\ \boldsymbol{\sigma}(\boldsymbol{w}_{L-1}^T \ldots(\boldsymbol{w}_1^T\ \mathbf{x} + b_1) \ldots) + b_L)$$

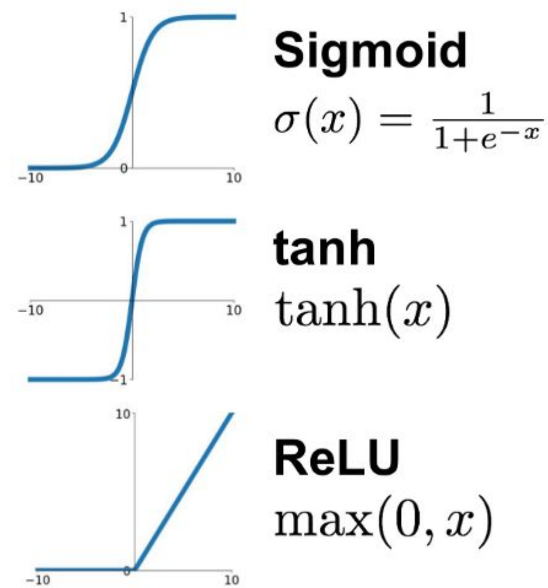


“Neuron” ≈ linear classifier

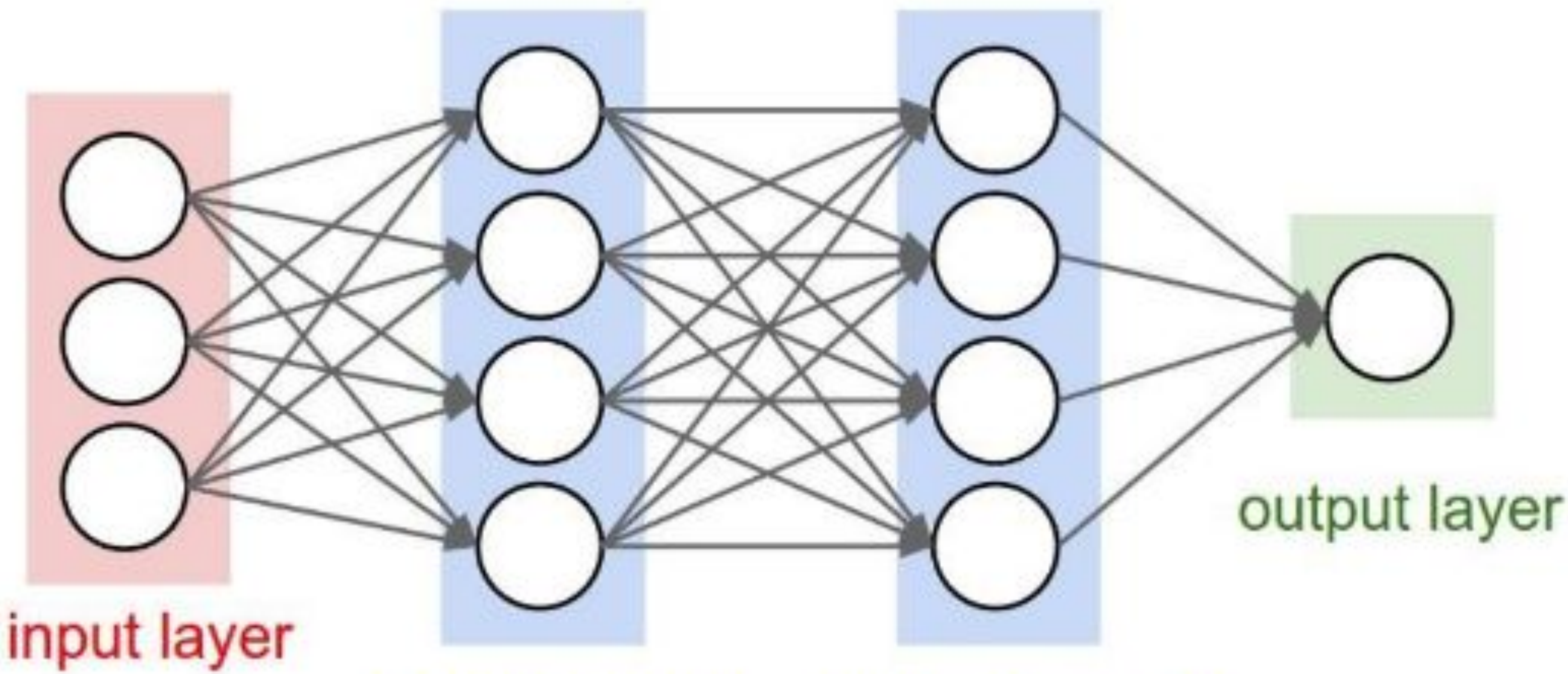
- Smoothed non-binary output
- No temporal dynamics
- Parameter learning ≈ Hebbian learning







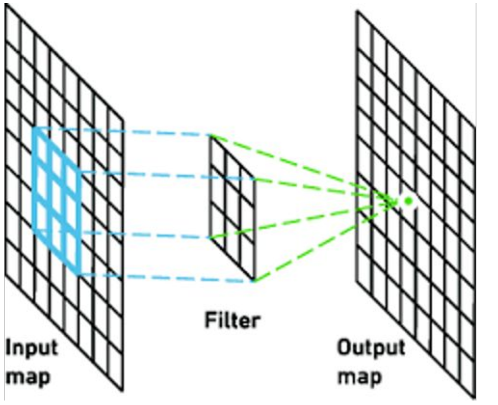
Fully connected network



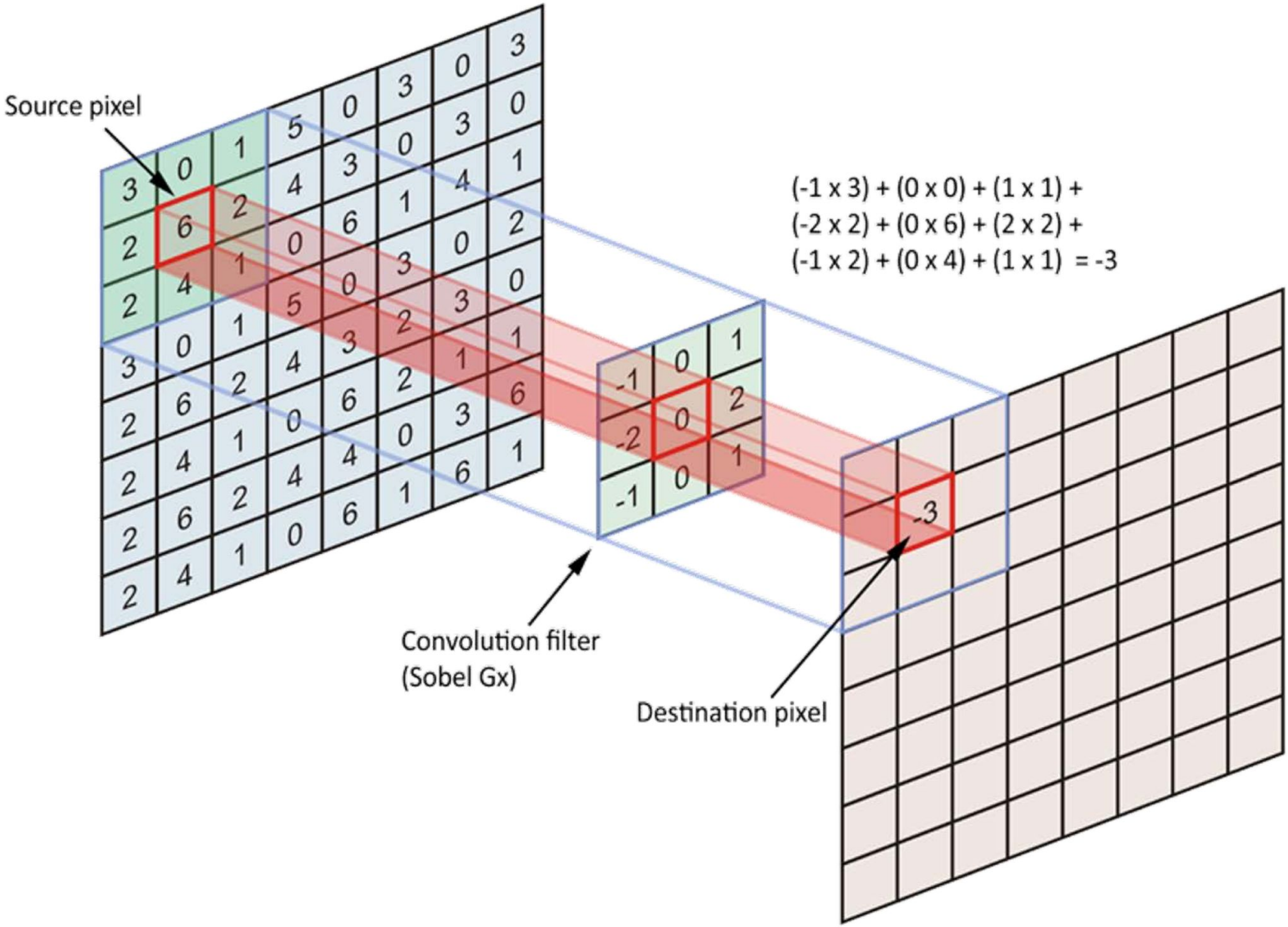
Convolutional neural network

Few changes from fully connected networks

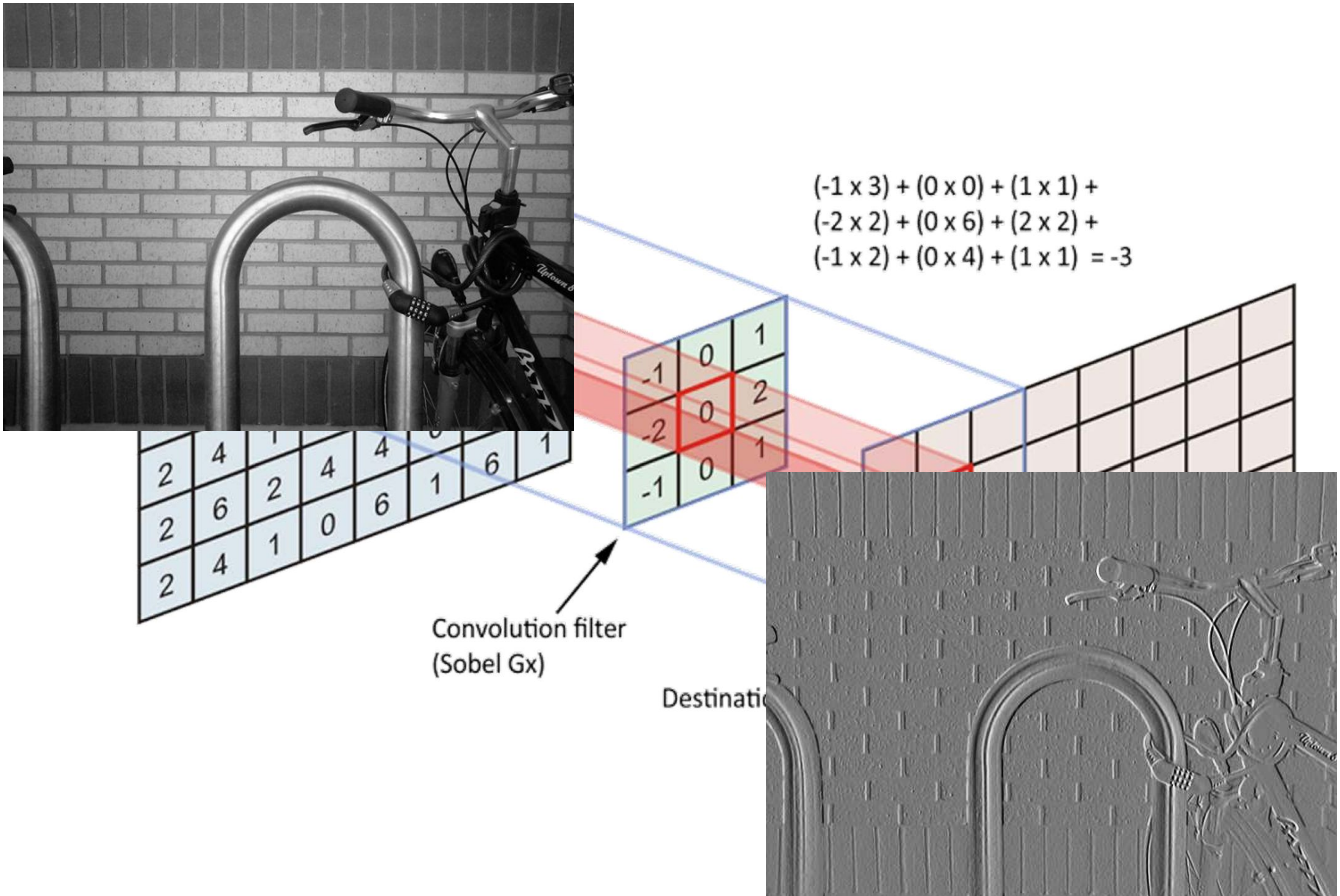
1. A neuron is not connected to all neurons (in prev. layer)
2. Keep it local
3. Use the same filter across all regions



Convolutional neural network - filters



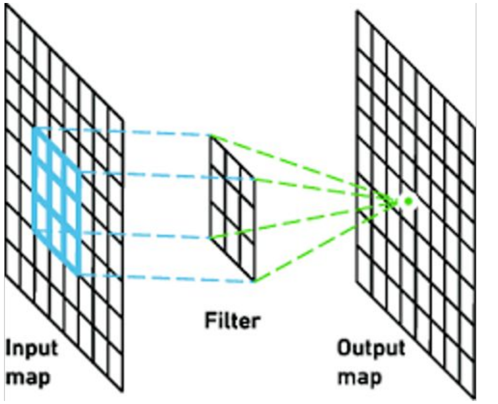
Convolutional neural network - filters

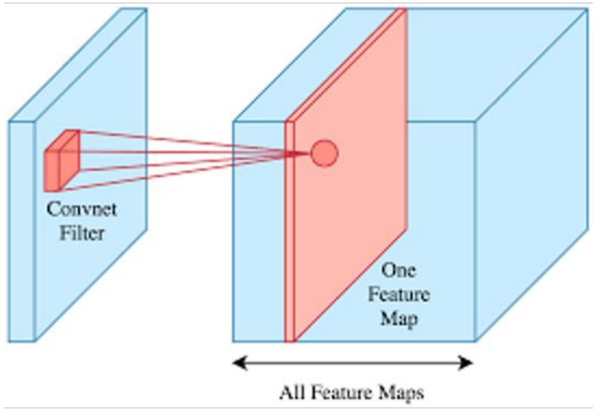


Convolutional neural network

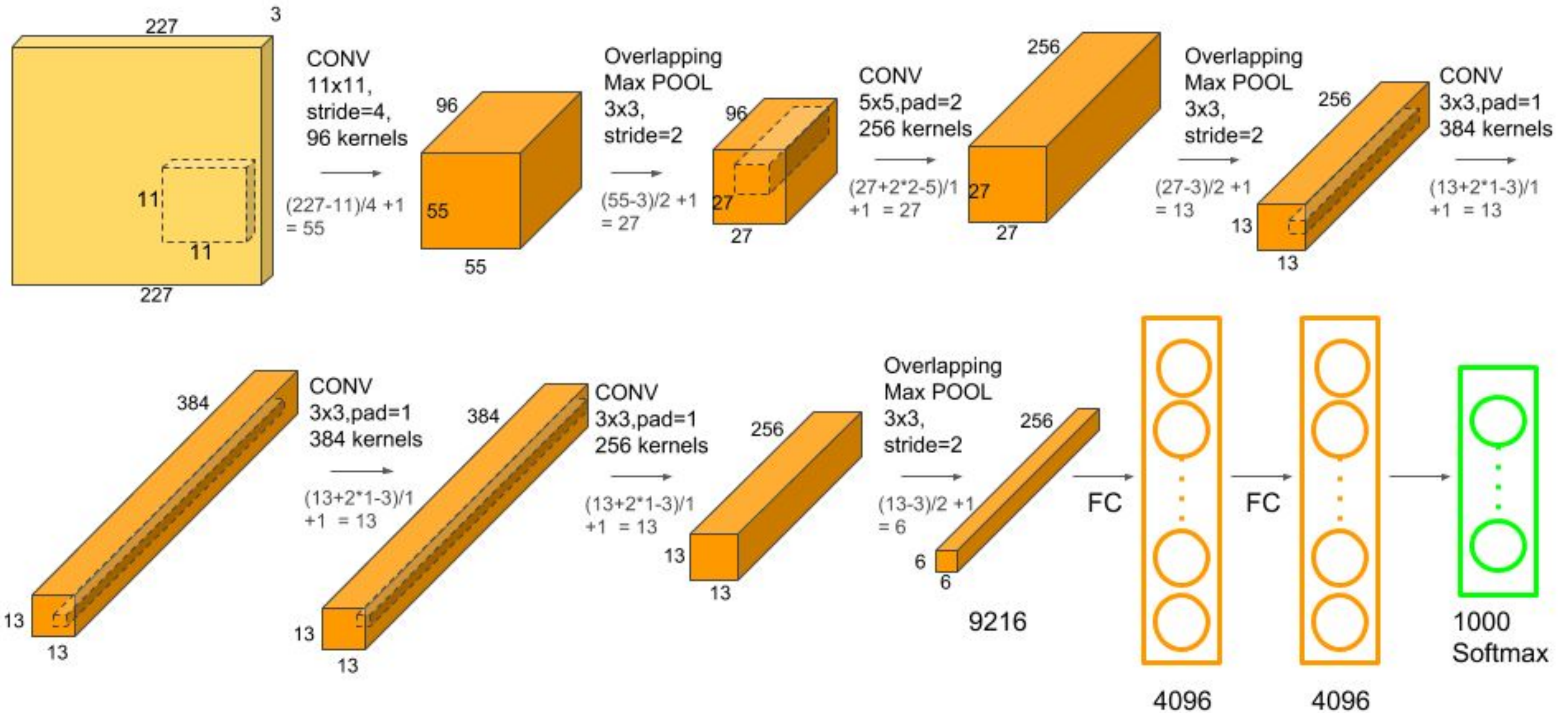
Few changes from fully connected networks

1. A neuron is not connected to all neurons (in prev. layer)
2. Keep it local
3. Use the same filter across all regions
4. Use more than one filter





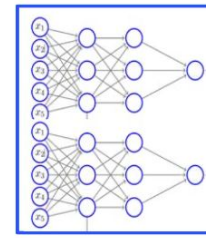
Convolutional neural network - architecture

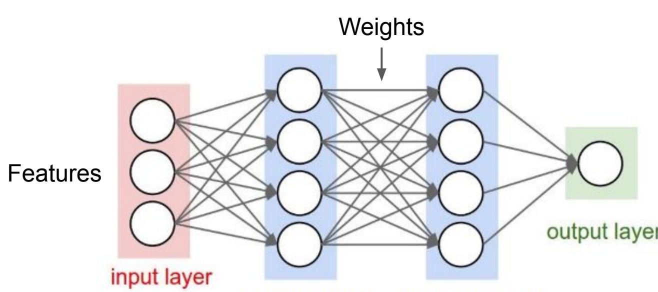


AlexNet, 2012

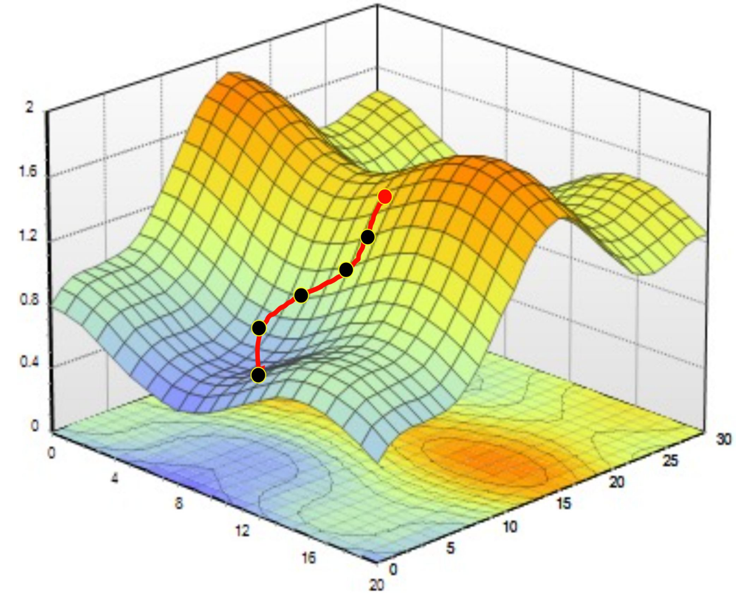
From engineering to learning to deep learning

Manual modeling		Machine learning		Deep learning	
 ***Features*** *intensity, texture shape, location*	MANUAL	***Features*** *intensity, texture shape, location*	MANUAL	***Features*** *Derived from data Implicit*	AUTOM
 ***Relations*** *Boundary differences, …*	MANUAL	***Relations*** *Derived by regression, SVM,…*	AUTOM	***Relations*** *Derived from data Implicit*	AUTOM

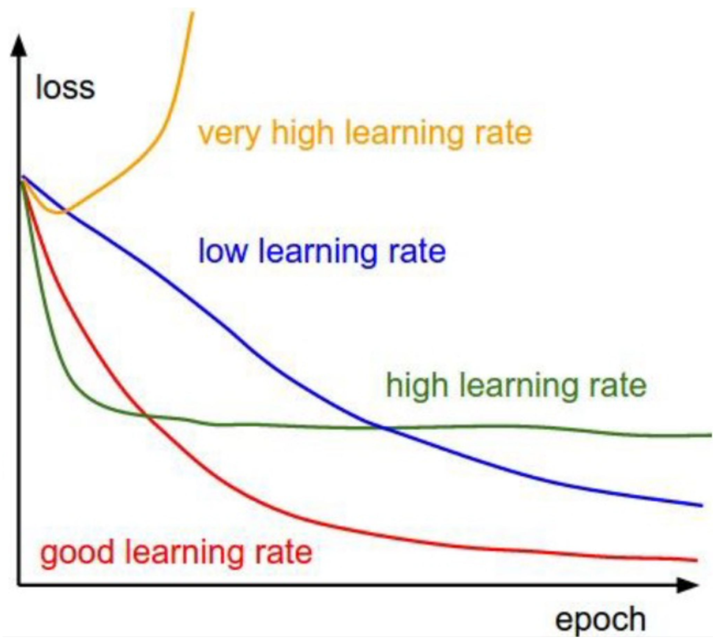




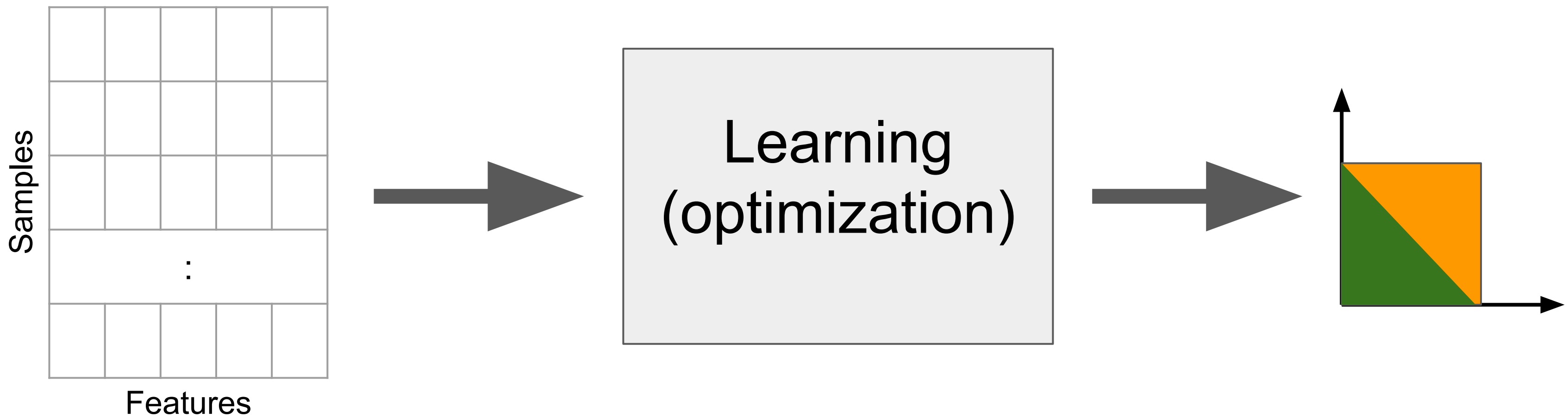
Stochastic Gradient Ascent



- Iteratively, approximate the direction at each optimization step using a small subset of samples (mini-batch)
- Epoch: a series of steps, using all training data
- Learning rate = step size
- Too large and you're over the mountain
- Too small and you won't get far



Revisiting our assumptions



Training set

- Training set - Samples X Features
- Every sample has value for all the features

Missing Data

Training set contains "?"

Samples

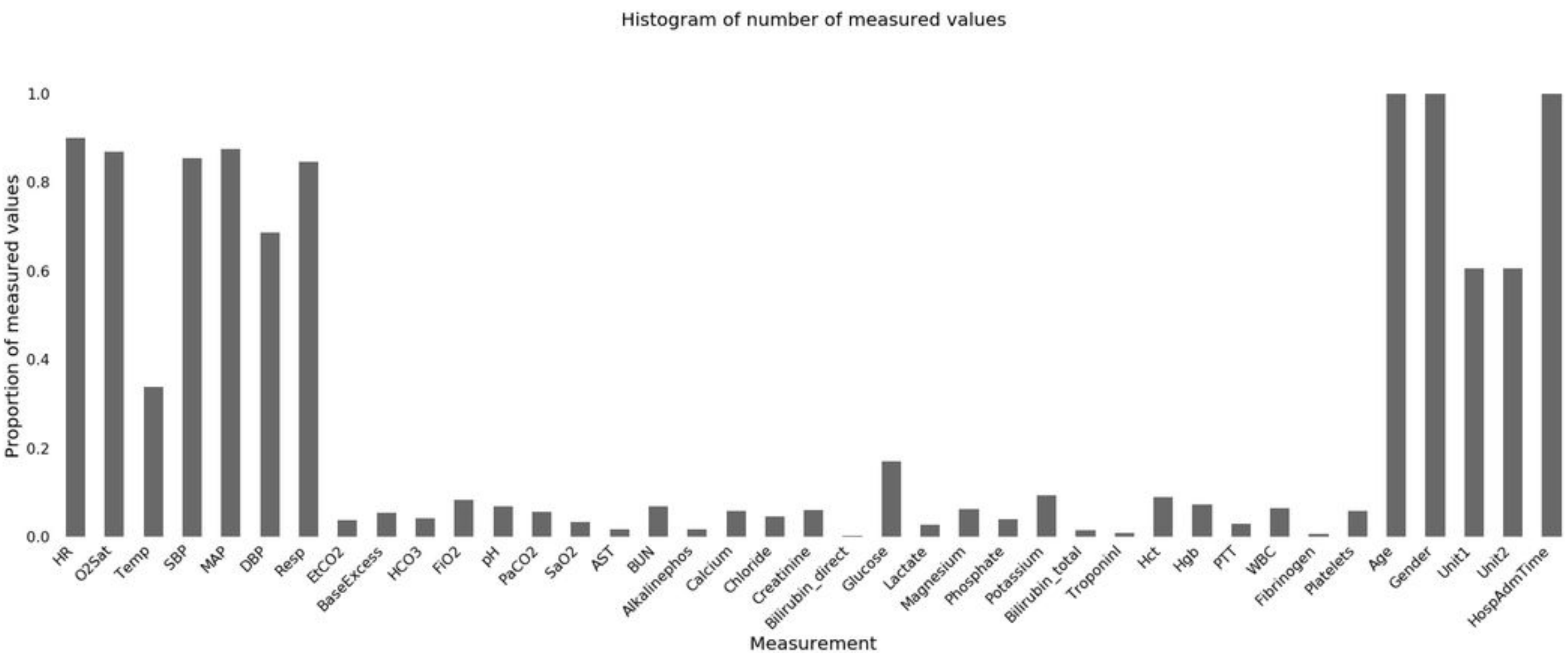
1	5	**?**	23	**?**
12	7	8	**?**	10
5	4	12	20	12
		:		
1	**?**	10	21	8

Features

Missing Data

Example:

- Basic parameters & blood works of patients in ER

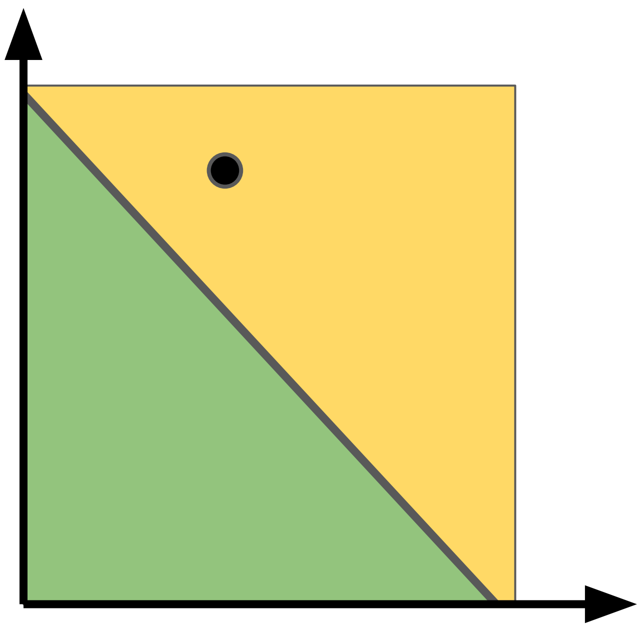


https://www.biosymetrics.com/blog/missing-values-healthcare-data

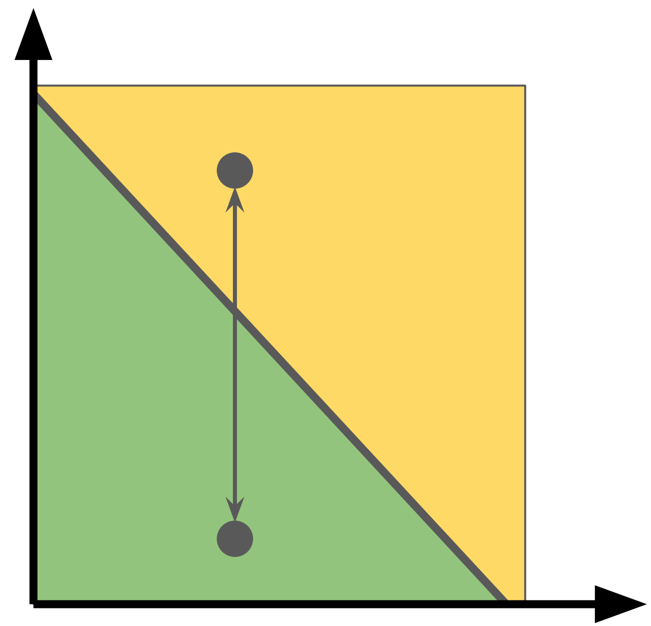
Missing Data

Why is that a problem?

Complete data - (10, 24)



Missing data - (10, ?)



Sources of Missing Data

- Missing completely at random
  Random "mechanism" removes values
  - Patients miss ~5-10% of questions on the form, each person different ones
  - Measurement device is flaky and not all results are measured

Sources of Missing Data

- Missing completely at random
- Missing specific values
  Hiding mechanism depends on actual value
  - Overweight people often do not report their weight
  - Only abnormal temperatures are recorded

Sources of Missing Data

- Missing completely at random
- Missing specific values
- Missing specific cases
  Other aspects of the sample determine whether the value is observed
    - Pathology report only when colonoscopy had positive findings

Sources of Missing Data

- Missing completely at random
- Missing specific values
- Missing specific cases
- Complex mechanism
  - Creatinine is typically measured for patients with potential kidney problems
  - Employees who fear their manager do not report their job satisfaction

Issues to consider

- Observed/missing status - is it informative?
  - Should we count it as another feature?
- Distribution of “missing values” - different than observed?
-

Approaches to Missing Data

New value that stands for “missing” or “unknown”

- Enables reasoning about the implications of not observing the values
- Can complicates the learning procedure

Approaches to Missing Data

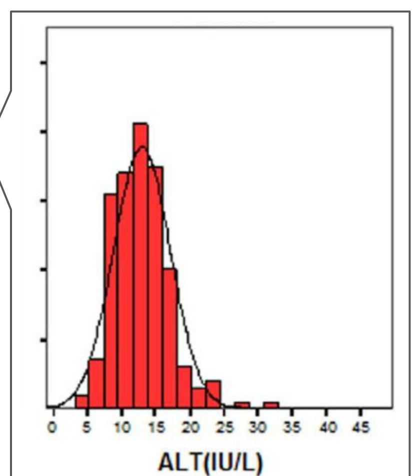
Special value: Danger of artifacts

- Missing weight value denoted as 0
- Mean / variance estimates are skewed
- Regression model treats it as another number

Samples

1	5	**?**	23	**?**
12	7	8	10	**?**
5	4	12	20	**?**
		:		
1	**?**	10	21	8

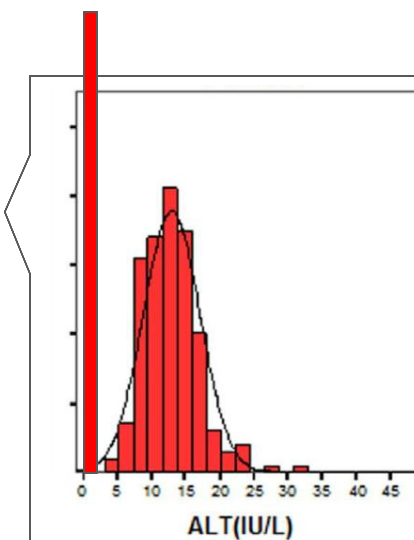
Features



Samples

1	5	**?**	23	**0**
12	7	8	10	**0**
5	4	12	20	**0**
		:		
1	**?**	10	21	8

Features



Approaches to Missing Data

Fill in missing values

- Use existing algorithms and procedures
- “Shields” the learning procedure from missing data
- Ignores information in observed/missing status

Issue - what values to fill in?

Imputation - Fill in the blanks

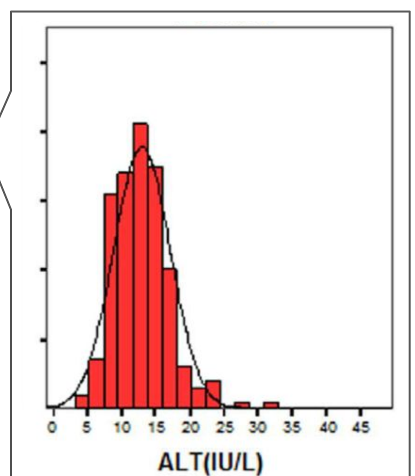
Default value

- Skews the distribution of values
- Underestimation of variance

Samples

1	5	**?**	23	**?**
12	7	8	10	**?**
5	4	12	20	**?**
		:		
1	**?**	10	21	8

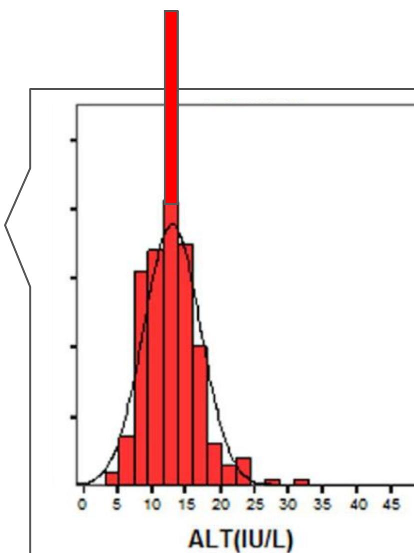
Features



Samples

1	5	**?**	23	**10**
12	7	8	10	**10**
5	4	12	20	**10**
		:		
1	**?**	10	21	8

Features



Imputation - Fill in the blanks

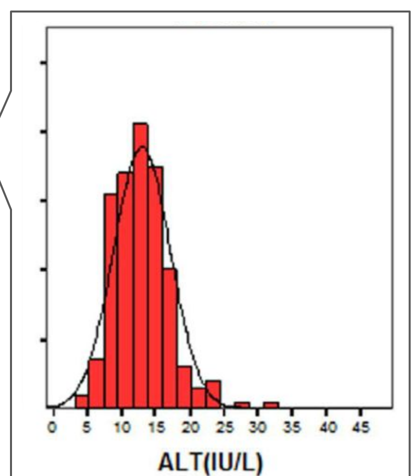
Use randomization

- Fixed distribution
- Empirical distribution

Samples

1	5	**?**	23	**?**
12	7	8	10	**?**
5	4	12	20	**?**
		:		
1	**?**	10	21	8

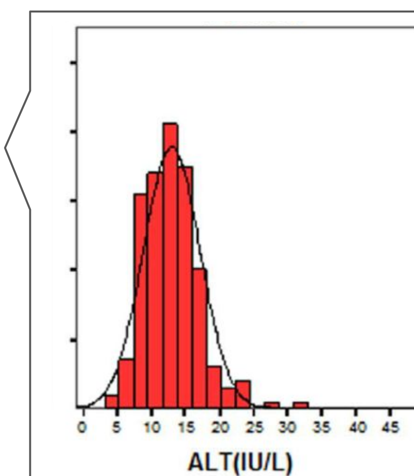
Features



Samples

1	5	**?**	23	**10**
12	7	8	10	**12**
5	4	12	20	**9**
		:		
1	**?**	10	21	8

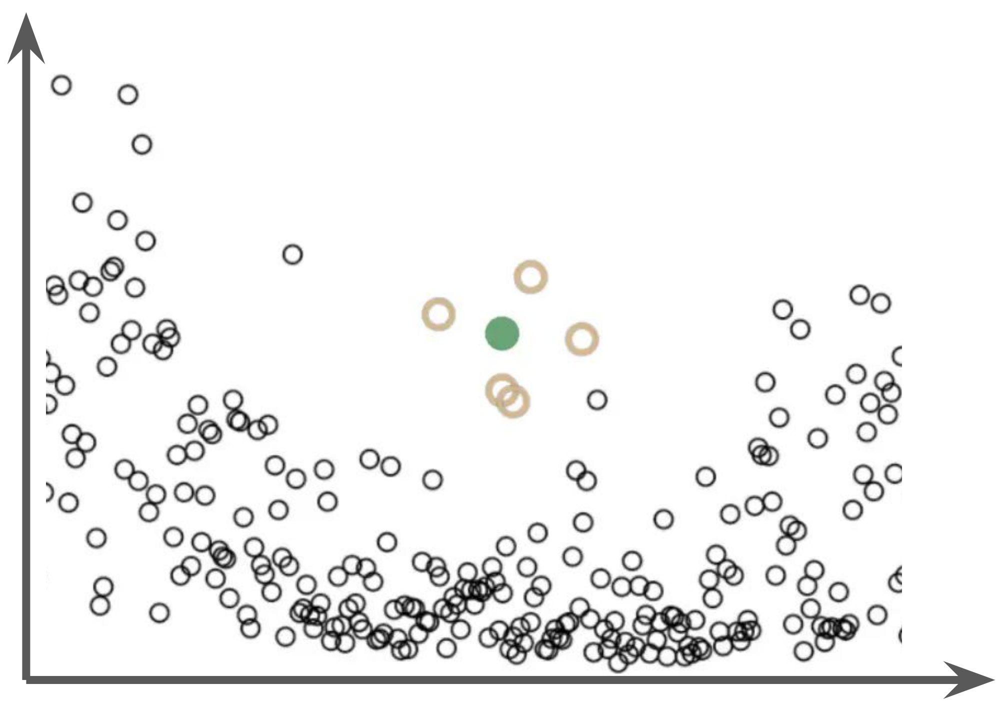
Features



Imputation - Fill in the blanks

More advanced methods

- Classifier to predict based on other examples
- Use nearest neighbors to predict missing values



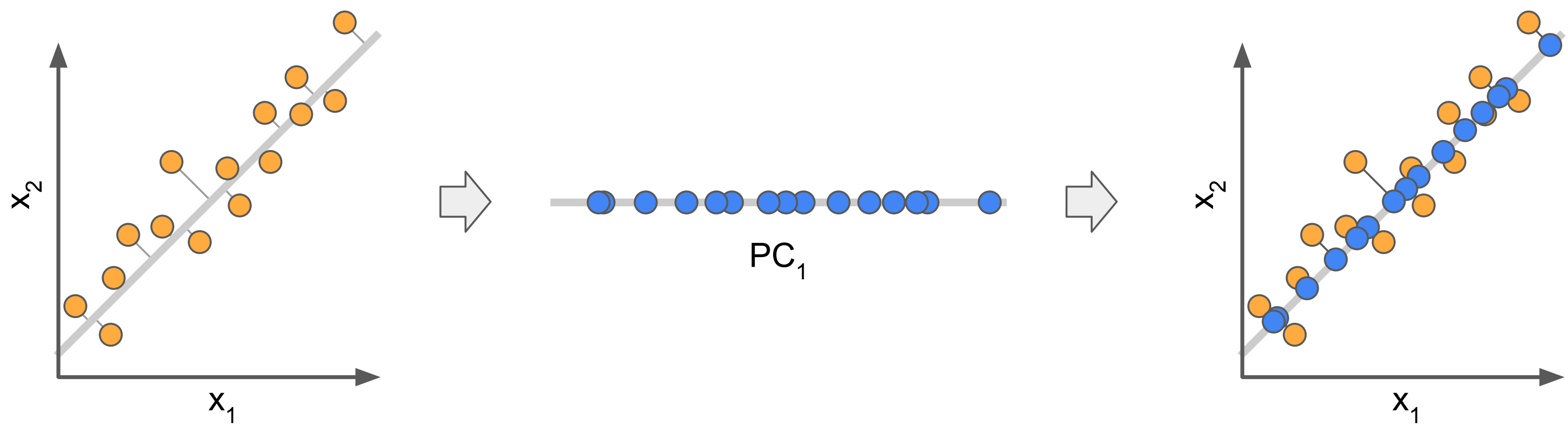
Skewed and imbalanced data

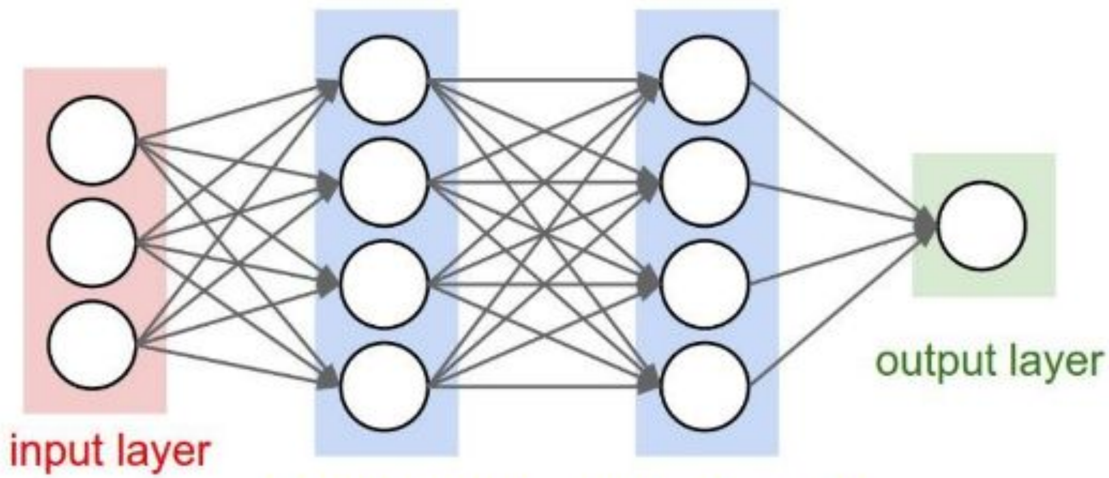
Remind the iid assumption (graphically)

Situations where this might not hold:

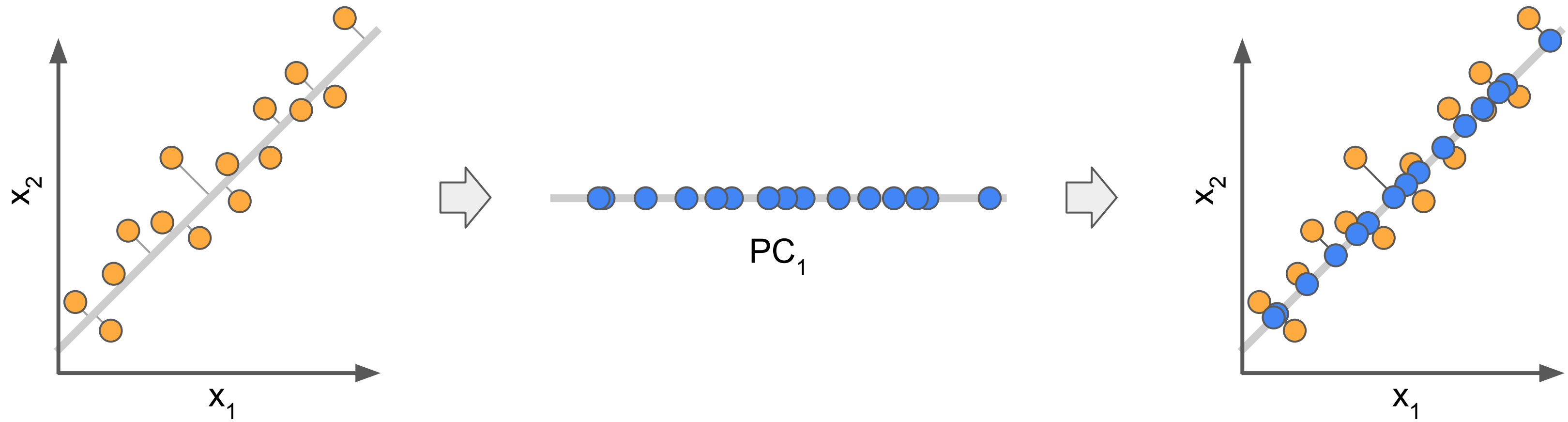
- Skewed probability of classes (only 2% are positive)
  → increased representation of rare cases
- Distribution in training cohort differs from test cohort
- Not all samples are independent of each other

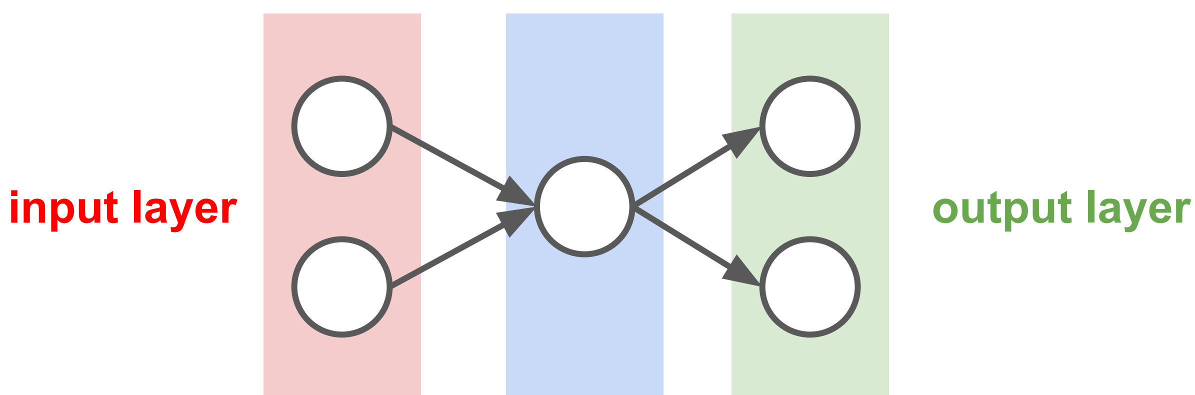
Remember PCA?





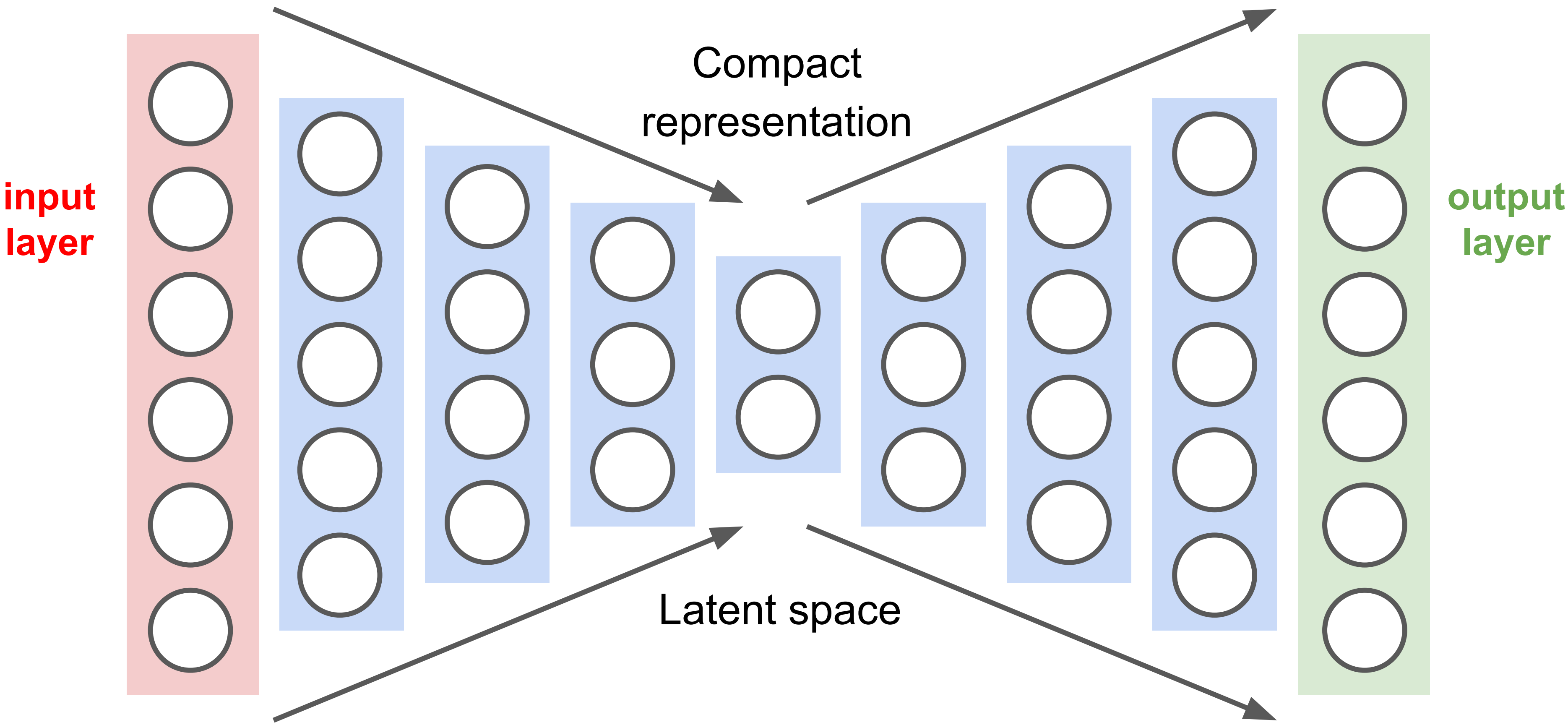
Remember PCA?





Auto-encoders

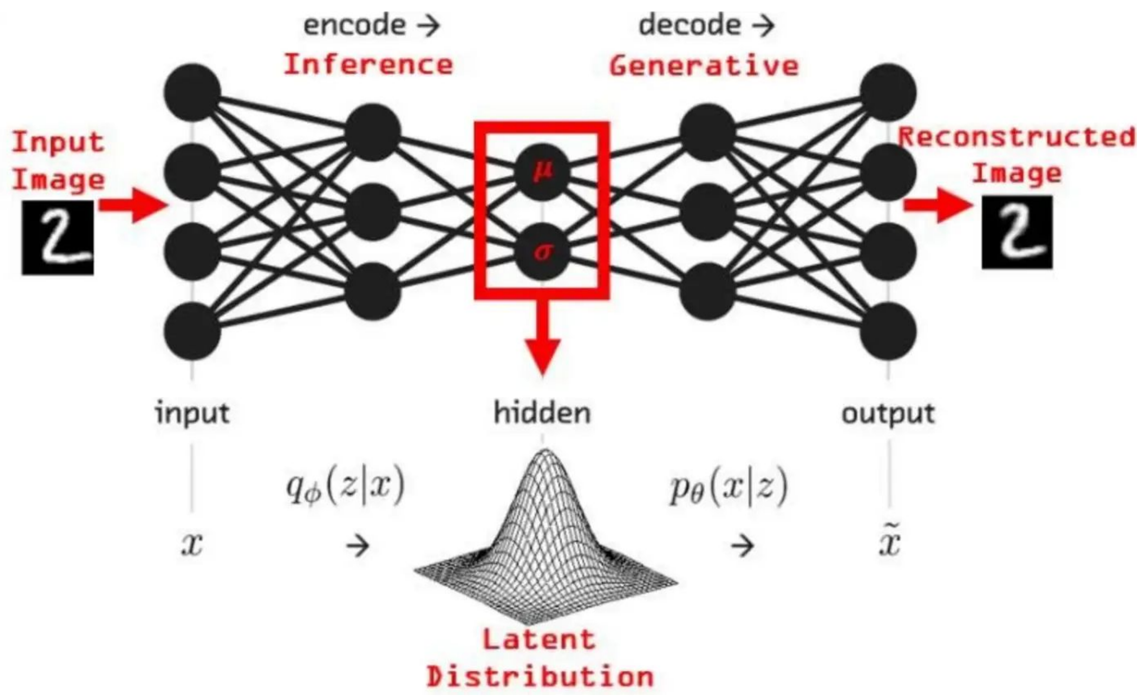
“Compress” data to lower dimension



then, “decompress” back to original dimension

Why?

- Learn hidden dependencies or patterns in data
- Denoise



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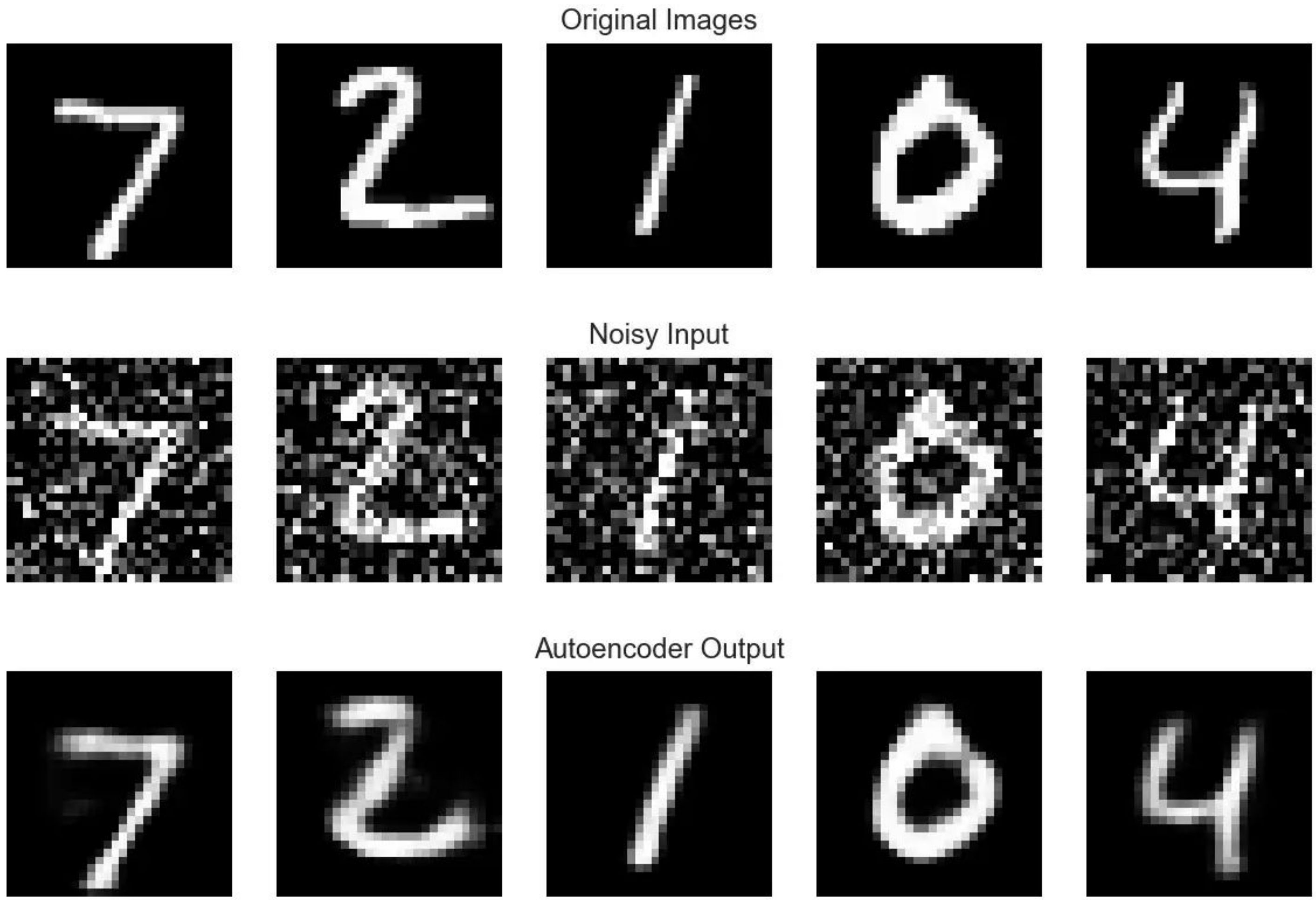


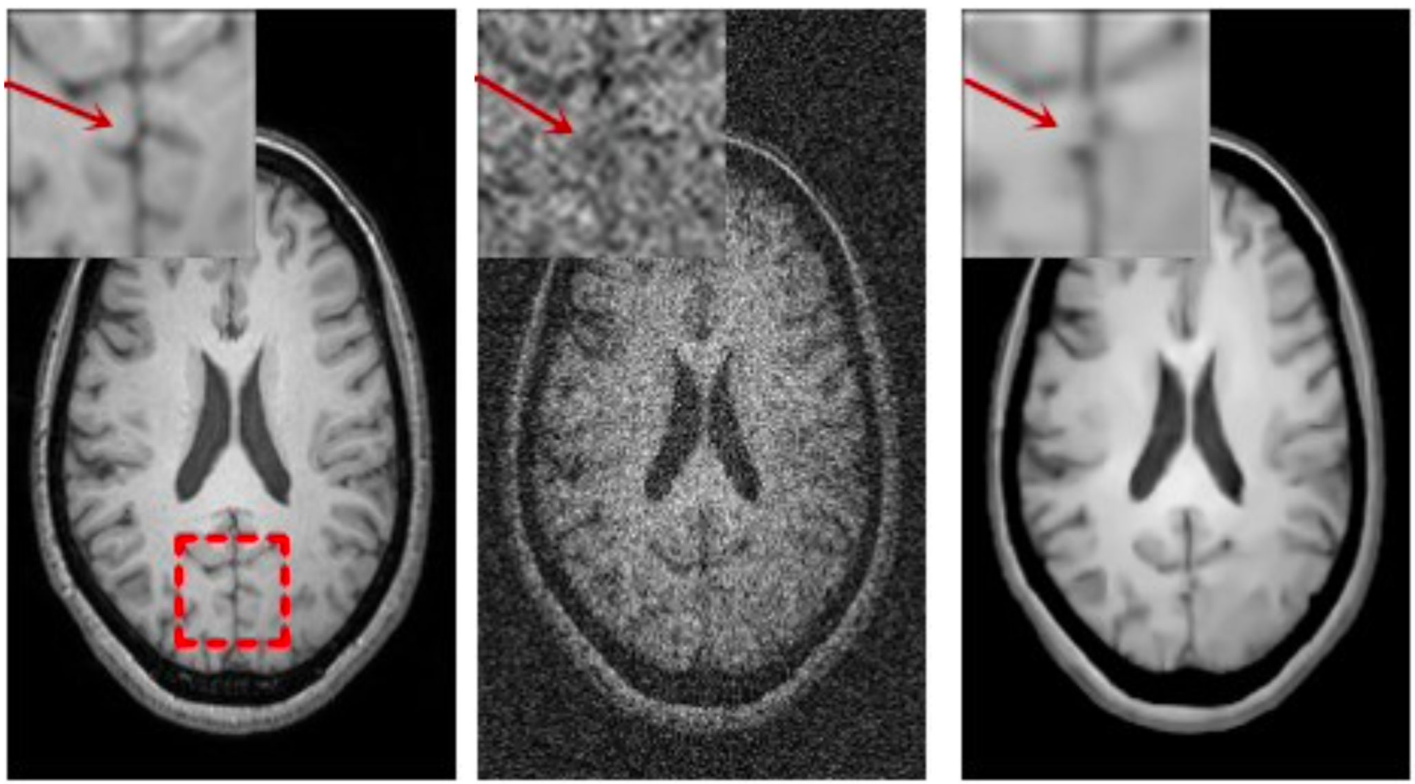
https://towardsdatascience.com/applied-deep-learning-part-3-autoencoders-1c083af4d798

Why?

- Learn hidden dependencies or patterns in data
- Denoise

Denoising of 3D Magnetic Resonance Images Using a Residual Encoder-Decoder Wasserstein Generative Adversarial Network

Maosong Ran[1], Jinrong Hu[2], Yang Chen[3,4,5], Hu Chen[1], Huaiqiang Sun[6], Jiliu Zhou[1], Yi Zhang[1,7,*]



(a) (b) (c)

Why?

- Learn hidden dependencies or patterns in data
- Denoise
- Impute

Extracting and Composing Robust Features with Denoising Autoencoders

Pascal Vincent, Hugo Larochelle, Yoshua Bengio, Pierre-Antoine Manzagol

MISSING DATA IMPUTATION IN THE ELECTRONIC HEALTH RECORD USING DEEPLY LEARNED AUTOENCODERS*

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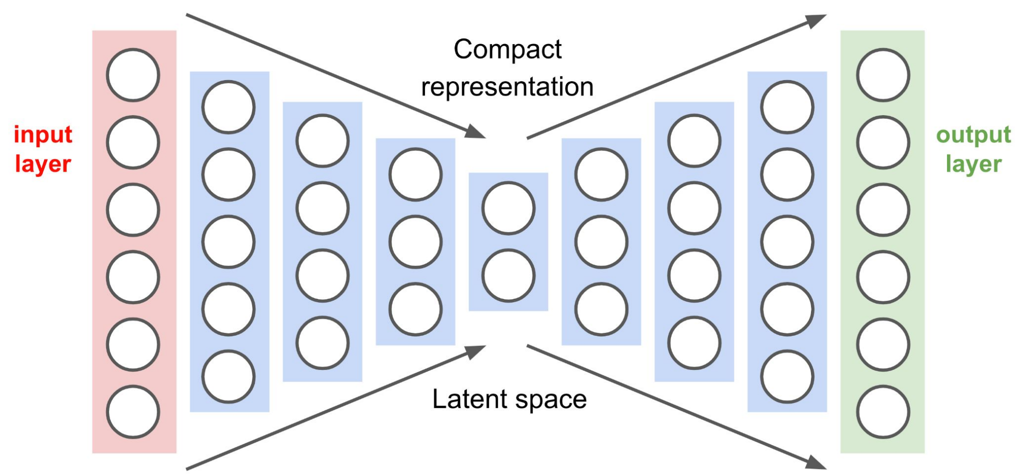
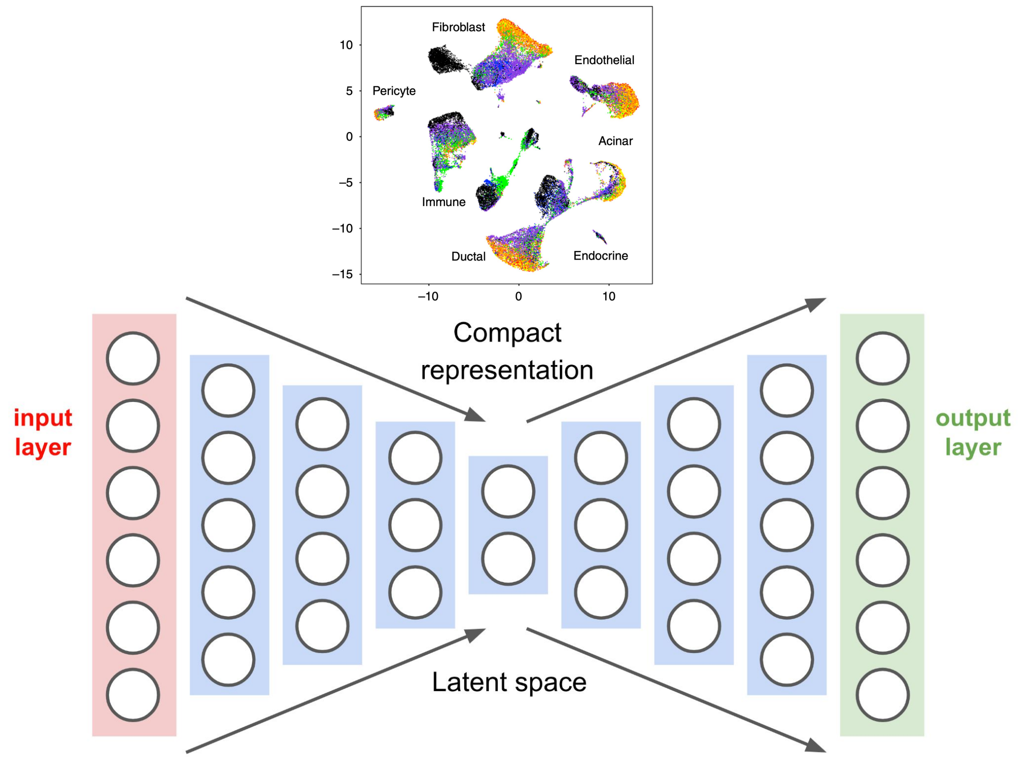


Why?

- Learn hidden dependencies or patterns in data
- Denoise
- Impute
- Visualize / cluster data in latent space



Why?

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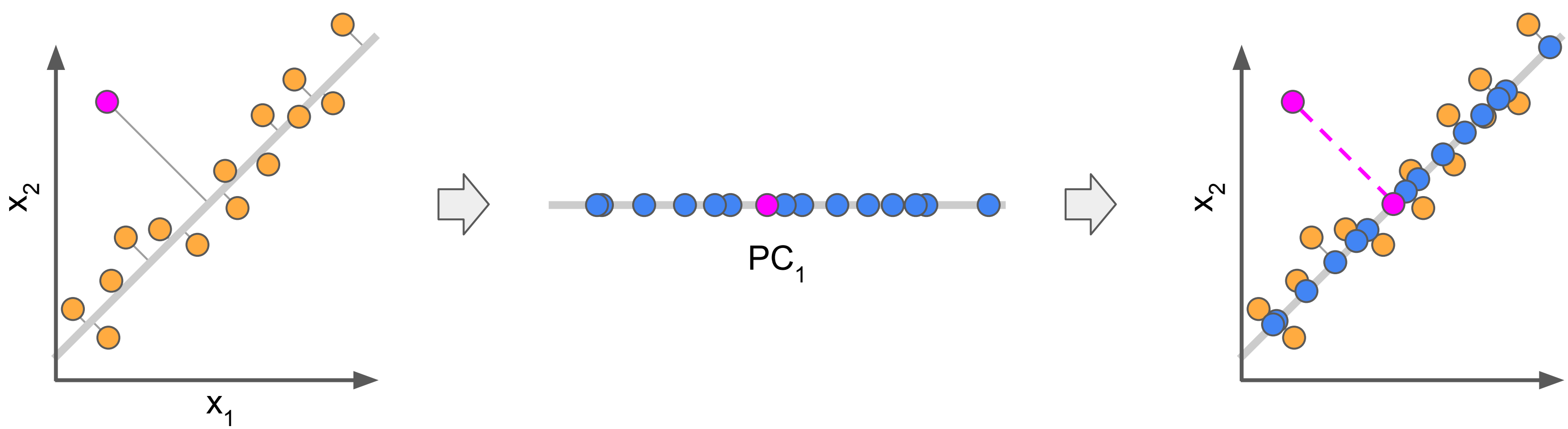
- Visualize / cluster data in latent space
- Anomaly detection (= reconstruction failures)



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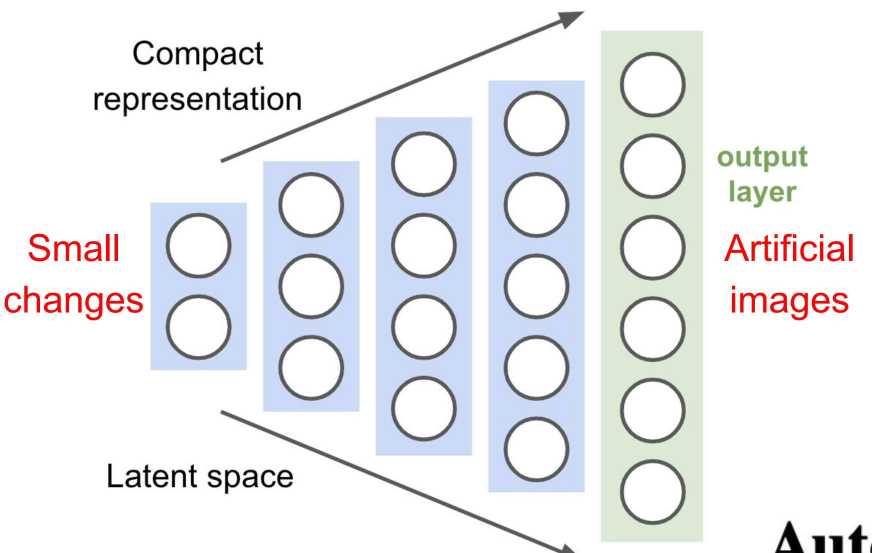
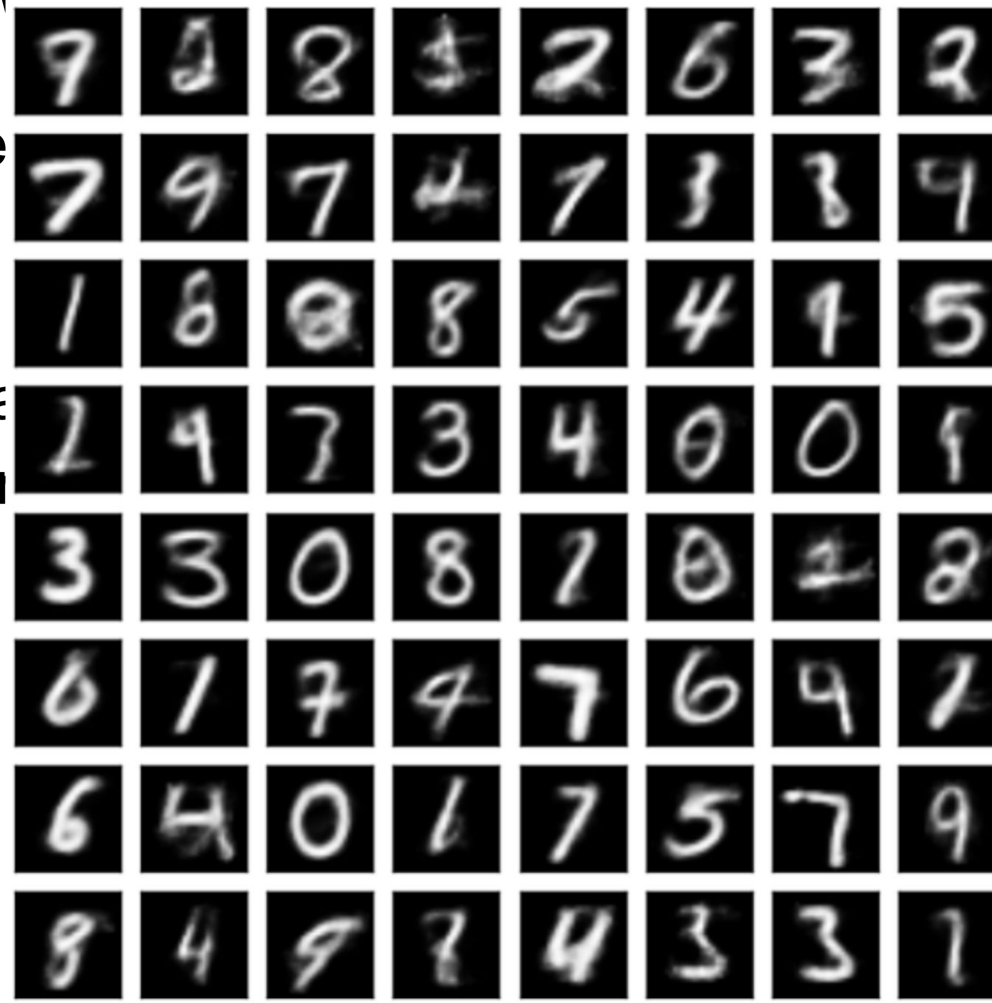
- Data generation



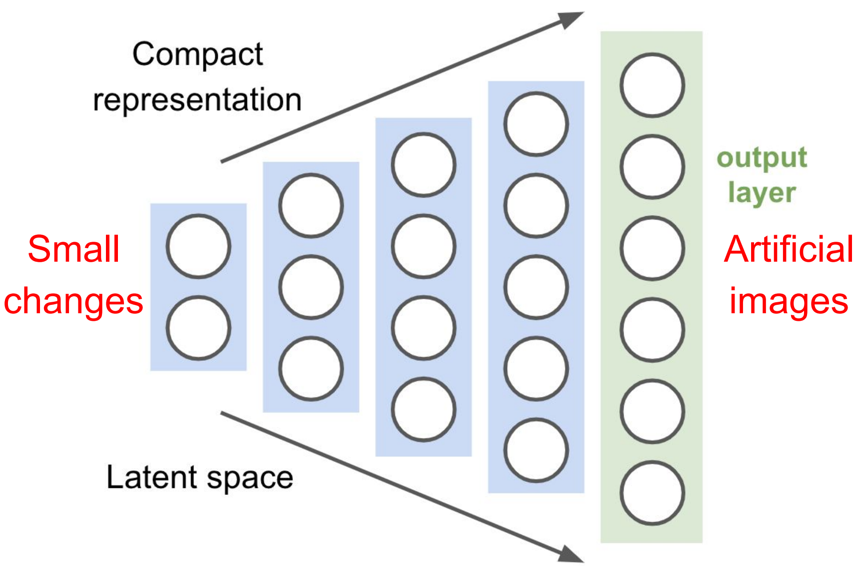


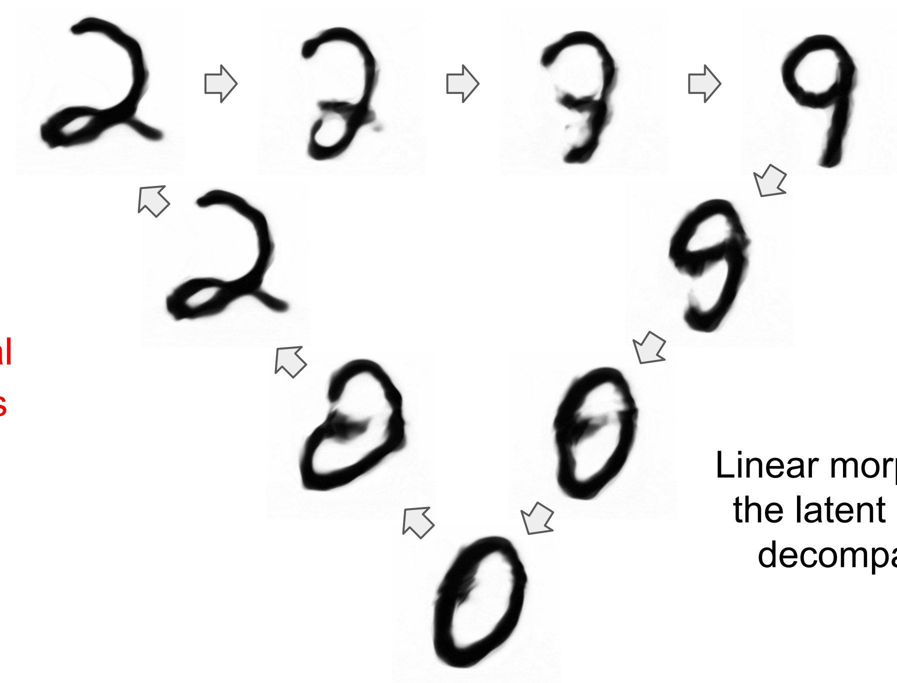
(b) VAE generated MNIST images.

Autoencoders Dor Bank, Noam Koenigstein, Raja Giryes

Why?

- Learn hidden dependencies or patterns in data
- Denoise
- Impute
- Visualize / cluster data in latent space
- Anomaly detection (= reconstruction failures)
- Data generation



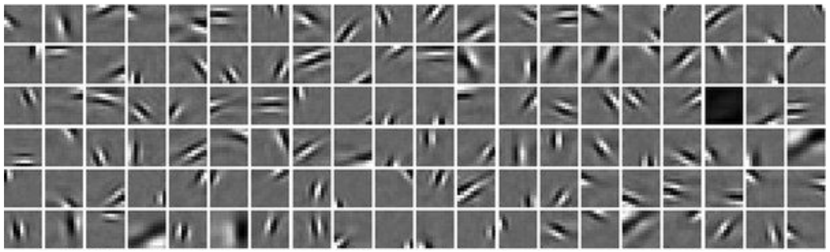


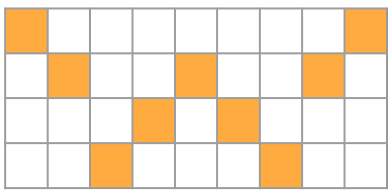
Linear morphing in the latent space, decompacted

https://blog.otoro.net/2016/04/01/generating-large-images-from-latent-vectors/

Transfer learning

- Re-use parts of a trained network (e.g., early filters/features)





ACTGCGTCA

Transfusion: Understanding Transfer Learning for Medical Imaging

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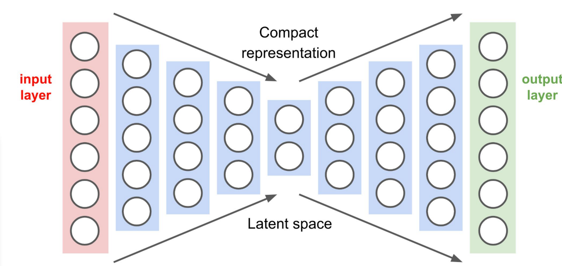
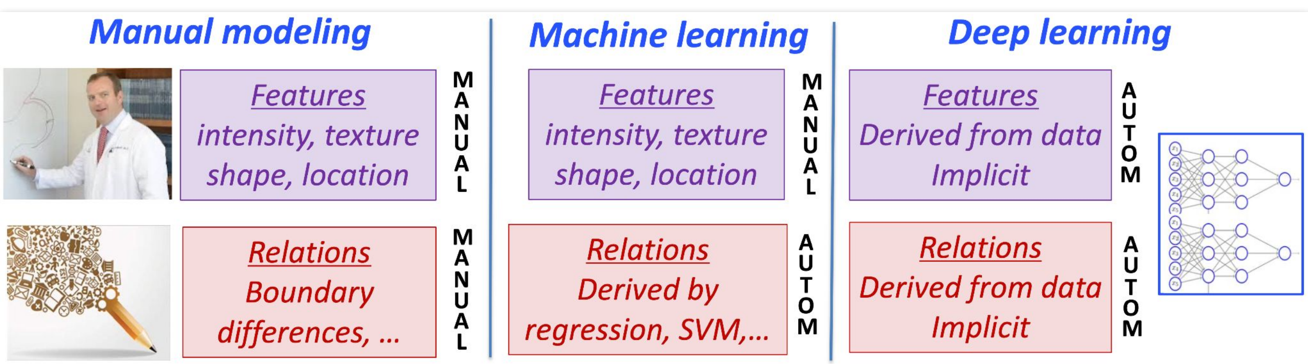
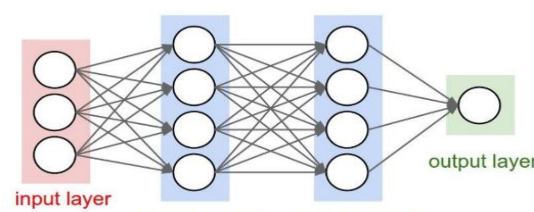
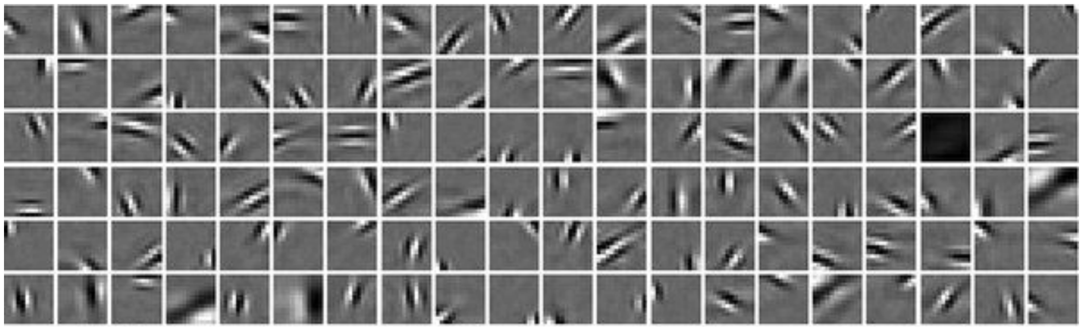






Transfer learning

- Re-use parts of a pre-trained network (early filters = basic visual features)



Transfusion: Understanding Transfer Learning for Medical Imaging

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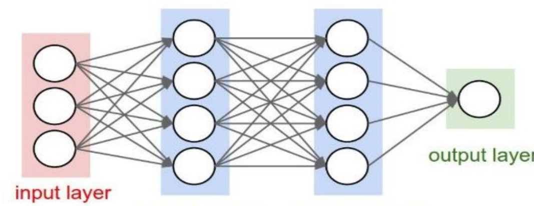

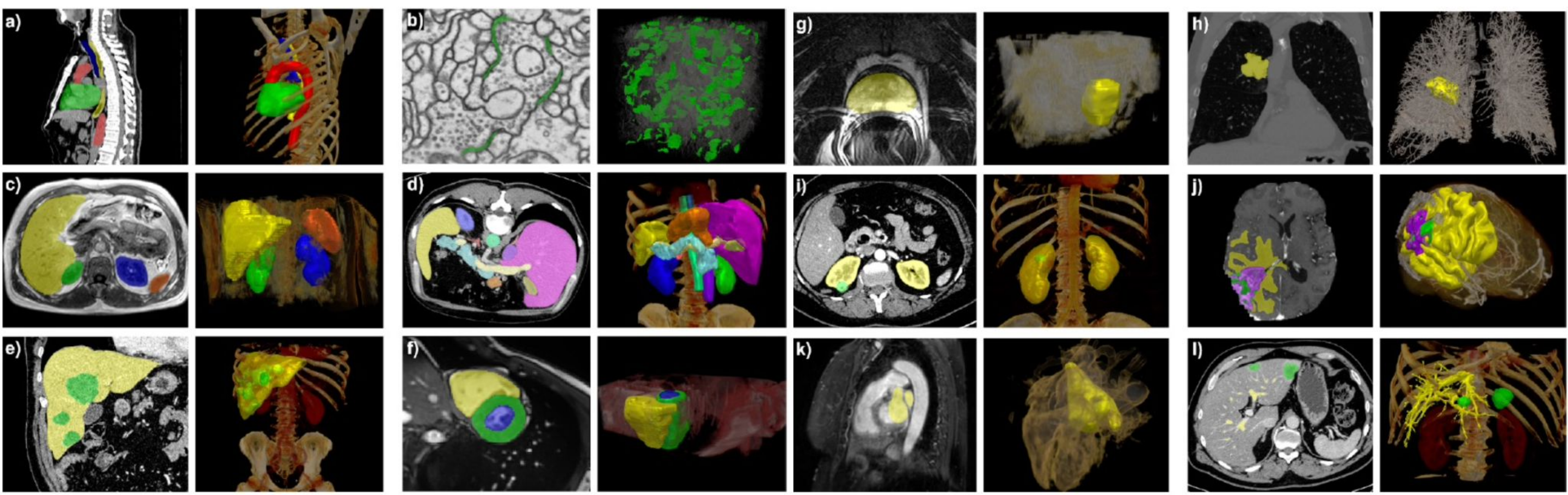

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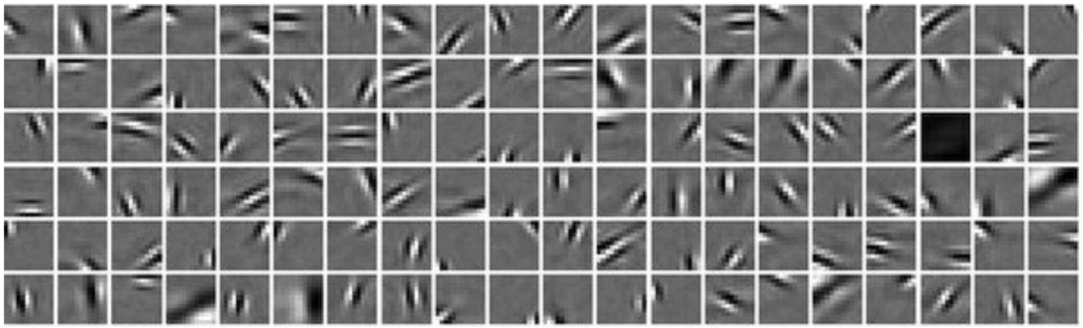

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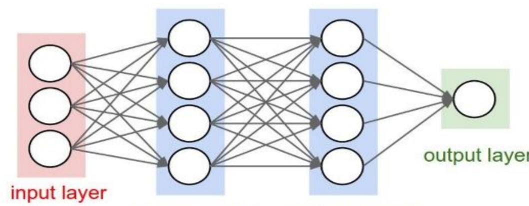
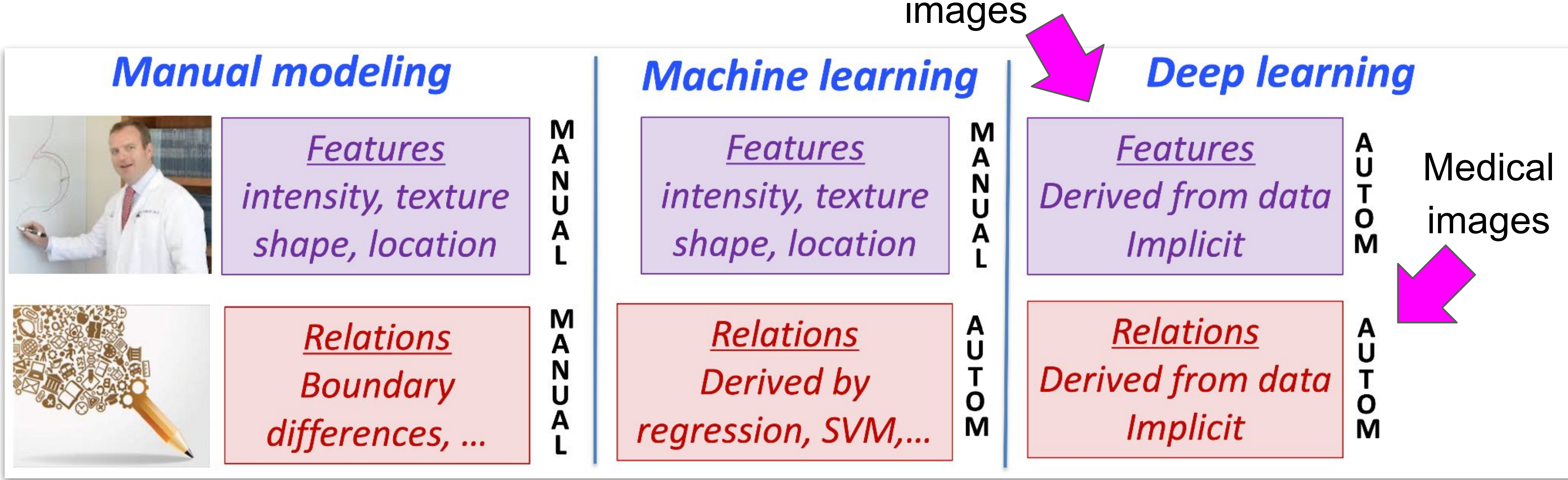


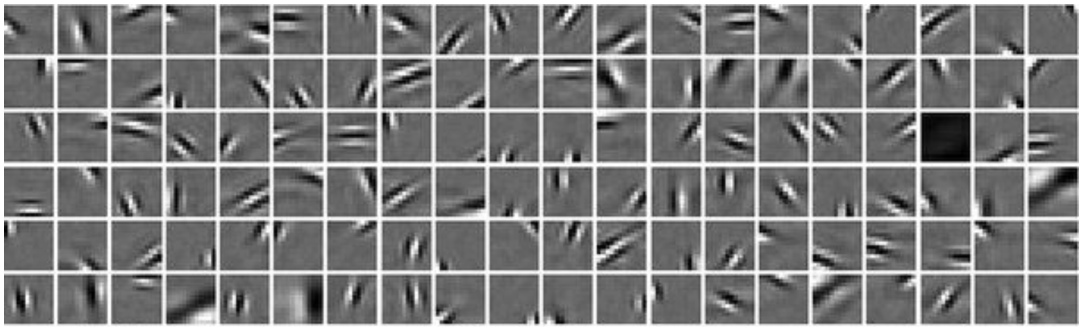
“Vanilla” images



Medical images

Transfer learning

- Re-use parts of a pre-trained network (early filters = basic visual features)



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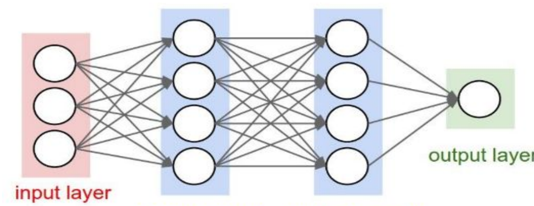
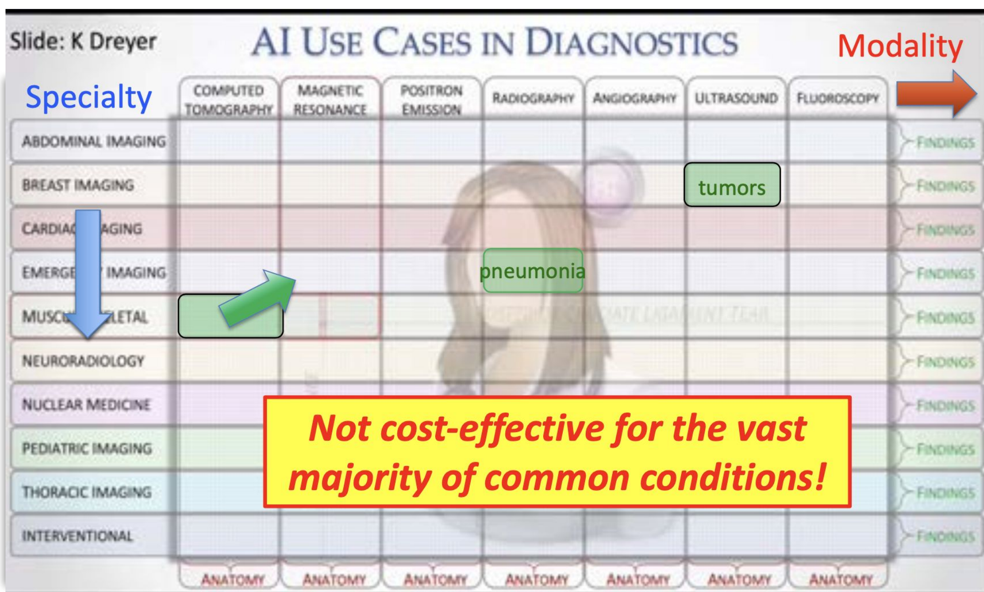
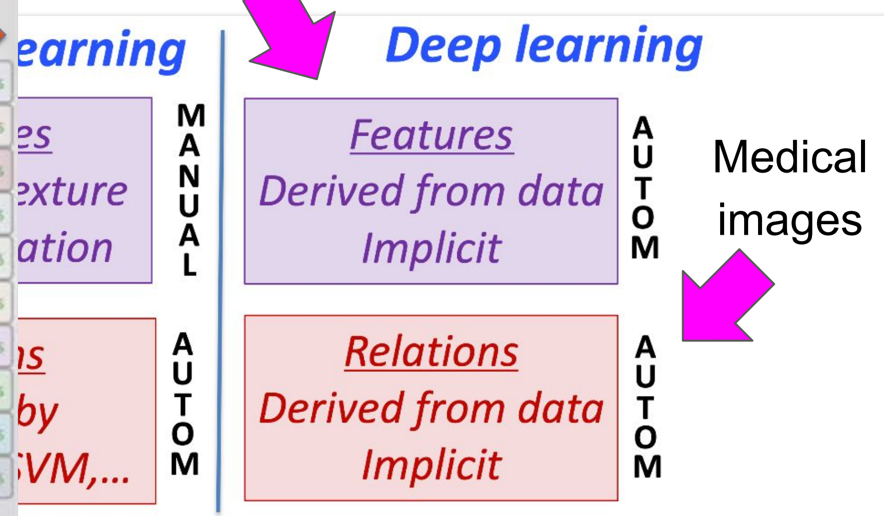


Narrow AI – long time and high costs!

“Vanilla” images





Medical images

What have we learned?

- Convolutional neural networks
- Missing data
- Imputation
- Auto-encoders
- Learning latent representations
- Multiple uses of latent representations
- Transfer learning

Medical AI idea competition

- Medical need
- Impact on individual
- Population size
- Machine Learning technique
- How will you get the data for the project?
- Similar works (and how are you different?)
- Supplementary material
- Team members
- Top projects to be presented in the last lesson

Syllabus

1. Introduction
2. Classification
3. Learning 1
4. AI in ophthalmology (Prof. Itay Chowers)
5. Learning 2
6. Regression
7. Clustering
8. Visualization (and dimensionality reduction)
9. Deep learning in image analysis (Prof. Leo Joskowicz)
10. Missing data, statistical dependencies
11. Decisions (utility)
12. Natural language in medicine (Dr. Gabi Stanovsky)
13. Longitudinal Data / Projects