Deep Generative Models

AIGenomics101
Week 4

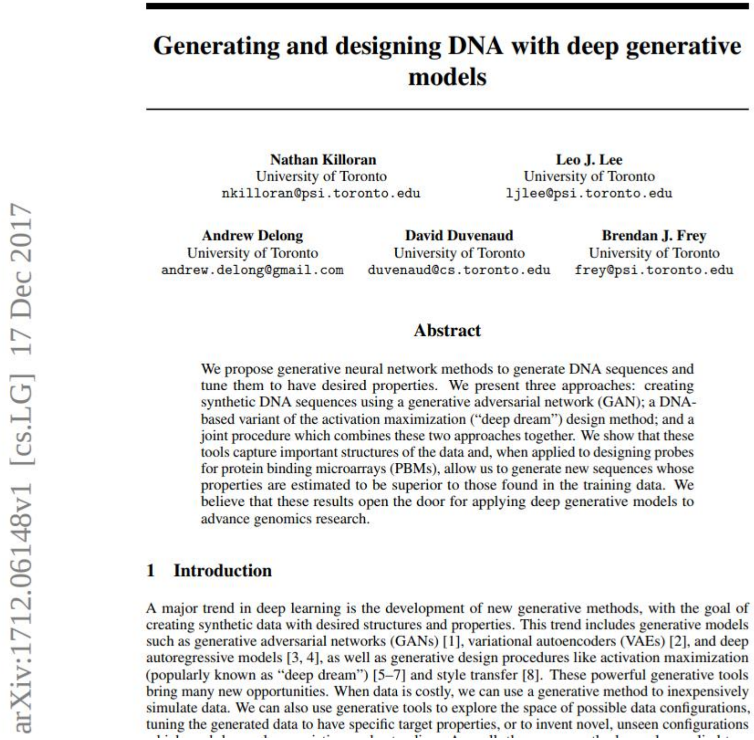
Many of slides borrowed from from: Fei-Fei Li & Serena Yeung, Stanford Course

Julie Hussin & Ahmad Pesaranghader

Overview

- Unsupervised Learning
- Generative Models
  - Variational Autoencoders (VAE)
  - Generative Adversarial Networks (GAN)

Generative Adversarial Nets in Genomics



arXiv:1712.06148v1 [cs.LG] 17 Dec 2017

Generating and designing DNA with deep generative models

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Abstract

We propose generative neural network methods to generate DNA sequences and tune them to have desired properties. We present three approaches: creating synthetic DNA sequences using a generative adversarial network (GAN); a DNA-based variant of the activation maximization ("deep dream") design method; and a joint procedure which combines these two approaches together. We show that these tools capture important structures of the data and, when applied to designing probes for protein binding microarrays (PBMs), allow us to generate new sequences whose properties are estimated to be superior to those found in the training data. We believe that these results open the door for applying deep generative models to advance genomics research.

1 Introduction

A major trend in deep learning is the development of new generative methods, with the goal of creating synthetic data with desired structures and properties. This trend includes generative models such as generative adversarial networks (GANs) [1], variational autoencoders (VAEs) [2], and deep autoregressive models [3, 4], as well as generative design procedures like activation maximization (popularly known as "deep dream") [5–7] and style transfer [8]. These powerful generative tools bring many new opportunities. When data is costly, we can use a generative method to inexpensively simulate data. We can also use generative tools to explore the space of possible data configurations, tuning the generated data to have specific target properties, or to invent novel, unseen configurations

Figure 7: Motif-matching experiment: a) Sequence logo for the PWM detected by the predictor. Letter heights reflect their relative frequency at each position. Sequences which have a strong match with this motif will score highly. b) Sample sequences tuned to have a high predictor score. The boxes indicate strong motif matches for each sequence.

Supervised vs Unsupervised Learning

Supervised Learning

Data: (x, y)
x is data, y is label

Goal: Learn a *function* to map x -> y

Examples: Classification, regression, object detection, semantic segmentation, image captioning, etc.

Supervised vs Unsupervised Learning

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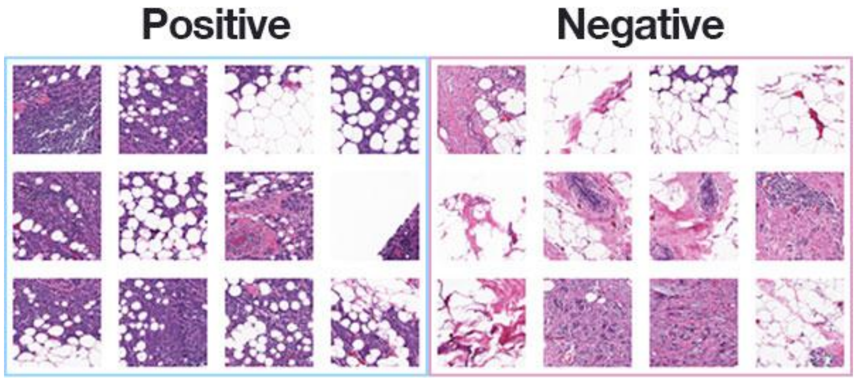
The breast cancer histology image dataset



Classification

Supervised vs Unsupervised Learning

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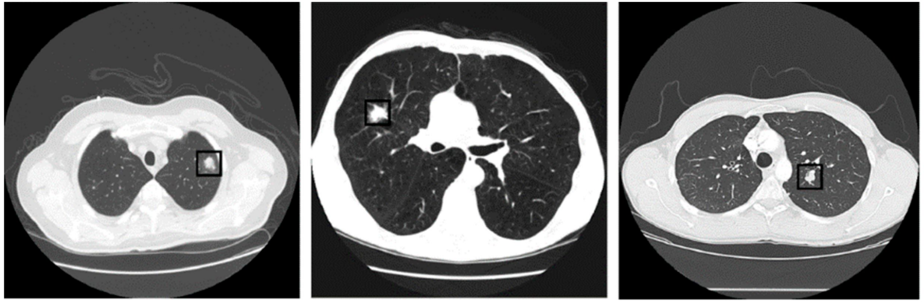
Lung nodule detection with several levels of malignancy (LIDC dataset)



Object Detection

Supervised vs Unsupervised Learning

Supervised Learning

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x is data, y is label

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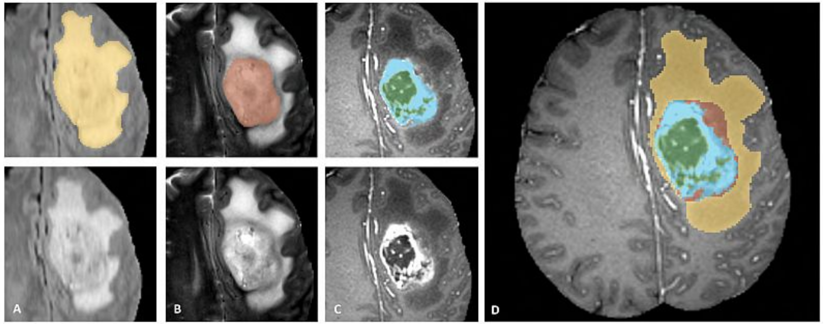
Examples: Classification, regression, object detection, semantic segmentation, image captioning, etc.

BraTs-Segmentation-Challenge
(Brain MRI)



Semantic Segmentation

Supervised vs Unsupervised Learning

Supervised Learning

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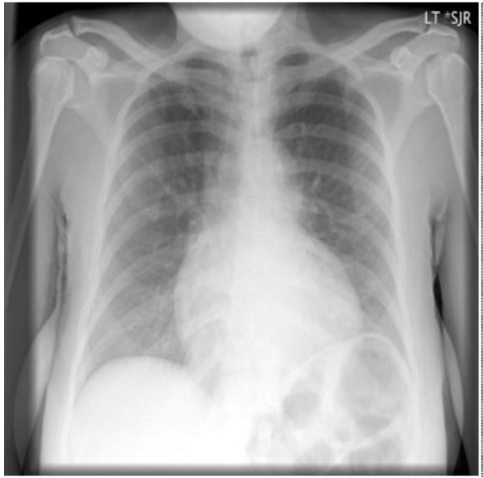
Examples: Classification, regression, object detection, semantic segmentation, image captioning, etc.

Medical Report Captioning



Findings:
The cardiac silhouette is enlarged and has a globular appearance. Mild bibasilar dependent atelectasis. No pneumothorax or large pleural effusion. No acute bone abnormality.

Impression:
Cardiomegaly with globular appearance of the cardiac silhouette. Considerations would include pericardial effusion or dilated cardiomyopathy.

Image captioning

Supervised vs Unsupervised Learning

Unsupervised Learning

Data: x
Just data, no labels!

Goal: Learn some underlying hidden *structure* of the data

Examples: Clustering, dimensionality reduction, feature learning, density estimation, etc.

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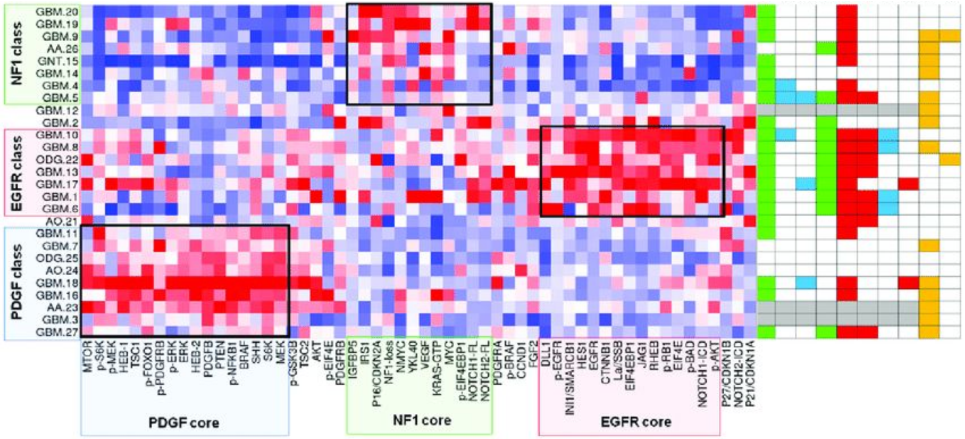
K-means clustering of gliomas by signature-defining proteins



K-means or t-SNE clustering

Supervised vs Unsupervised Learning

Unsupervised Learning

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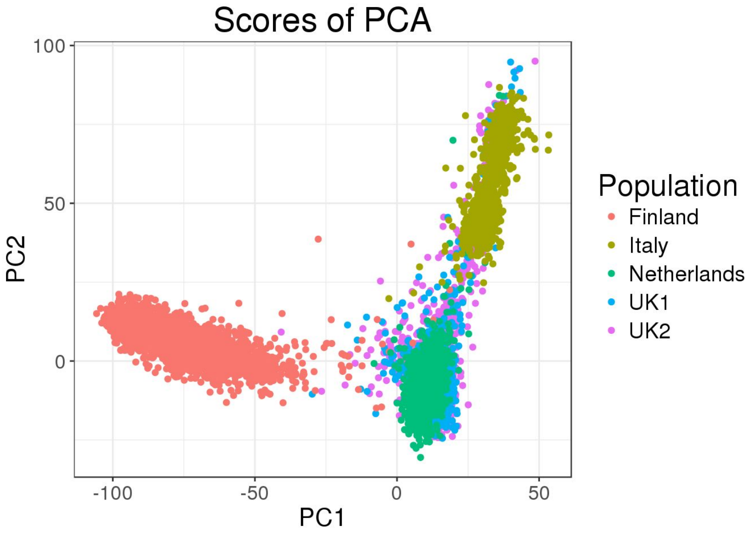
Just data, no labels!

Goal: Learn some underlying hidden *structure* of the data

Examples: Clustering, dimensionality reduction, feature learning, density estimation, etc.



Principal Component Analysis
(Dimensionality reduction)

Supervised vs Unsupervised Learning

Unsupervised Learning

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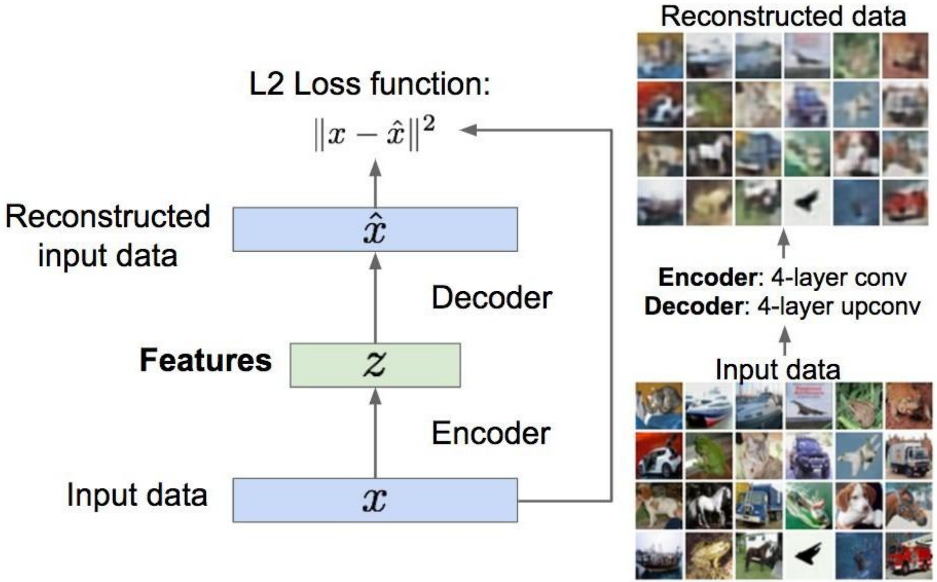
Just data, no labels!

Goal: Learn some underlying hidden *structure* of the data

Examples: Clustering, dimensionality reduction, feature learning, density estimation, etc.



Autoencoders
(Feature learning/representation)

Supervised vs Unsupervised Learning

Unsupervised Learning

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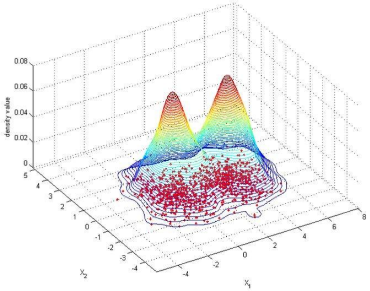
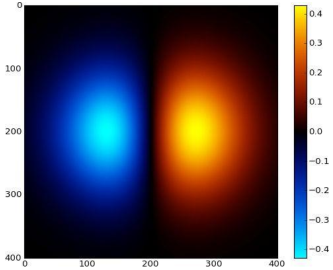
Just data, no labels!

Goal: Learn some underlying hidden *structure* of the data

Examples: Clustering, dimensionality reduction, feature learning, density estimation, etc.

1-d density estimation





2-d density estimation

Supervised vs Unsupervised Learning

Supervised Learning

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Examples: Classification, regression, object detection, semantic segmentation, image captioning, etc.

Unsupervised Learning

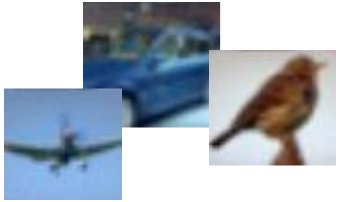
Data: x
Just data, no labels!

Goal: Learn some underlying hidden *structure* of the data

Examples: Clustering, dimensionality reduction, feature learning, density estimation, etc.

Generative Models

Given training data, generate new samples from same distribution

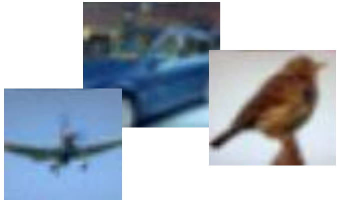


Training data ~ $p_{data}(x)$ Generated samples ~ $p_{model}(x)$

Want to learn $p_{model}(x)$ similar to $p_{data}(x)$

Generative Models

Given training data, generate new samples from same distribution



Training data ~ $p_{data}(x)$

Generated samples ~ $p_{model}(x)$

Want to learn $p_{model}(x)$ similar to $p_{data}(x)$

Addresses density estimation, a core problem in unsupervised learning

Several flavors:

- Explicit density estimation: explicitly define and solve for $p_{model}(x)$
- Implicit density estimation: learn model that can sample from $p_{model}(x)$ w/o explicitly defining it

Taxonomy of Generative Models

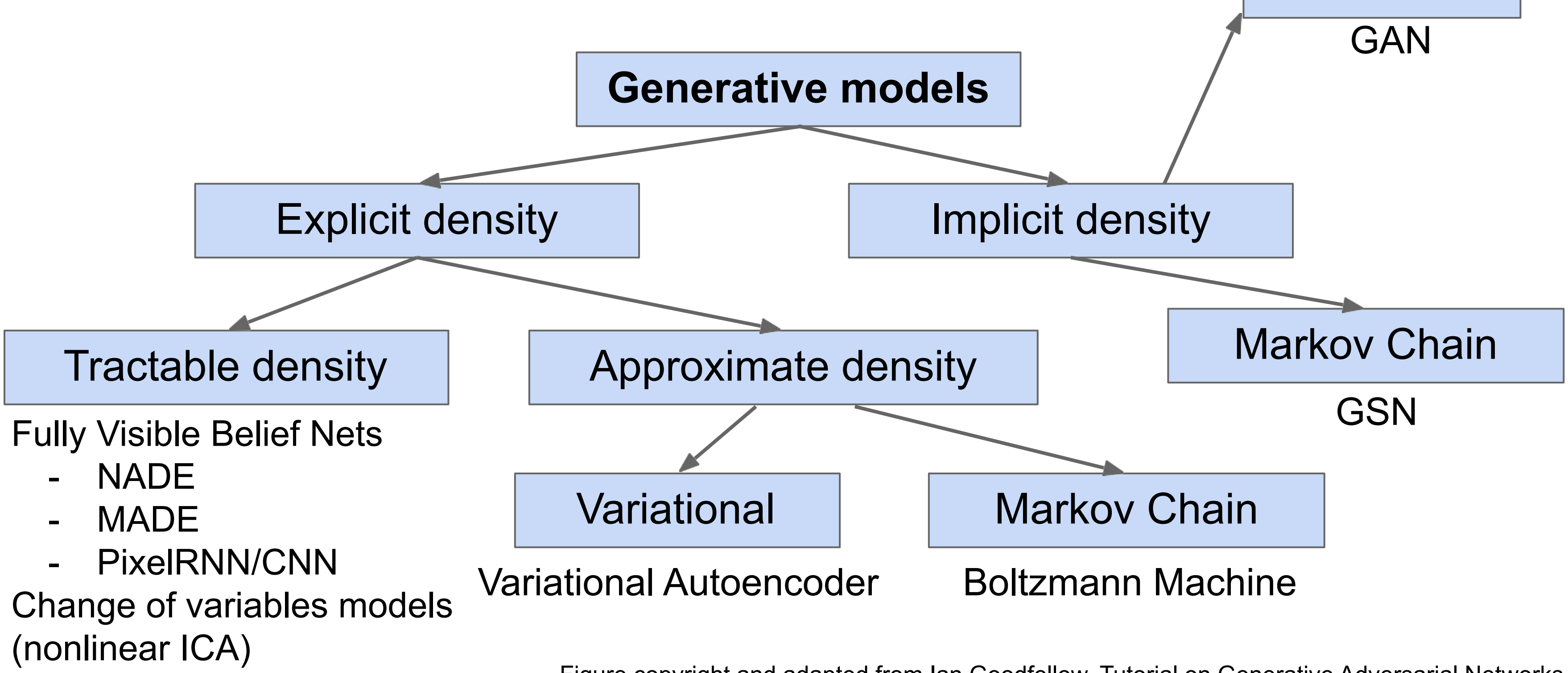
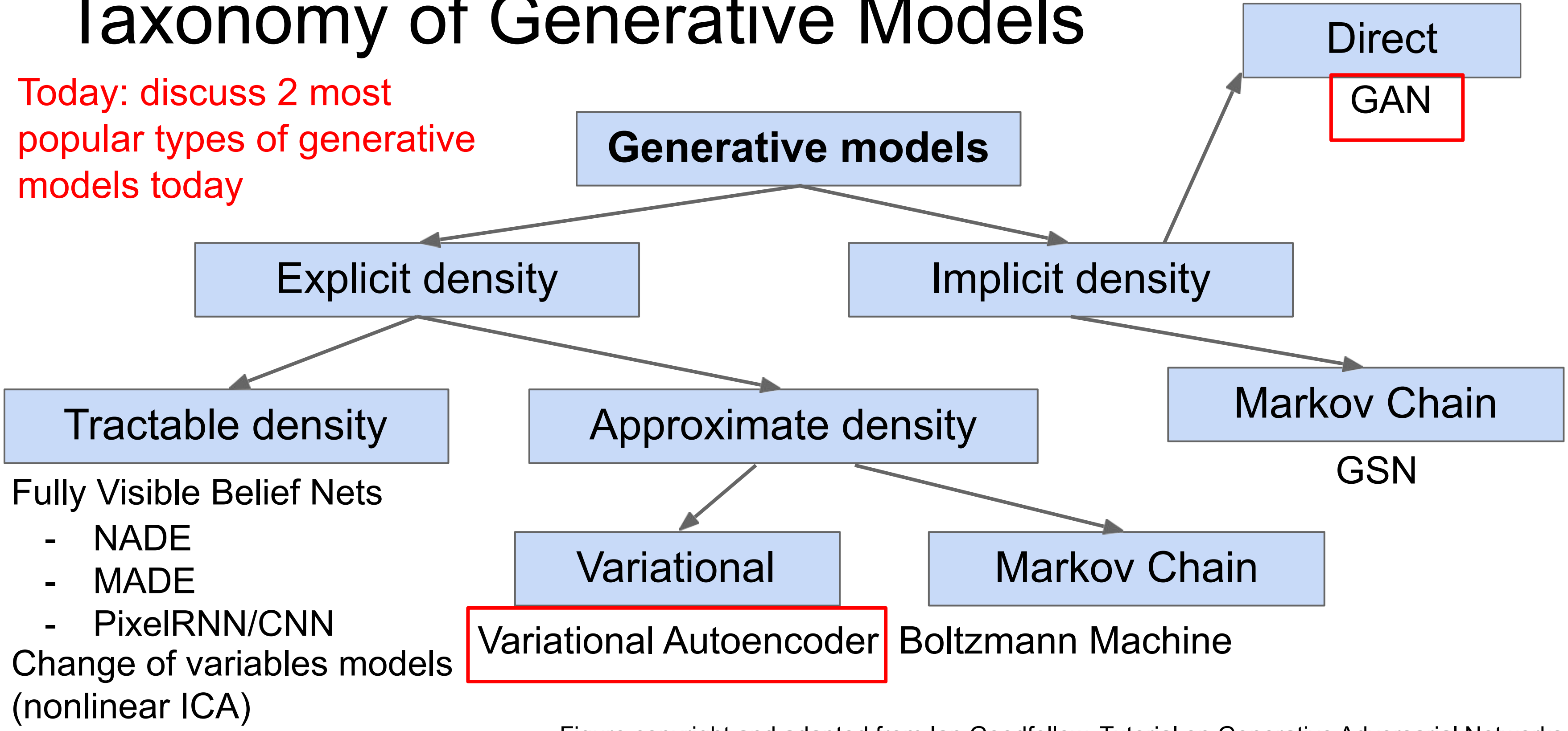


Figure copyright and adapted from Ian Goodfellow, Tutorial on Generative Adversarial Networks, 2017.

Taxonomy of Generative Models

Today: discuss 2 most popular types of generative models today



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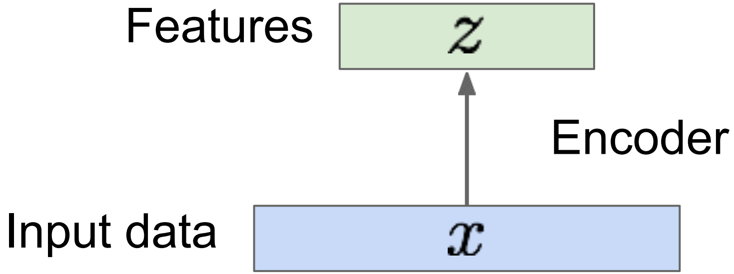
Variational Autoencoders (VAE)

Some background first: Autoencoders

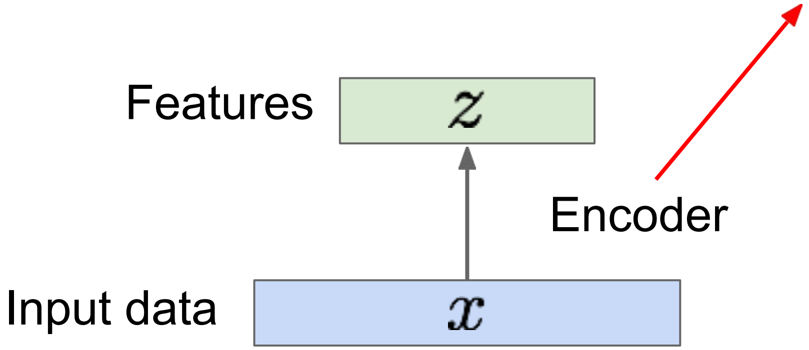
Unsupervised approach for learning a lower-dimensional feature representation from unlabeled training data



Some background first: Autoencoders

Unsupervised approach for learning a lower-dimensional feature representation from unlabeled training data

Originally: Linear + nonlinearity (sigmoid)
Later: Deep, fully-connected
Later: ReLU CNN



Some background first: Autoencoders

Unsupervised approach for learning a lower-dimensional feature representation from unlabeled training data

z usually smaller than **x** (dimensionality reduction)

Q: Why dimensionality reduction?

Originally: Linear + nonlinearity (sigmoid)
Later: Deep, fully-connected
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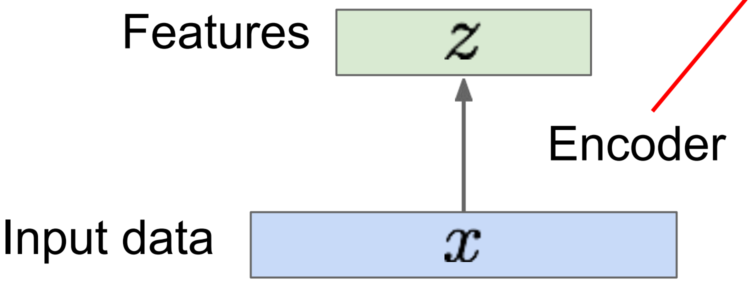


Some background first: Autoencoders

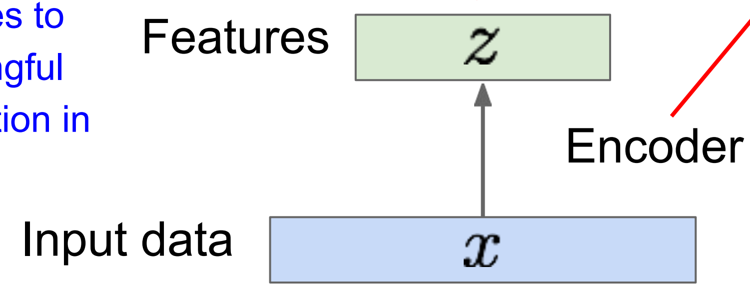
Unsupervised approach for learning a lower-dimensional feature representation from unlabeled training data

z usually smaller than **x** (dimensionality reduction)

Q: Why dimensionality reduction?

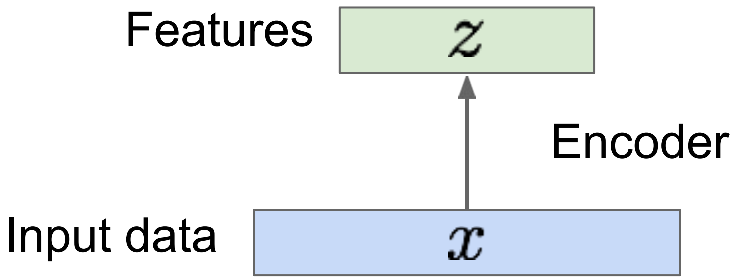
A: Want features to capture meaningful factors of variation in data

Originally: Linear + nonlinearity (sigmoid)
Later: Deep, fully-connected
Later: ReLU CNN



Some background first: Autoencoders

How to learn this feature representation?

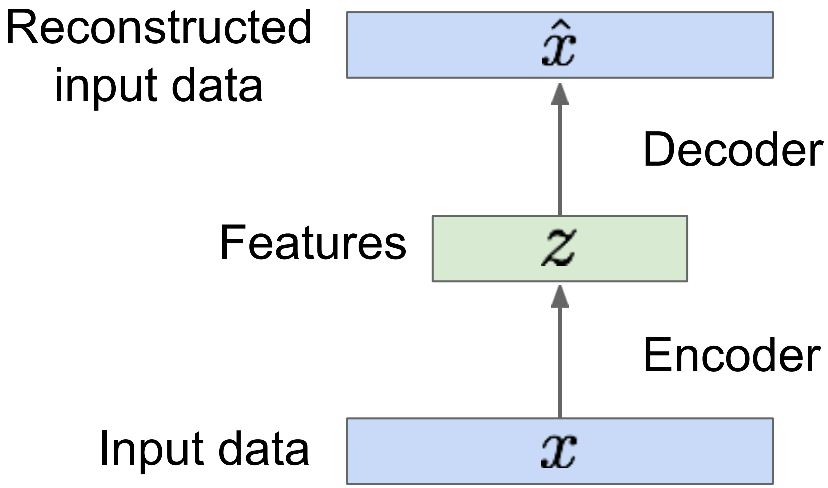


Some background first: Autoencoders

How to learn this feature representation?

Train such that features can be used to reconstruct original data

“Autoencoding” - encoding itself



Some background first: Autoencoders

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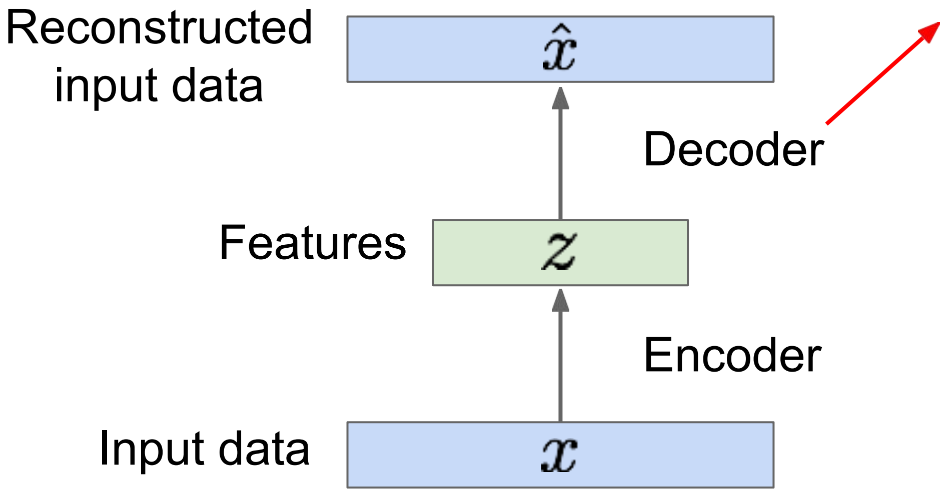


Originally: Linear + nonlinearity (sigmoid)

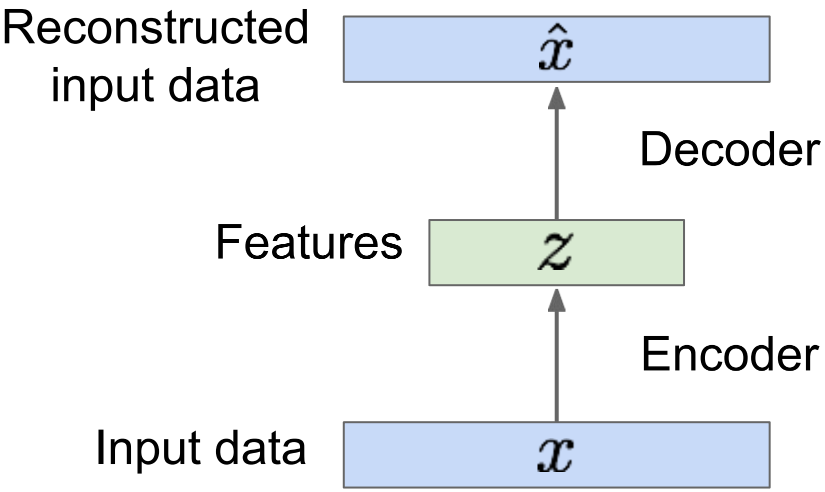
Later: Deep, fully-connected

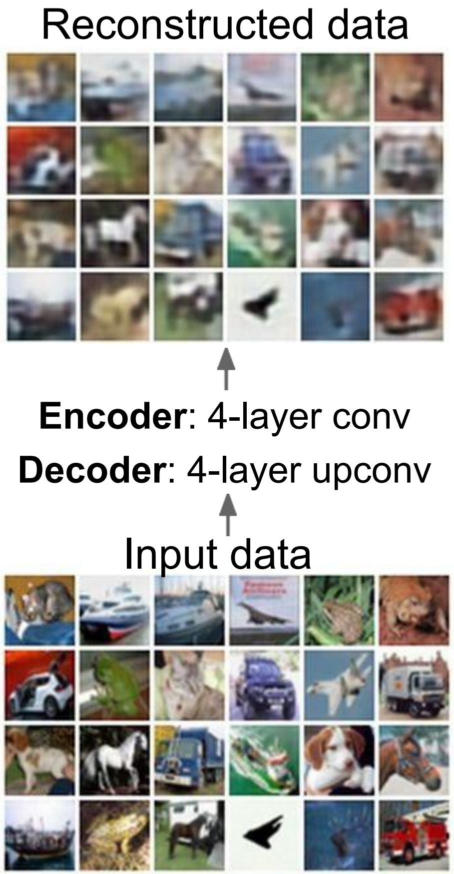
Later: ReLU CNN (upconv)

Some background first: Autoencoders

How to learn this feature representation?

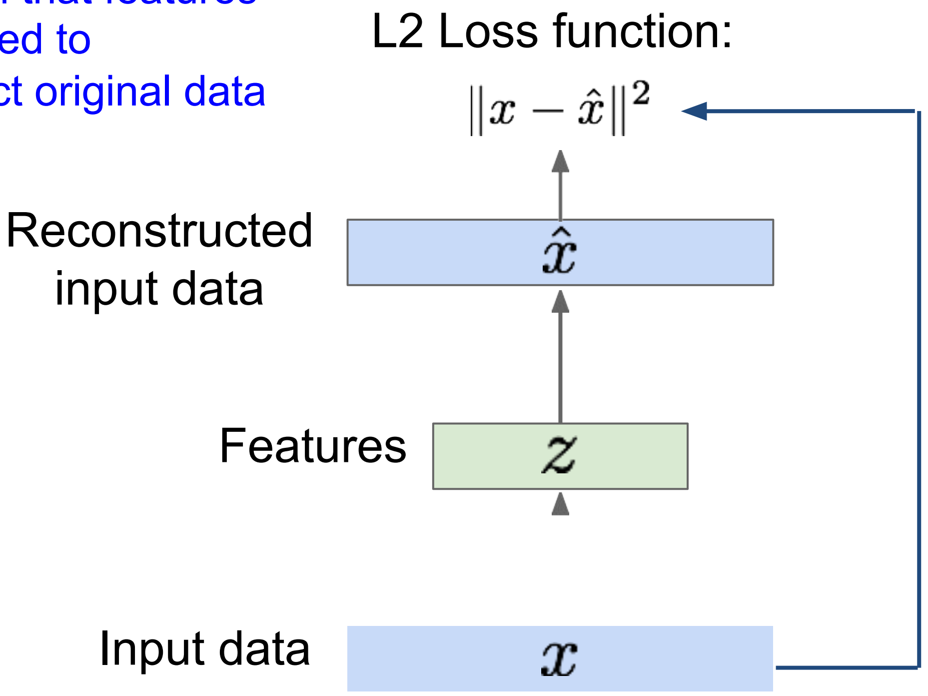
Train such that features can be used to reconstruct original data
"Autoencoding" - encoding itself

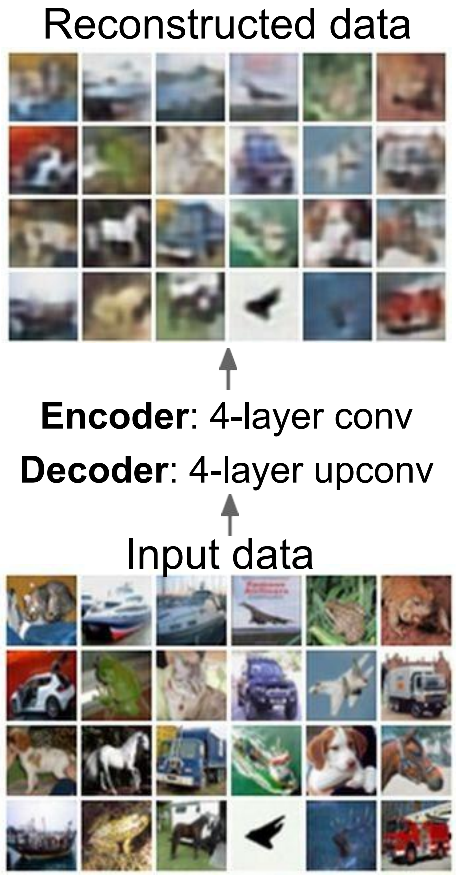




Some background first: Autoencoders

Train such that features can be used to reconstruct original data

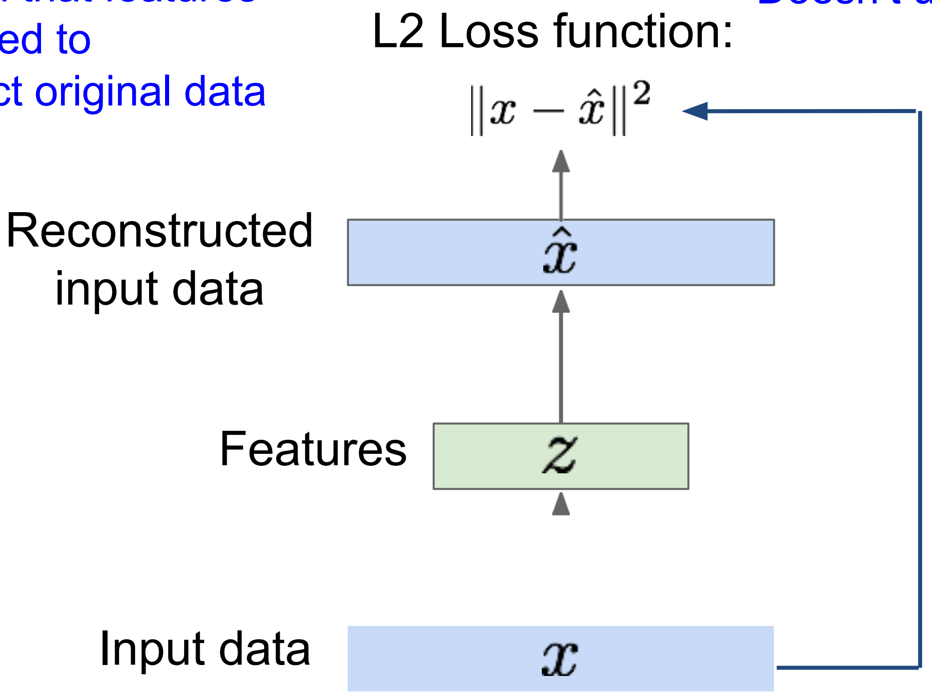


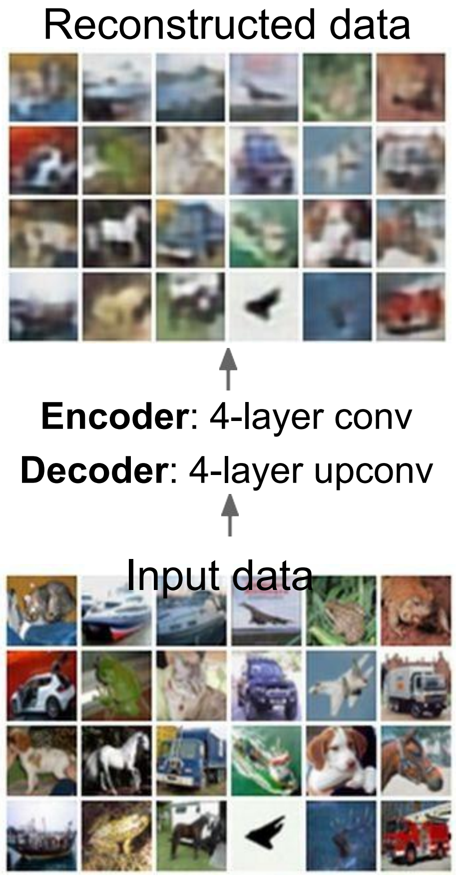


Some background first: Autoencoders

Train such that features can be used to reconstruct original data

Doesn't use labels!





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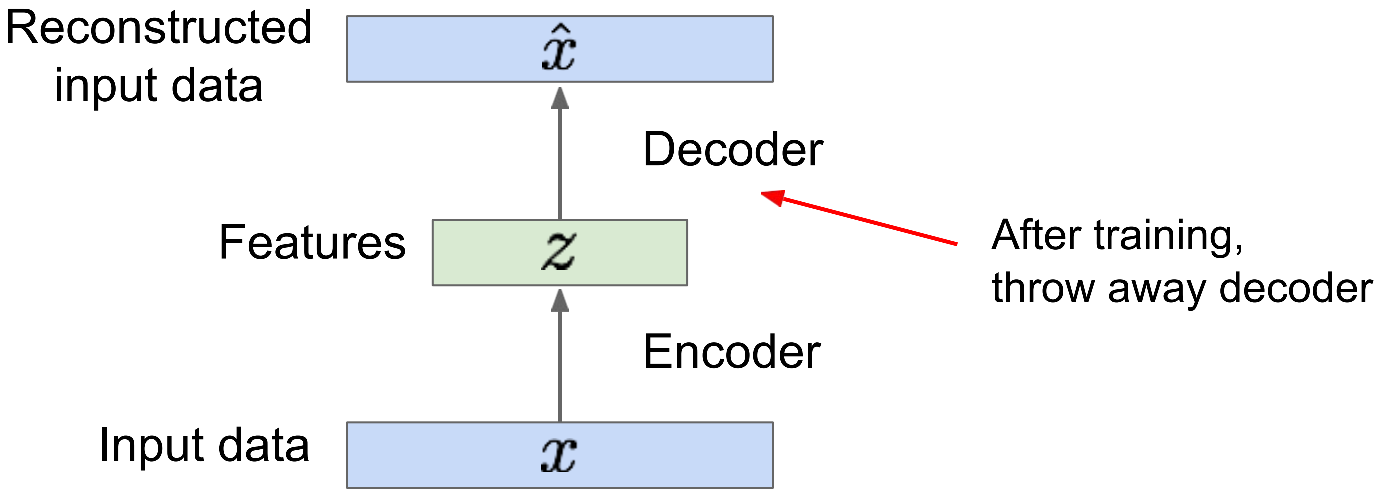

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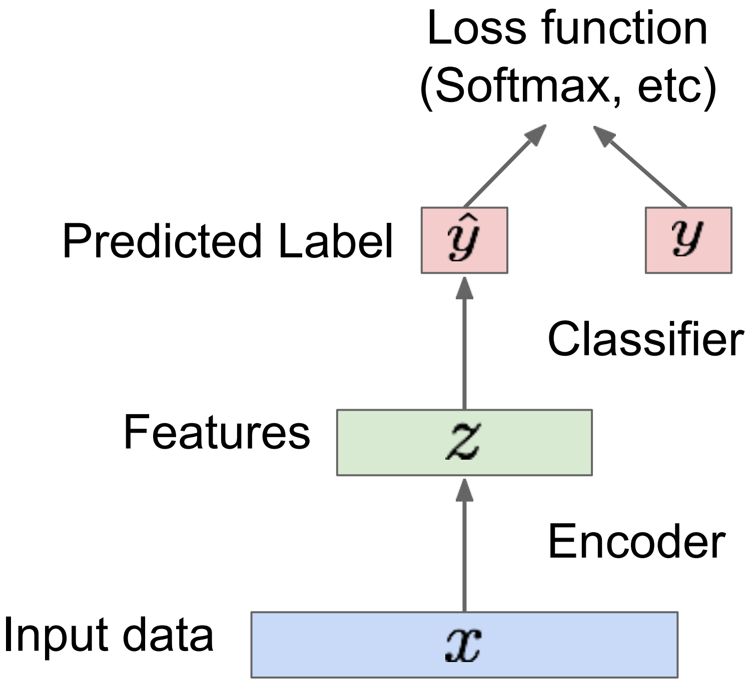


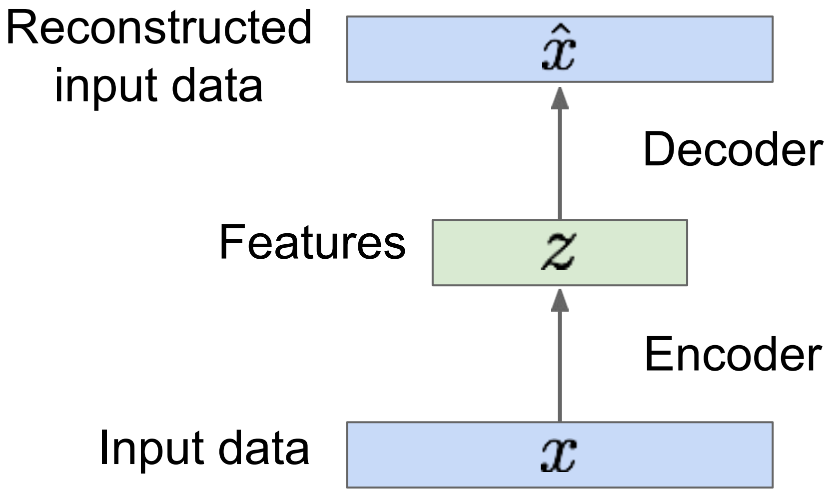
Encoder can be used to initialize a **supervised** model

Fine-tune encoder jointly with classifier

Train for final task (sometimes with small data)

bird plane
dog deer truck

Some background first: Autoencoders



Autoencoders can reconstruct data, and can learn features to initialize a supervised model

Features capture factors of variation in training data. Can we generate new images from an autoencoder?

Variational Autoencoders

Probabilistic spin on autoencoders - will let us sample from the model to generate data!

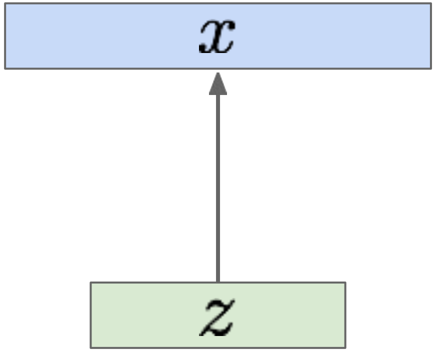
Variational Autoencoders

Probabilistic spin on autoencoders - will let us sample from the model to generate data!

Assume training data $\{x^{(i)}\}_{i=1}^{N}$ is generated from underlying unobserved (latent) representation **z**

Sample from true conditional $p_{\theta^*}(x \mid z^{(i)})$

Sample from true prior $p_{\theta^*}(z)$



Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders

Probabilistic spin on autoencoders - will let us sample from the model to generate data!

Assume training data $\{x^{(i)}\}_{i=1}^{N}$ is generated from underlying unobserved (latent) representation **z**

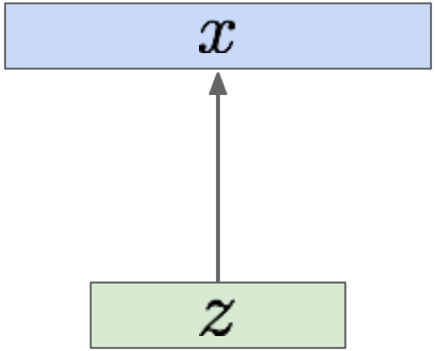
Intuition (remember from autoencoders!): **x** is an image, **z** is latent factors used to generate **x:** attributes, orientation, etc.

Sample from true conditional

$p_{\theta^*}(x \mid z^{(i)})$

Sample from true prior

$p_{\theta^*}(z)$



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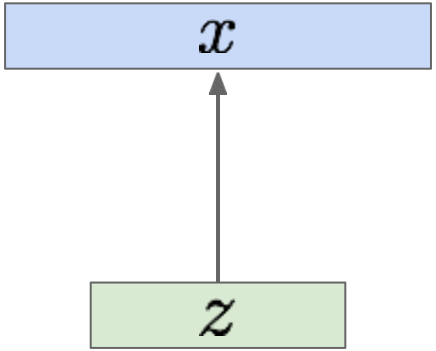
Variational Autoencoders

We want to estimate the true parameters θ^* of this generative model.

Sample from true conditional

$p_{\theta^*}(x \mid z^{(i)})$



Sample from true prior

$p_{\theta^*}(z)$

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders

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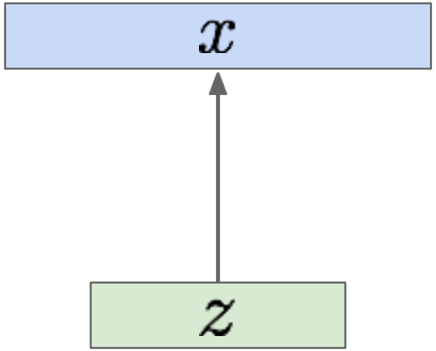

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How should we represent this model?

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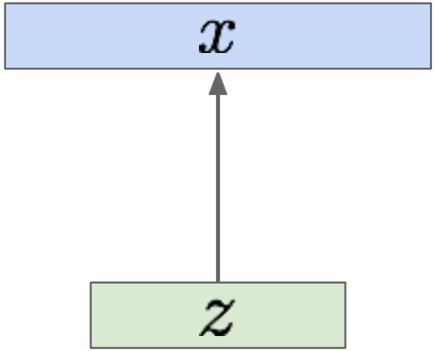

We want to estimate the true parameters θ^* of this generative model.

How should we represent this model?

Choose prior p(z) to be simple, e.g. Gaussian. Reasonable for latent attributes, e.g. pose, how much smile.

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders

Sample from
true conditional

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Sample from
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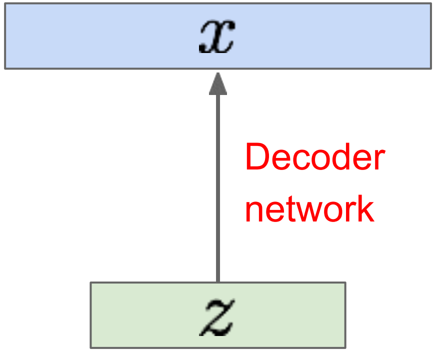


We want to estimate the true parameters θ^* of this generative model.

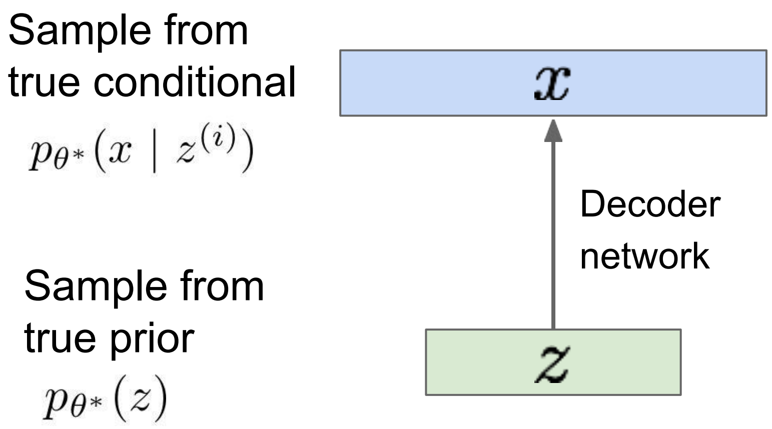
How should we represent this model?

Choose prior p(z) to be simple, e.g. Gaussian.

Conditional p(x|z) is complex (generates image) => represent with neural network

Kingma and Welling, “Auto-Encoding Variational Bayes”, ICLR 2014

Variational Autoencoders



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How to train the model?

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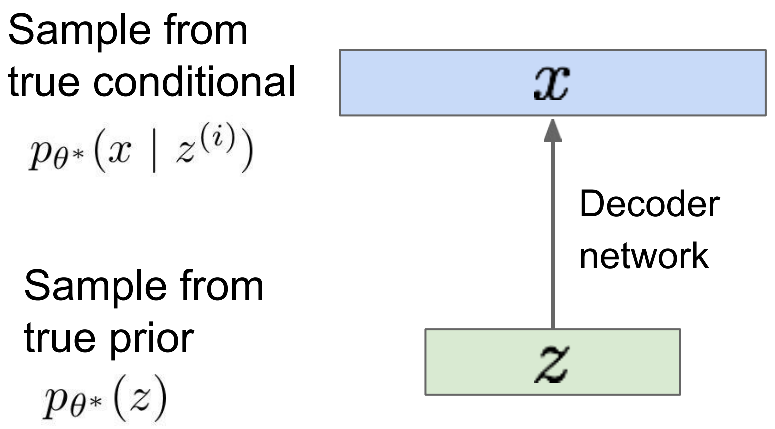
Variational Autoencoders



We want to estimate the true parameters θ^* of this generative model.

How to train the model?

Learn model parameters to maximize likelihood of training data

$$p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$$

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Variational Autoencoders

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How to train the model?

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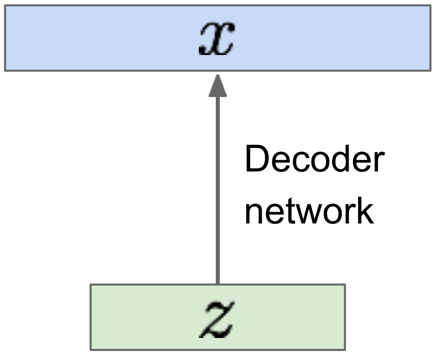

Sample from true prior

$p_{\theta^*}(z)$

Learn model parameters to maximize likelihood of training data

$$p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$$

Now with latent z

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders

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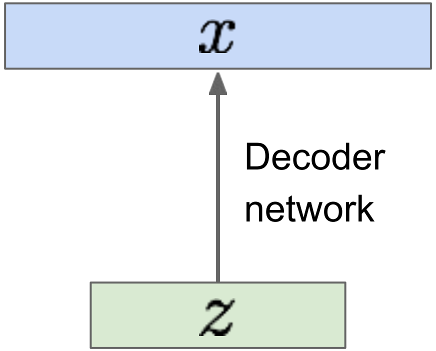
Sample from true prior

$p_{\theta^*}(z)$



We want to estimate the true parameters θ^* of this generative model.

How to train the model?

Learn model parameters to maximize likelihood of training data

$$p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$$

Q: What is the problem with this?

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders

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Sample from
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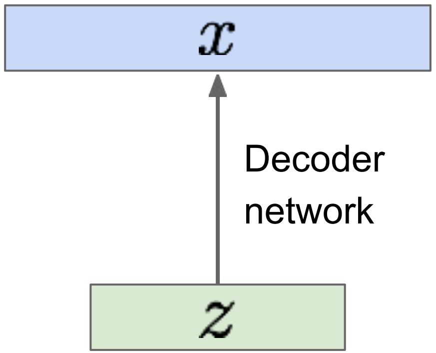

We want to estimate the true parameters θ^* of this generative model.

How to train the model?

Learn model parameters to maximize likelihood of training data

$$p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$$

Q: What is the problem with this?

Intractable!

Kingma and Welling, “Auto-Encoding Variational Bayes”, ICLR 2014

Variational Autoencoders: Intractability

Data likelihood: $p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$

Kingma and Welling, “Auto-Encoding Variational Bayes”, ICLR 2014

Variational Autoencoders: Intractability

✔

Data likelihood: $p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$

Simple Gaussian prior

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders: Intractability

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Decoder neural network

Kingma and Welling, “Auto-Encoding Variational Bayes”, ICLR 2014

Variational Autoencoders: Intractability

:(✔ ✔

Data likelihood: $p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$

Intractible to compute
p(x|z) for every z!

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders: Intractability

:(✔ ✔

Data likelihood: $p_\theta(x) = \int p_\theta(z) p_\theta(x|z) dz$

Posterior density also intractable: $p_\theta(z|x) = p_\theta(x|z) p_\theta(z) / p_\theta(x)$

Kingma and Welling, “Auto-Encoding Variational Bayes”, ICLR 2014

Variational Autoencoders: Intractability

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✔ ✔ :(

Posterior density also intractable: $p_\theta(z|x) = p_\theta(x|z) p_\theta(z) / p_\theta(x)$

Intractable data likelihood

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders: Intractability

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Data likelihood: $p_\theta(x) = \int p_\theta(z)p_\theta(x|z)dz$

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Posterior density also intractable: $p_\theta(z|x) = p_\theta(x|z)p_\theta(z)/p_\theta(x)$

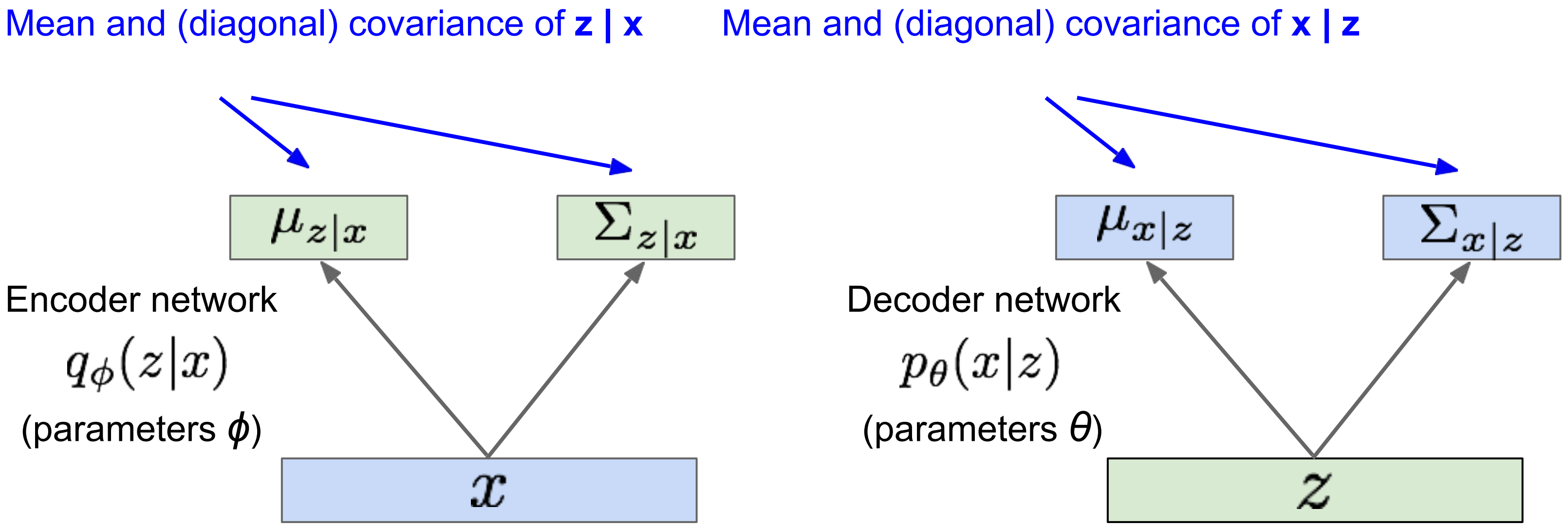
Solution: In addition to decoder network modeling $p_\theta(x|z)$, define additional encoder network $q_\phi(z|x)$ that approximates $p_\theta(z|x)$

Will see that this allows us to derive a lower bound on the data likelihood that is tractable, which we can optimize

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders

Since we're modeling probabilistic generation of data, encoder and decoder networks are probabilistic



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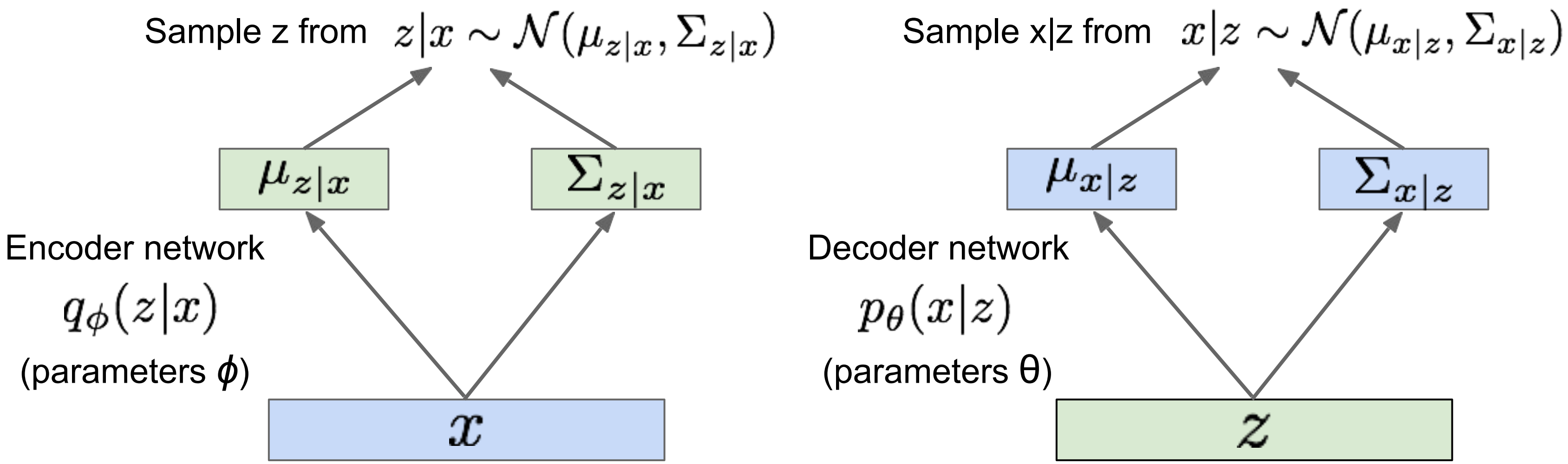

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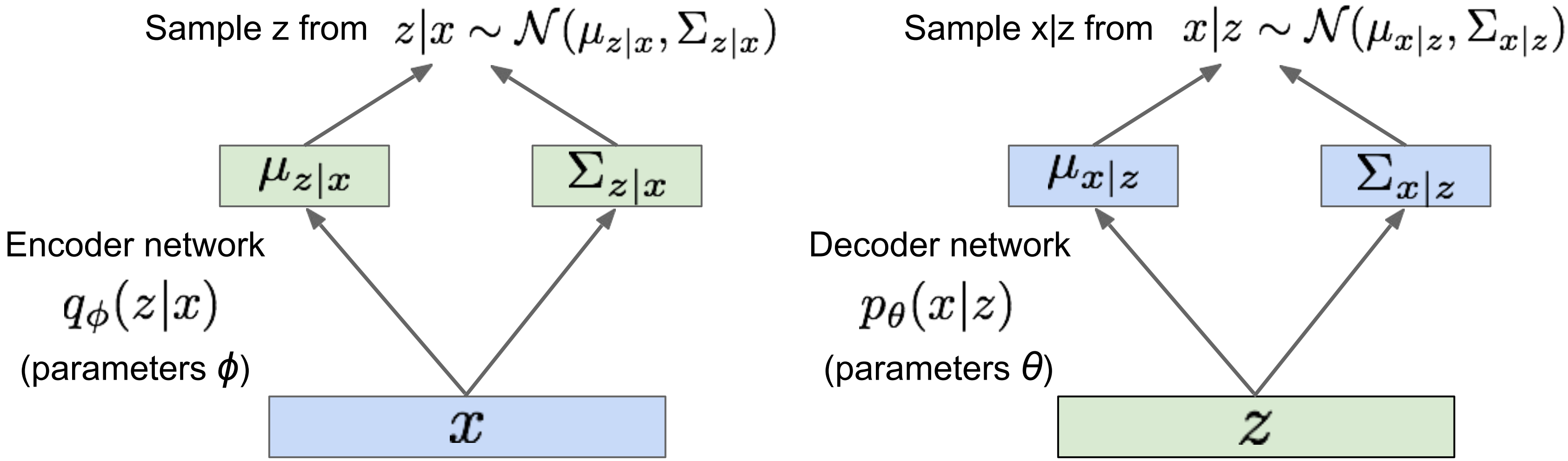

Encoder and decoder networks also called "recognition"/"inference" and "generation" networks

Kingma and Welling, "Auto-Encoding Variational Bayes", ICLR 2014

Variational Autoencoders

Now equipped with our encoder and decoder networks, let's work out the (log) data likelihood:

$$\log p_\theta(x^{(i)}) = \mathbf{E}_{z \sim q_\phi(z|x^{(i)})} \left[\log p_\theta(x^{(i)}) \right] \qquad (p_\theta(x^{(i)}) \text{ Does not depend on } z)$$

Variational Autoencoders

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Taking expectation wrt. z (using encoder network) will come in handy later

Variational Autoencoders

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Variational Autoencoders

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Variational Autoencoders

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The expectation wrt. z (using encoder network) let us write nice KL terms

Variational Autoencoders

Now equipped with our encoder and decoder networks, let's work out the (log) data likelihood:

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Decoder network gives $p_\theta(x|z)$, can compute estimate of this term through sampling. (Sampling differentiable through reparam. trick, see paper.)

This KL term (between Gaussians for encoder and z prior) has nice closed-form solution!

$p_\theta(z|x)$ intractable (saw earlier), can't compute this KL term :(But we know KL divergence always >= 0.

Variational Autoencoders

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Tractable lower bound which we can take gradient of and optimize! ($p_\theta(x|z)$ differentiable, KL term differentiable)

Variational Autoencoders

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$$\log p_\theta(x^{(i)}) \geq \mathcal{L}(x^{(i)},\theta,\phi)$$

Variational lower bound ("ELBO")

$$\theta^*, \phi^* = \arg\max_{\theta,\phi} \sum_{i=1}^{N} \mathcal{L}(x^{(i)},\theta,\phi)$$

Training: Maximize lower bound

Variational Autoencoders

Now equipped with our encoder and decoder networks, let's work out the (log) data likelihood:

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Reconstruct the input data

Make approximate posterior distribution close to prior

$$\log p_\theta(x^{(i)}) \geq \mathcal{L}(x^{(i)},\theta,\phi)$$

Variational lower bound ("ELBO")

$$\theta^*, \phi^* = \arg\max_{\theta,\phi} \sum_{i=1}^{N} \mathcal{L}(x^{(i)},\theta,\phi)$$

Training: Maximize lower bound

Variational Autoencoders

Putting it all together: maximizing the likelihood lower bound

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Variational Autoencoders

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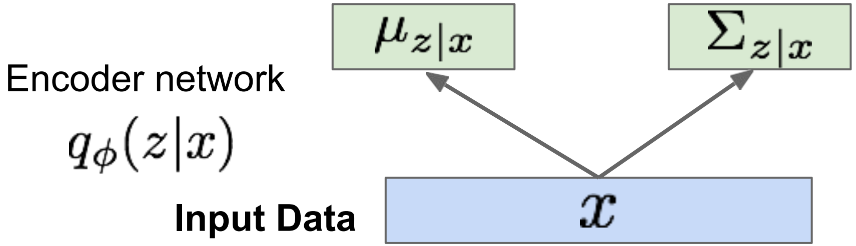
Let's look at computing the bound (forward pass) for a given minibatch of input data

Input Data x

Variational Autoencoders

Putting it all together: maximizing the likelihood lower bound

$$\underbrace{\mathbf{E}_z\left[\log p_\theta(x^{(i)} \mid z)\right] - D_{KL}(q_\phi(z \mid x^{(i)}) \,||\, p_\theta(z))}_{\mathcal{L}(x^{(i)},\theta,\phi)}$$



Variational Autoencoders

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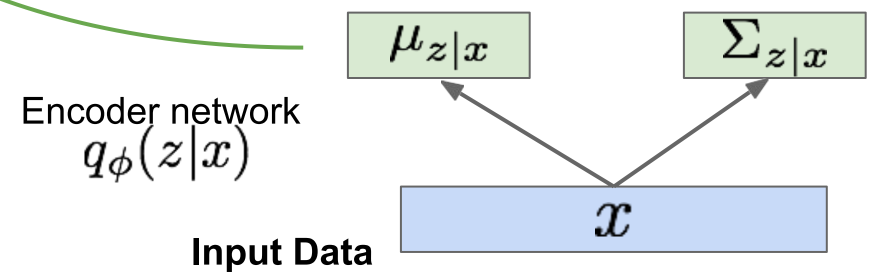

Variational Autoencoders

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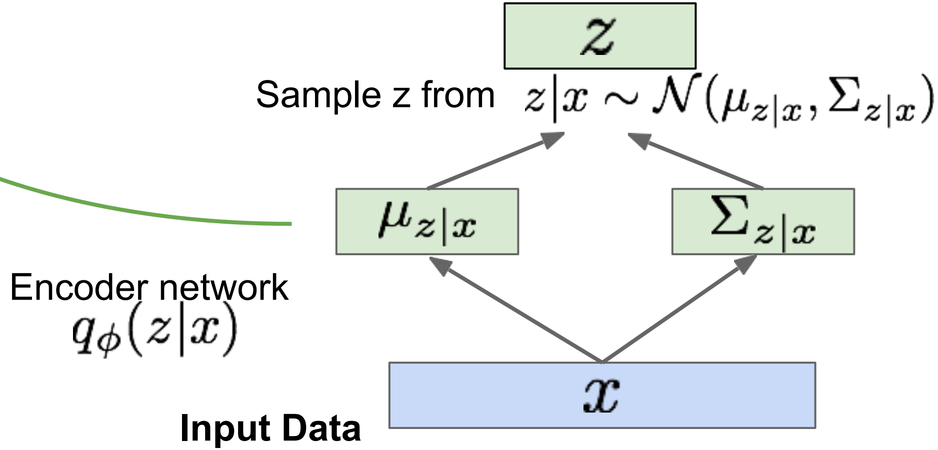

Variational Autoencoders

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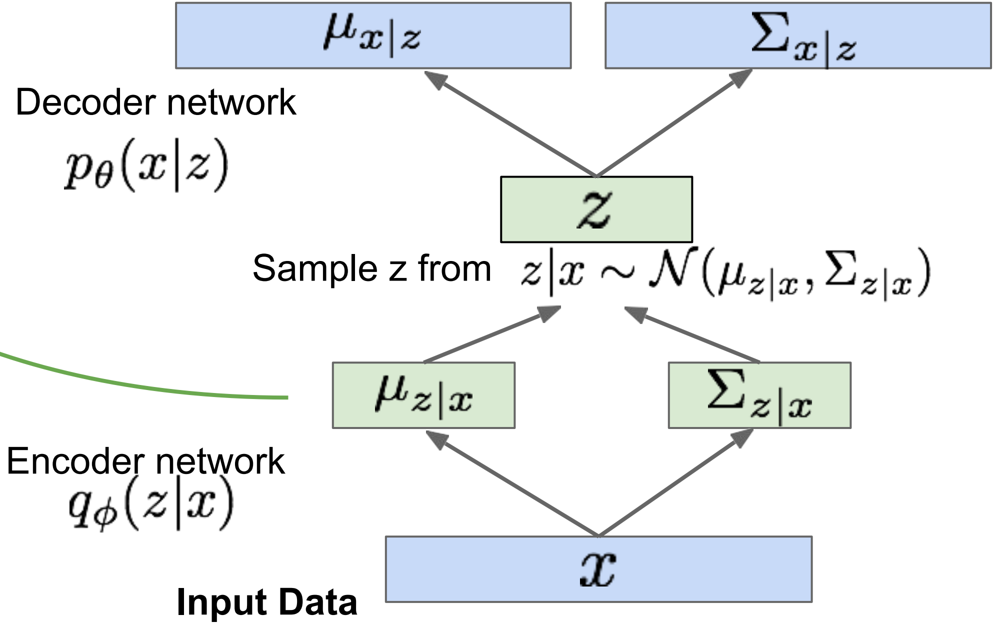

Variational Autoencoders

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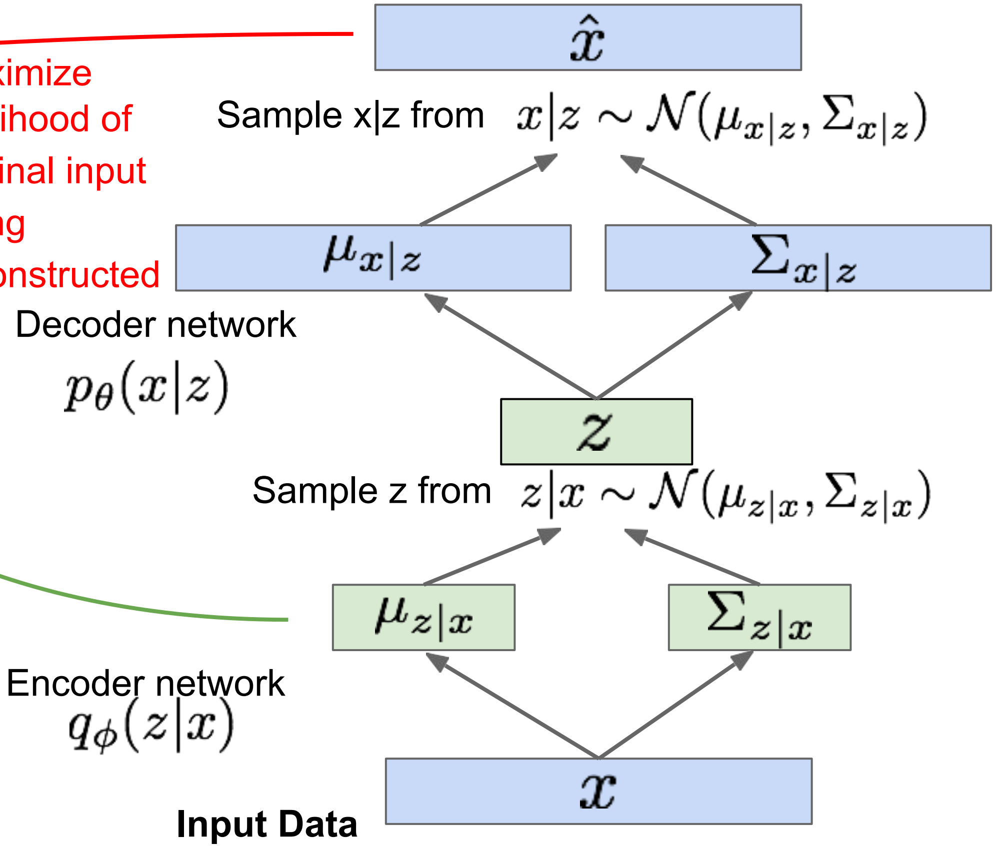
Maximize likelihood of original input being reconstructed

Make approximate posterior distribution close to prior



Variational Autoencoders

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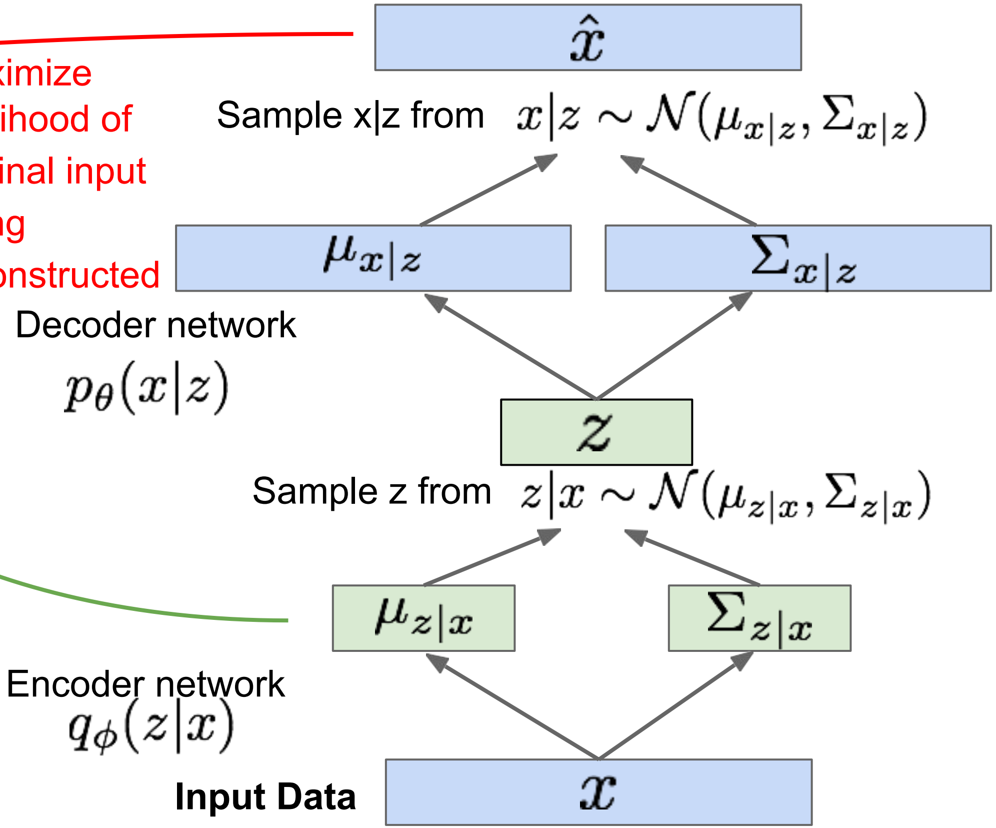
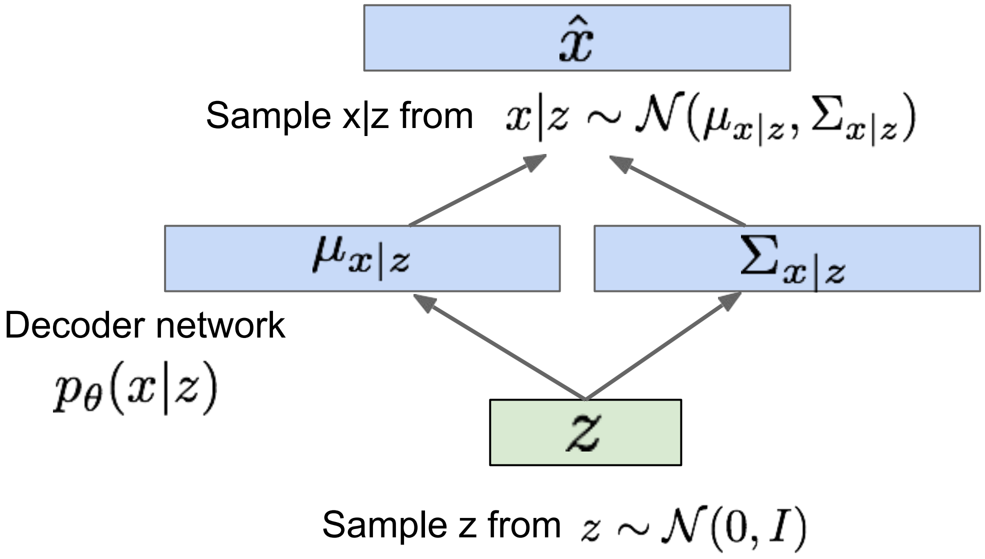


For every minibatch of input data: compute this forward pass, and then backprop!

Variational Autoencoders: Generating Data!

Use decoder network. Now sample z from prior!



Kingma and Welling, “Auto-Encoding Variational Bayes”, ICLR 2014

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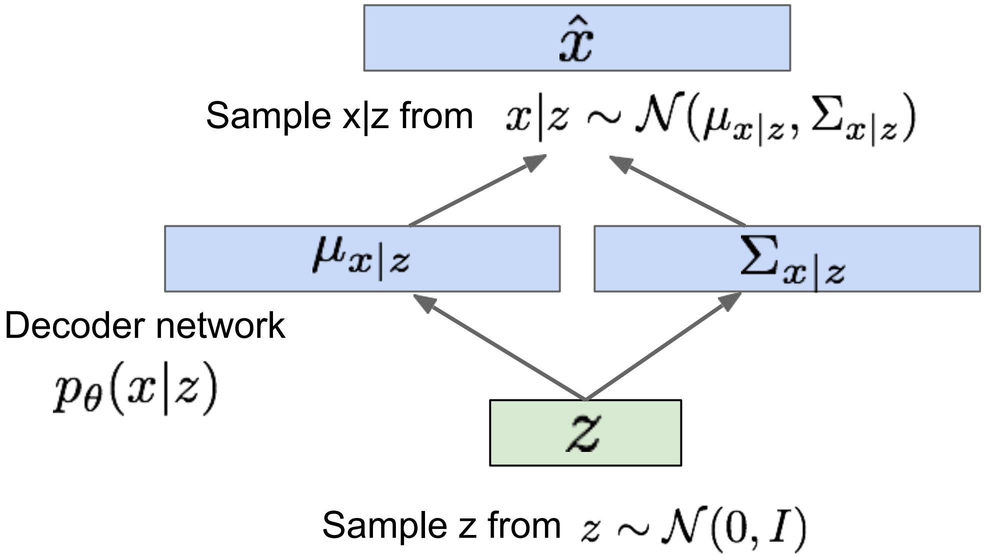

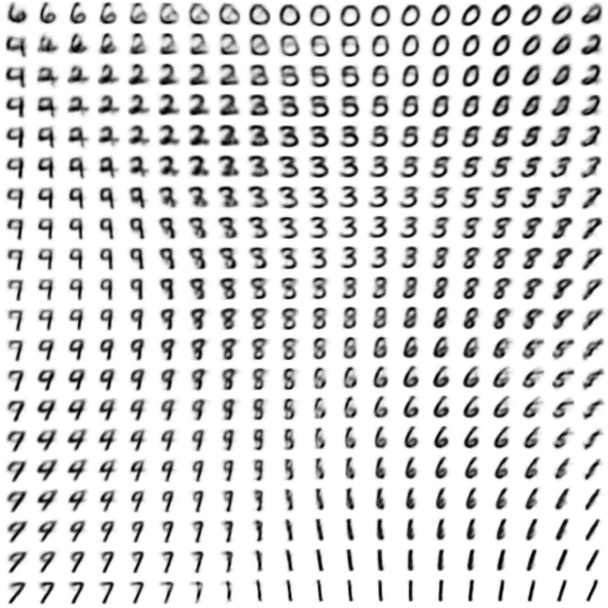

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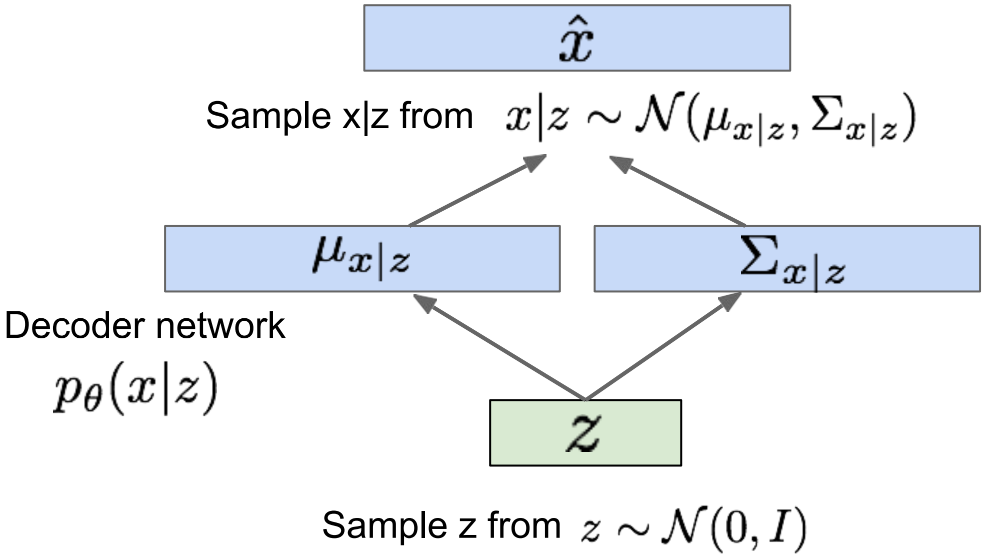
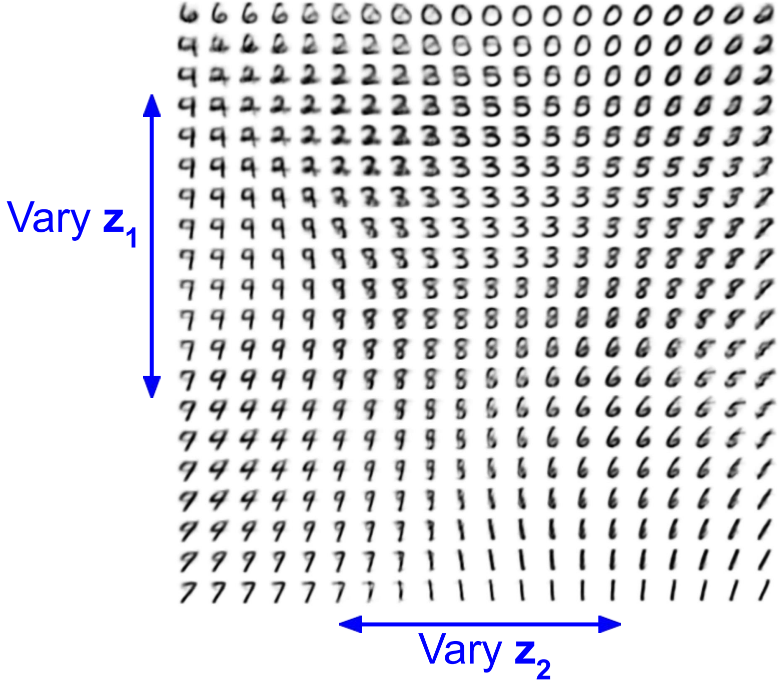


Data manifold for 2-d **z**



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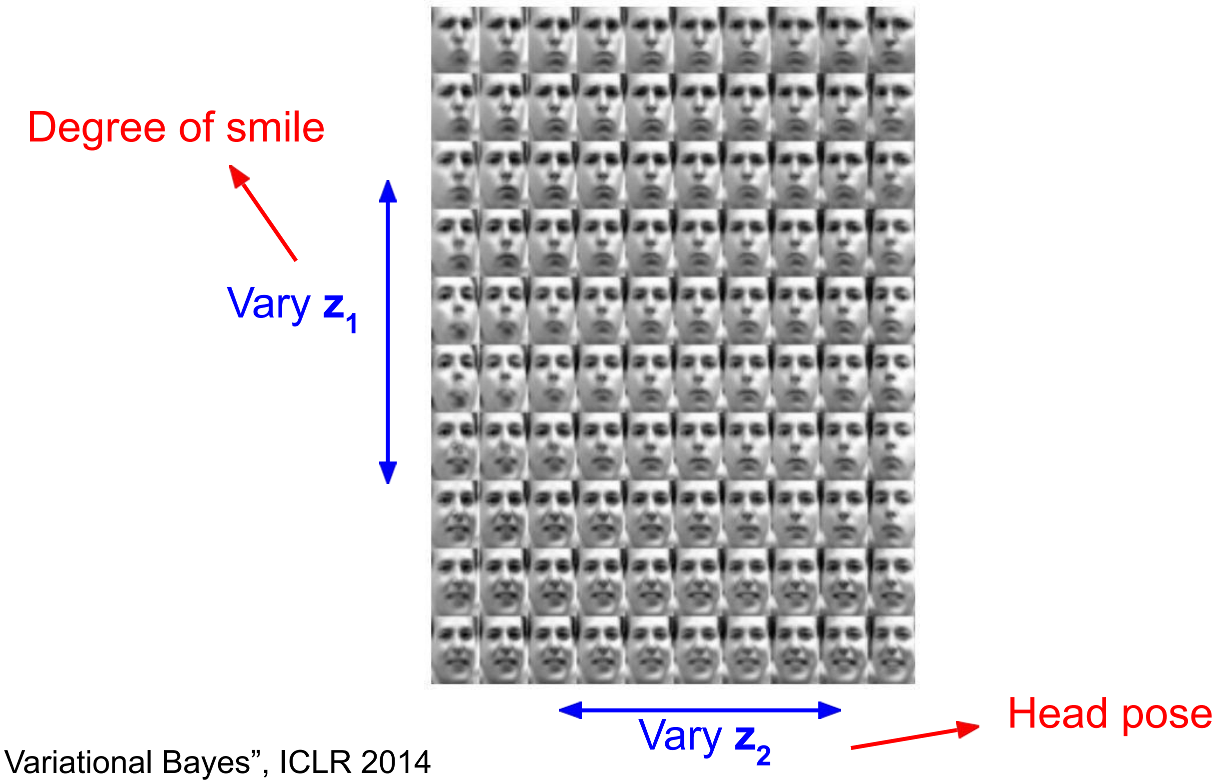
Variational Autoencoders: Generating Data!

Diagonal prior on **z**
=> independent
latent variables

Different
dimensions of **z**
encode
interpretable factors
of variation



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Variational Autoencoders: Generating Data!

Diagonal prior on **z** => independent latent variables

Different dimensions of **z** encode interpretable factors of variation

Also good feature representation that can be computed using $q_\phi(z|x)$!

Degree of smile

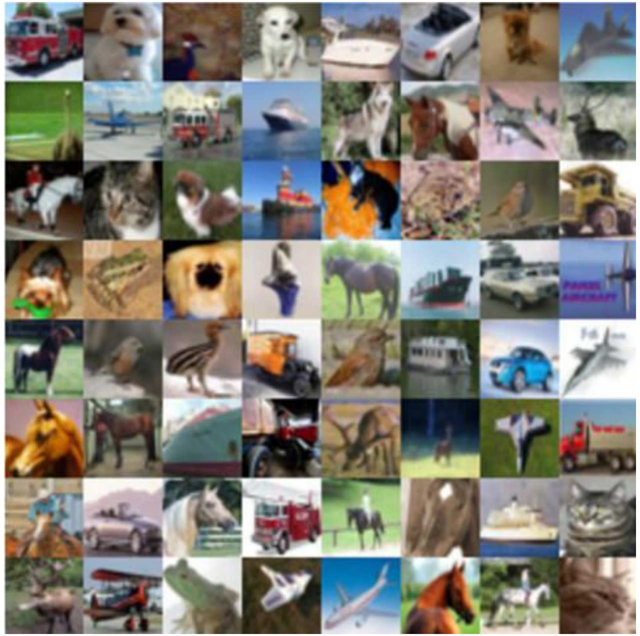
Vary $\mathbf{z}_1$

Vary $\mathbf{z}_2$

Head pose

Kingma and Welling, “Auto-Encoding Variational Bayes”, ICLR 2014

Variational Autoencoders: Generating Data!



32x32 CIFAR-10

Labeled Faces in the Wild

Variational Autoencoders in Genomics

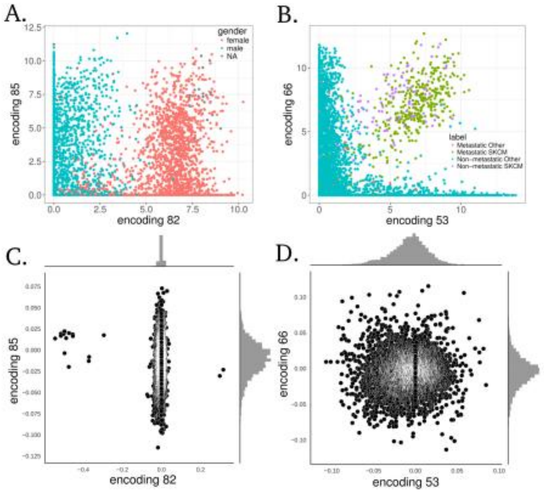


Fig. 3. *Specific examples of Tybalt features capturing biological signals.* **(A)** Encoding 82 stratified patient sex. **(B)** Together, encodings 53 and 66 separated melanoma tumors. Distributions of gene coefficients contributing to each plot above for **(C)** patient sex and **(D)** melanoma. The gene coefficients consist of the Tybalt learned weights for each feature encoding.

Extracting a biologically relevant latent space from cancer transcriptomes with variational autoencoders

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The Cancer Genome Atlas (TCGA) has profiled over 10,000 tumors across 33 different cancer-types for many genomic features, including gene expression levels. Gene expression measurements capture substantial information about the state of each tumor. Certain classes of deep neural network models are capable of learning a meaningful latent space. Such a latent space could be used to explore and generate hypothetical gene expression profiles under various types of molecular and genetic perturbation. For example, one might wish to use such a model to predict a tumor's response to specific therapies or to characterize complex gene expression activations existing in differential proportions in different tumors. Variational autoencoders (VAEs) are a deep neural network approach capable of generating meaningful latent spaces for image and text data. In this work, we sought to determine the extent to which a VAE can be trained to model cancer gene expression, and whether or not such a VAE would capture biologically-relevant features. In the following report, we introduce a VAE trained on TCGA pan-cancer RNA-seq data, identify specific patterns in the VAE encoded features, and discuss potential merits of the approach. We name our method "Tybalt" after an instigative, cat-like character who sets a cascading chain of events in motion in Shakespeare's "*Romeo and Juliet*". From a systems biology perspective, Tybalt could one day aid in cancer stratification or predict specific activated expression patterns that would result from genetic changes or treatment effects.

Keywords: Deep Learning; Gene Expression; Variational Autoencoder, The Cancer Genome Atlas

Variational Autoencoders in Genomics

They present a two-step VAE-based models for drug response prediction, which first predicts the post- from the pre-treatment state in an unsupervised manner, then extends it to the final semi-supervised prediction. The model is based on data from Genomics of Drug Sensitivity in Cancer (GDSC; Yang et al., 2013) and Cancer Cell Line Encyclopedia (CCLE; Barretina et al., 2012).

Dr.VAE: Drug Response Variational Autoencoder

Ladislav Rampasek*†‡ Daniel Hidru†‡ Petr Smirnov§
Benjamin Haibe-Kains§¶†‖ Anna Goldenberg*‡†

Abstract

We present two deep generative models based on Variational Autoencoders to improve the accuracy of drug response prediction. Our models, Perturbation Variational Autoencoder and its semi-supervised extension, Drug Response Variational Autoencoder (Dr.VAE), learn latent representation of the underlying gene states before and after drug application that depend on: (i) drug-induced biological change of each gene and (ii) overall treatment response outcome. Our VAE-based models outperform the current published benchmarks in the field by anywhere from 3 to 11% AUROC and 2 to 30% AUPR. In addition, we found that better reconstruction accuracy does not necessarily lead to improvement in classification accuracy and that jointly trained models perform better than models that minimize reconstruction error independently.

1 Introduction

Despite tremendous advances in the pharmaceutical industry, many patients worldwide do not respond to the first medication they are prescribed. Personalized medicine, an approach that uses patients' own genomic data, promises to tailor the treatment program to increase

Variational Autoencoders

Probabilistic spin to traditional autoencoders => allows generating data
Defines an intractable density => derive and optimize a (variational) lower bound

Pros:

- Principled approach to generative models
- Allows inference of q(z|x), can be useful feature representation for other tasks

Cons:

- Maximizes lower bound of likelihood
- Samples blurrier and lower quality compared to state-of-the-art (GANs)

Active areas of research:

- More flexible approximations, e.g. richer approximate posterior instead of diagonal Gaussian
- Incorporating structure in latent variables

Generative Adversarial Networks (GAN)

Generative Adversarial Networks (GAN)

GANs don't work with any explicit density function!
What they care the most, is the samples which are close to real data
(ie. learn to generate from training distribution through 2-player game)

Generative Adversarial Networks

Ian Goodfellow et al., "Generative Adversarial Nets", NIPS 2014

Problem: Want to sample from complex, high-dimensional training distribution. No direct way to do this!

Solution: Sample from a simple distribution, e.g. random noise. Learn transformation to training distribution.

Q: What can we use to represent this complex transformation?

Generative Adversarial Networks

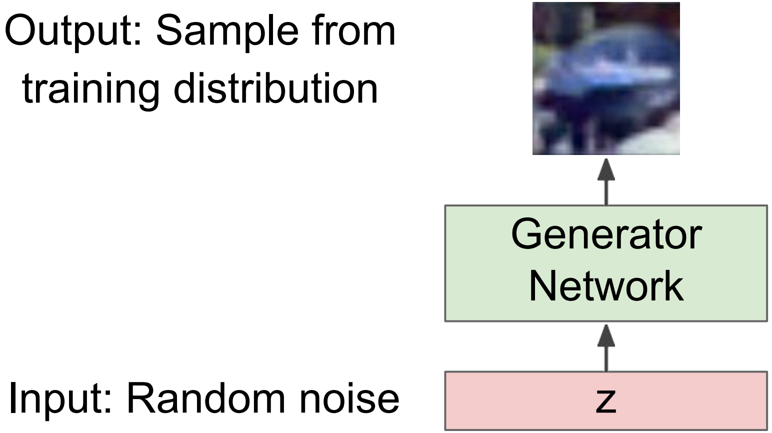
Ian Goodfellow et al., "Generative Adversarial Nets", NIPS 2014

Problem: Want to sample from complex, high-dimensional training distribution. No direct way to do this!

Solution: Sample from a simple distribution, e.g. random noise. Learn transformation to training distribution.

Q: What can we use to represent this complex transformation?

A: A neural network!



Training GANs: Two-player game

Ian Goodfellow et al., “Generative Adversarial Nets”, NIPS 2014

Generator network: try to fool the discriminator by generating real-looking images (or DNAs, etc)
Discriminator network: try to distinguish between real and fake images (or DNAs, etc)

Training GANs: Two-player game

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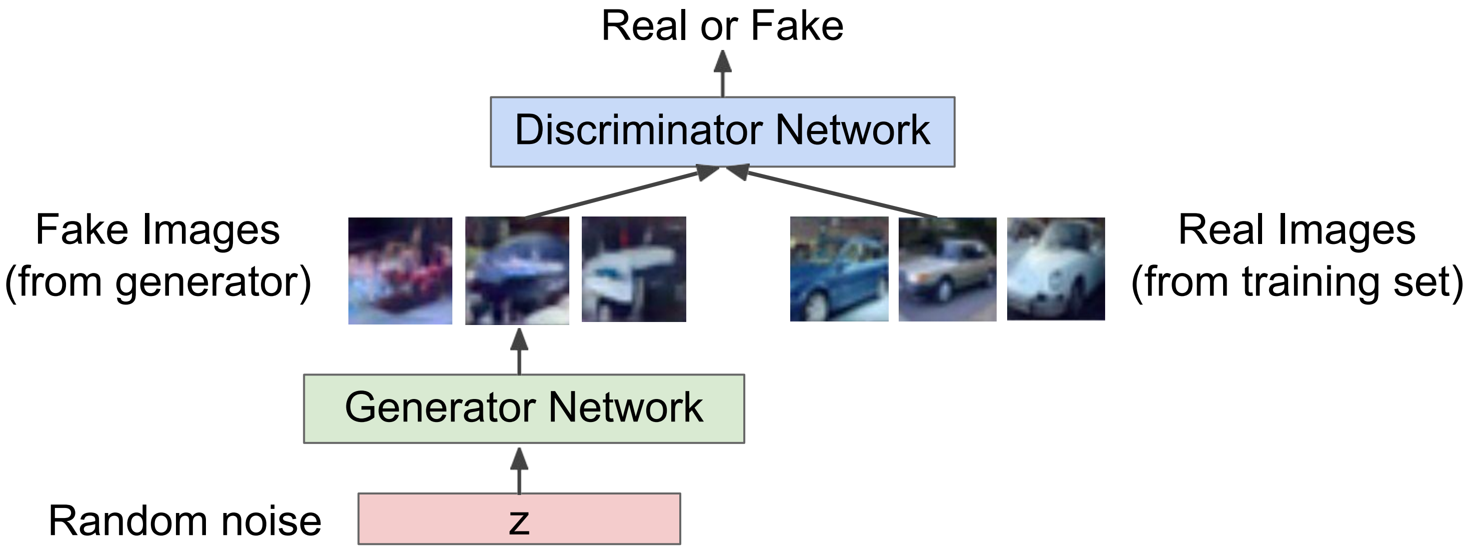

Training GANs: Two-player game

Ian Goodfellow et al., “Generative Adversarial Nets”, NIPS 2014

Generator network: try to fool the discriminator by generating real-looking images
Discriminator network: try to distinguish between real and fake images

Train jointly in **minimax game**

Minimax objective function:

$$\min_{\theta_g} \max_{\theta_d} \left[\mathbb{E}_{x \sim p_{data}} \log D_{\theta_d}(x) + \mathbb{E}_{z \sim p(z)} \log(1 - D_{\theta_d}(G_{\theta_g}(z))) \right]$$

Training GANs: Two-player game

Ian Goodfellow et al., “Generative Adversarial Nets”, NIPS 2014

Generator network: try to fool the discriminator by generating real-looking images
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Discriminator outputs likelihood in (0,1) of real image

Minimax objective function:

$$\min_{\theta_g} \max_{\theta_d} \left[\mathbb{E}_{x \sim p_{data}} \log \underbrace{D_{\theta_d}(x)}_{\text{Discriminator output for real data x}} + \mathbb{E}_{z \sim p(z)} \log(1 - \underbrace{D_{\theta_d}(G_{\theta_g}(z))}_{\text{Discriminator output for generated fake data G(z)}}) \right]$$

Discriminator output for real data x

Discriminator output for generated fake data G(z)

Training GANs: Two-player game

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- Discriminator (θ_d) wants to **maximize objective** such that D(x) is close to 1 (real) and D(G(z)) is close to 0 (fake)
- Generator (θ_g) wants to **minimize objective** such that D(G(z)) is close to 1 (discriminator is fooled into thinking generated G(z) is real)

Training GANs: Two-player game

Ian Goodfellow et al., “Generative Adversarial Nets”, NIPS 2014

Minimax objective function:

$$\min_{\theta_g} \max_{\theta_d} \left[\mathbb{E}_{x \sim p_{data}} \log D_{\theta_d}(x) + \mathbb{E}_{z \sim p(z)} \log(1 - D_{\theta_d}(G_{\theta_g}(z))) \right]$$

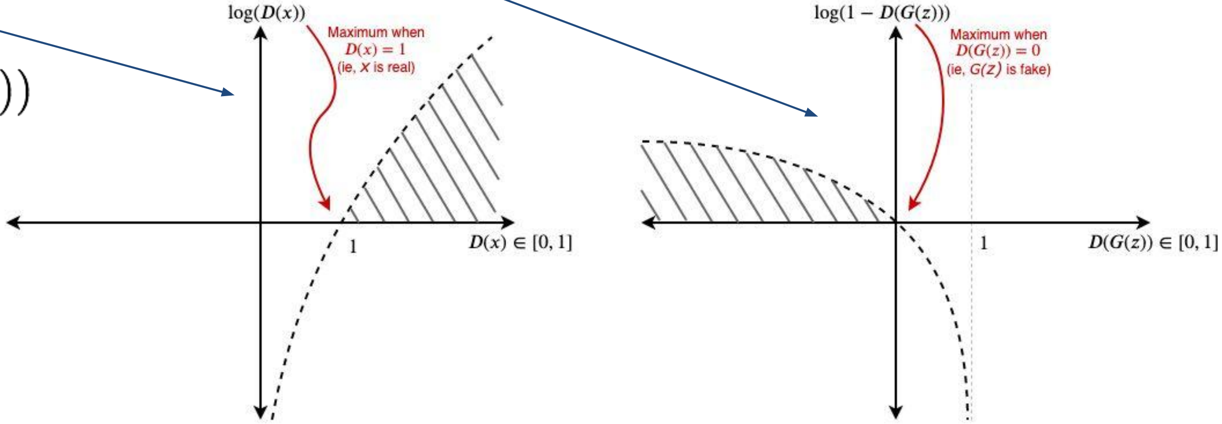
Alternate between:

1. For **Discriminator**

$$\max_{\theta_d} \left[\mathbb{E}_{x \sim p_{data}} \log D_{\theta_d}(x) + \mathbb{E}_{z \sim p(z)} \log(1 - D_{\theta_d}(G_{\theta_g}(z))) \right]$$

2. For **Generator**

$$\min_{\theta_g} \mathbb{E}_{z \sim p(z)} \log(1 - D_{\theta_d}(G_{\theta_g}(z)))$$



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Ian Goodfellow et al., “Generative Adversarial Nets”, NIPS 2014

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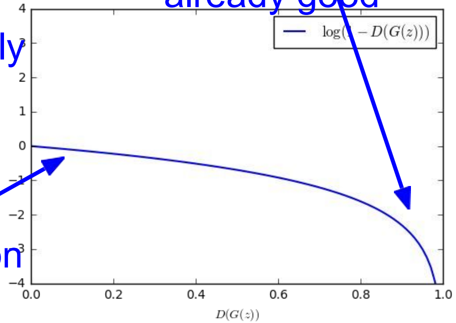
2. For **Generator**

$$\min_{\theta_g} \mathbb{E}_{z \sim p(z)} \log(1 - D_{\theta_d}(G_{\theta_g}(z)))$$

In practice, optimizing this generator objective does not work well!

When sample is likely fake, want to learn from it to improve generator. But gradient in this region is relatively flat!

Gradient signal dominated by region where sample is already good



Training GANs: Two-player game

Ian Goodfellow et al., "Generative Adversarial Nets", NIPS 2014

Minimax objective function:

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Alternate between:

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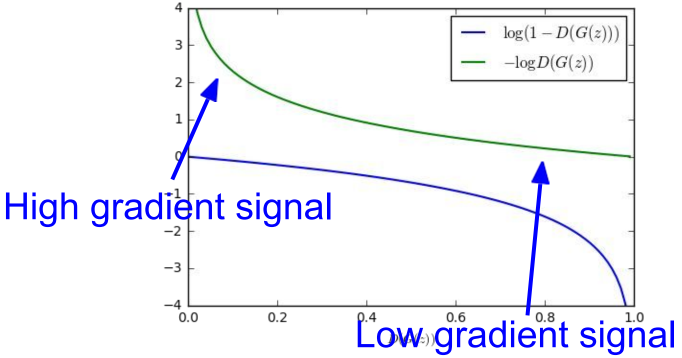
$$\max_{\theta_d} \left[\mathbb{E}_{x \sim p_{data}} \log D_{\theta_d}(x) + \mathbb{E}_{z \sim p(z)} \log(1 - D_{\theta_d}(G_{\theta_g}(z))) \right]$$

2. For **Generator**

different objective

$$\max_{\theta_g} \mathbb{E}_{z \sim p(z)} \log(D_{\theta_d}(G_{\theta_g}(z)))$$

Instead of minimizing likelihood of discriminator being correct, now maximize likelihood of discriminator being wrong.
Same objective of fooling discriminator, but now higher gradient signal for bad samples => works much better! Standard in practice.



Training GANs: Two-player game

Ian Goodfellow et al., "Generative Adversarial Nets", NIPS 2014

Minimax objective function:

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Aside: Jointly training two networks is challenging, can be unstable. Choosing objectives with better loss landscapes helps training, is an active area of research.

Alternate between:

1. For **Discriminator**

$$\max_{\theta_d} \left[\mathbb{E}_{x \sim p_{data}} \log D_{\theta_d}(x) + \mathbb{E}_{z \sim p(z)} \log(1 - D_{\theta_d}(G_{\theta_g}(z))) \right]$$

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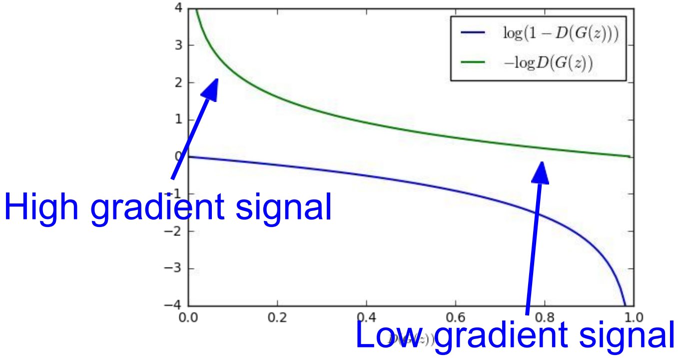

Training GANs: Two-player game

Ian Goodfellow et al., "Generative Adversarial Nets", NIPS 2014

Generator network: try to fool the discriminator by generating real-looking images
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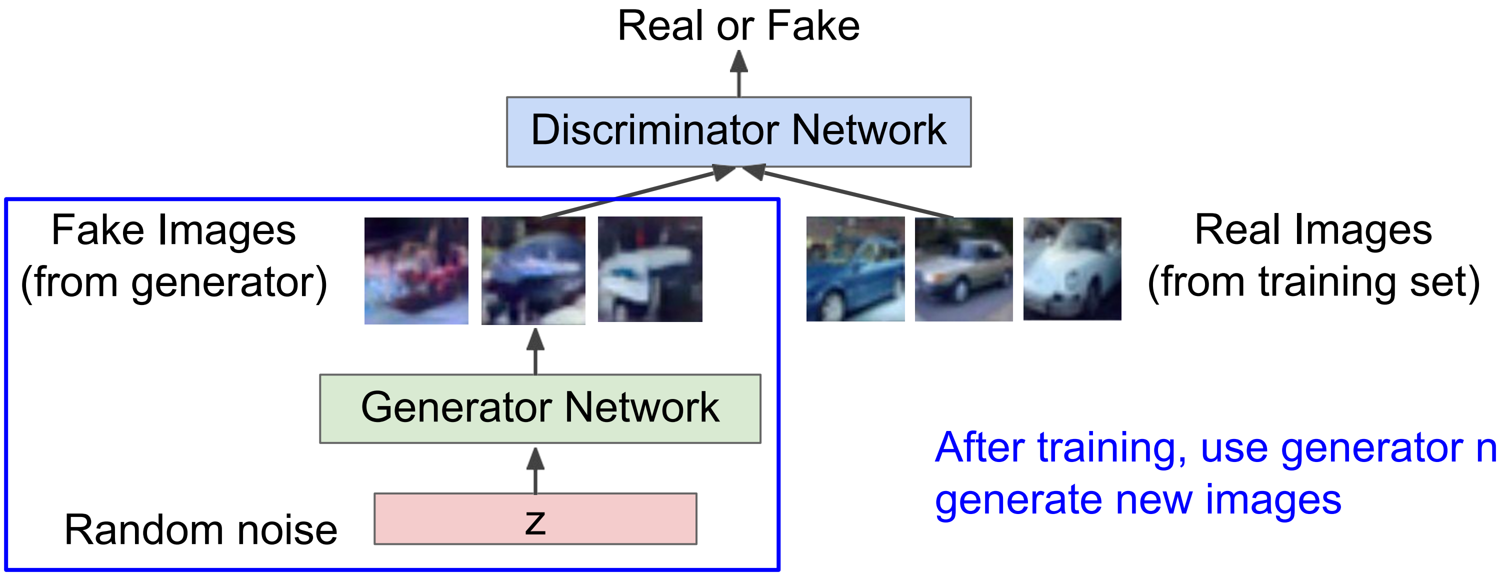
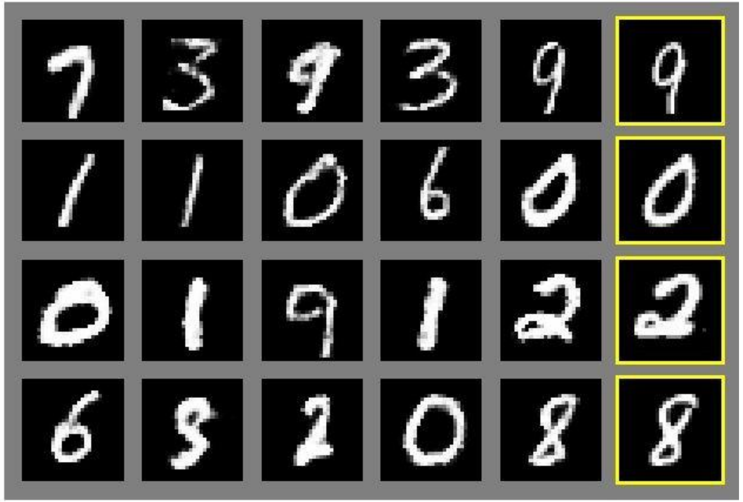


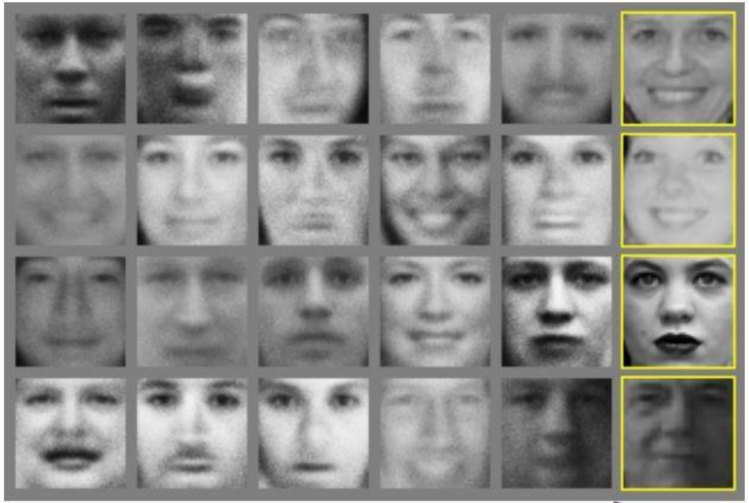
After training, use generator network to generate new images

Generative Adversarial Nets

Ian Goodfellow et al., "Generative Adversarial Nets", NIPS 2014

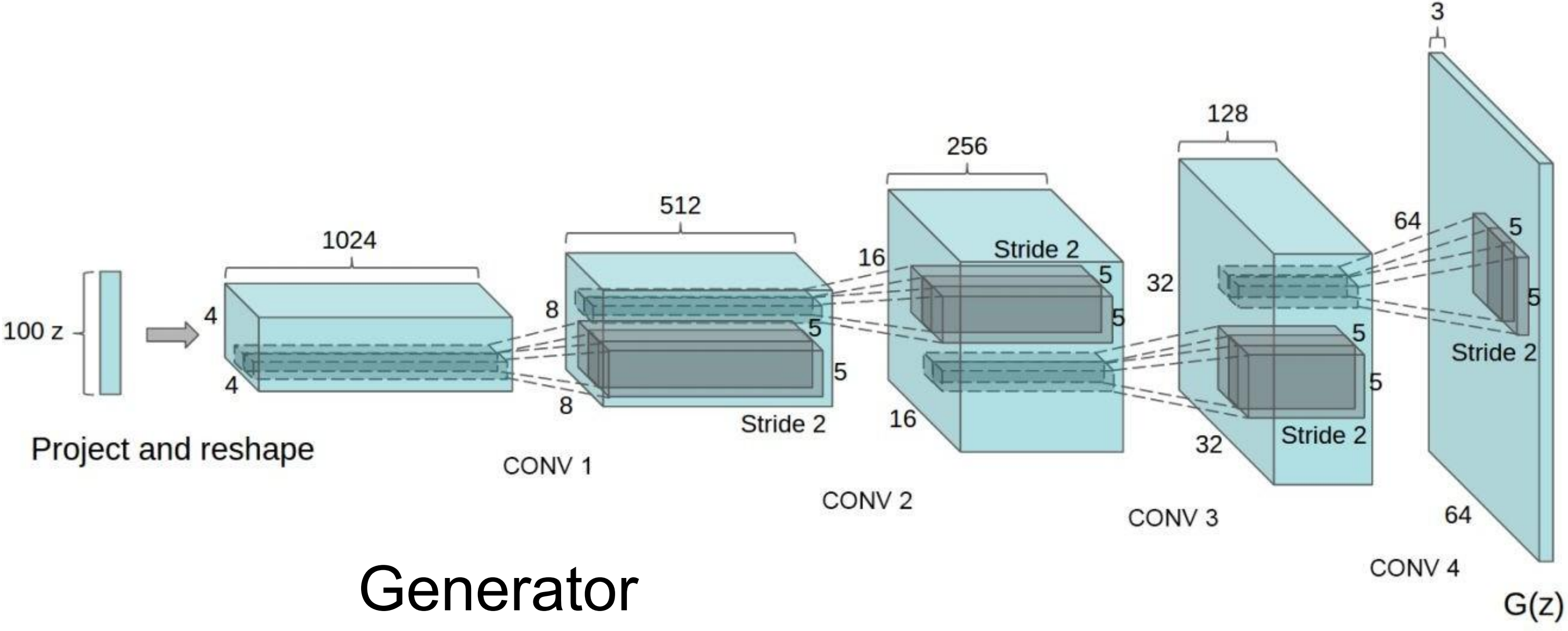
Generated samples





Nearest neighbor from training set

Generative Adversarial Nets: Convolutional Architectures



Generator

Radford et al, “Unsupervised Representation Learning with Deep Convolutional Generative Adversarial Networks”, ICLR 2016

Generative Adversarial Nets: Convolutional Architectures

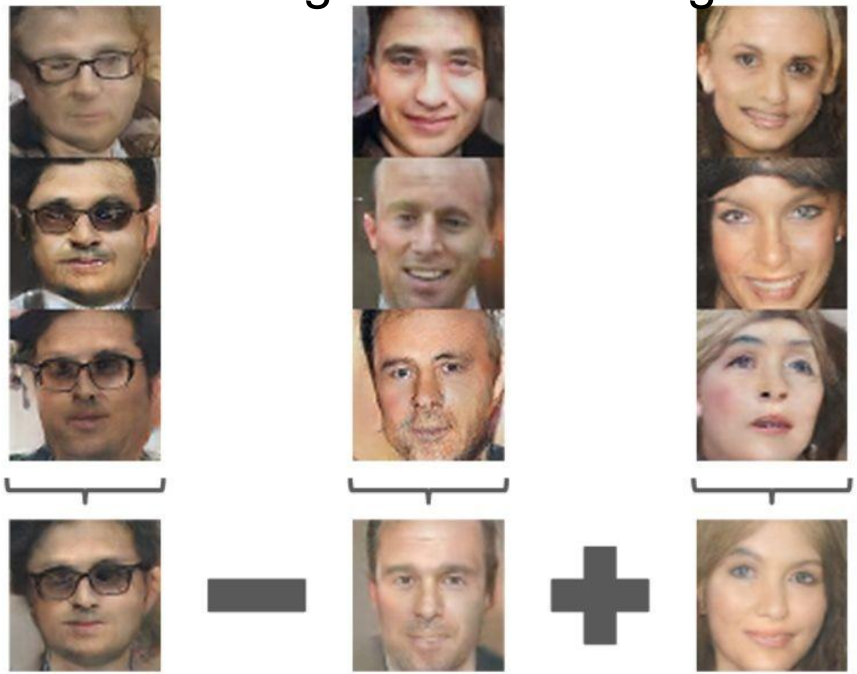
Samples from the model look amazing!

Radford et al,

Generative Adversarial Nets: Interpretable Vector Math

Glasses man

No glasses manNo glasses woman



Radford et al,

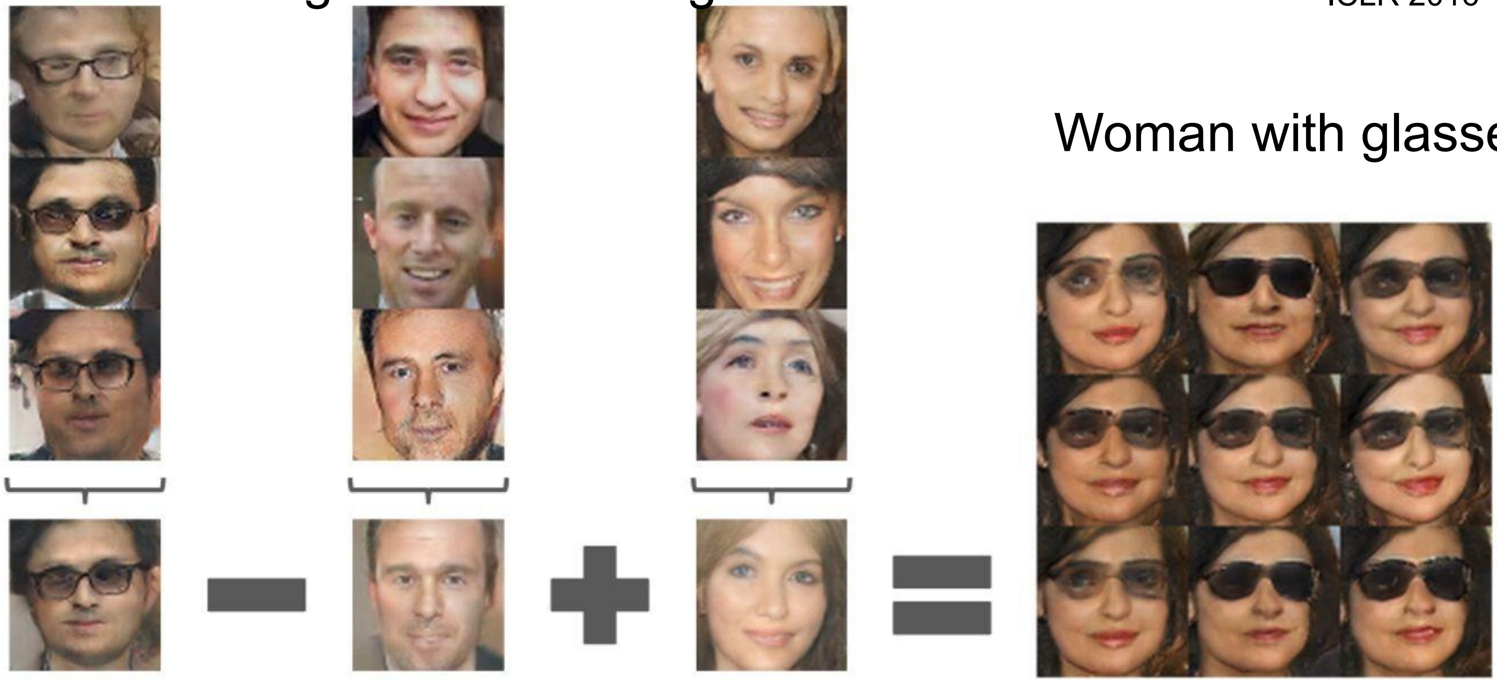
Generative Adversarial Nets: Interpretable Vector Math

Glasses man

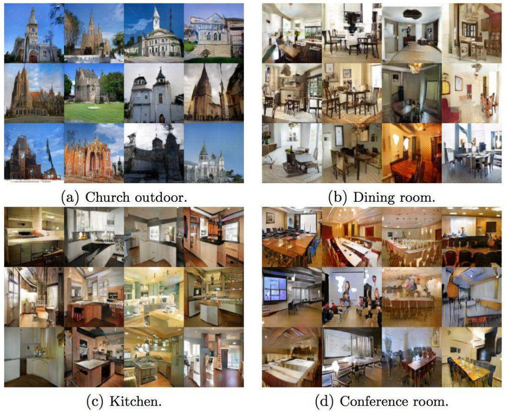
No glasses man No glasses woman

Radford et al, ICLR 2016

Woman with glasses



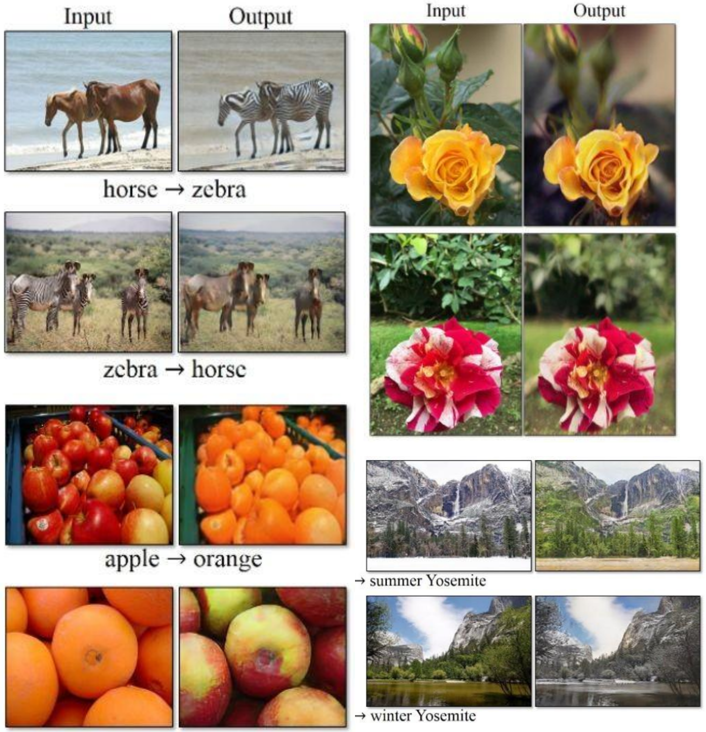
Better training and generation



LSGAN. Mao et al. 2017.

BEGAN. Bertholet et al. 2017.

Source->Target domain transfer



CycleGAN. Zhu et al. 2017.

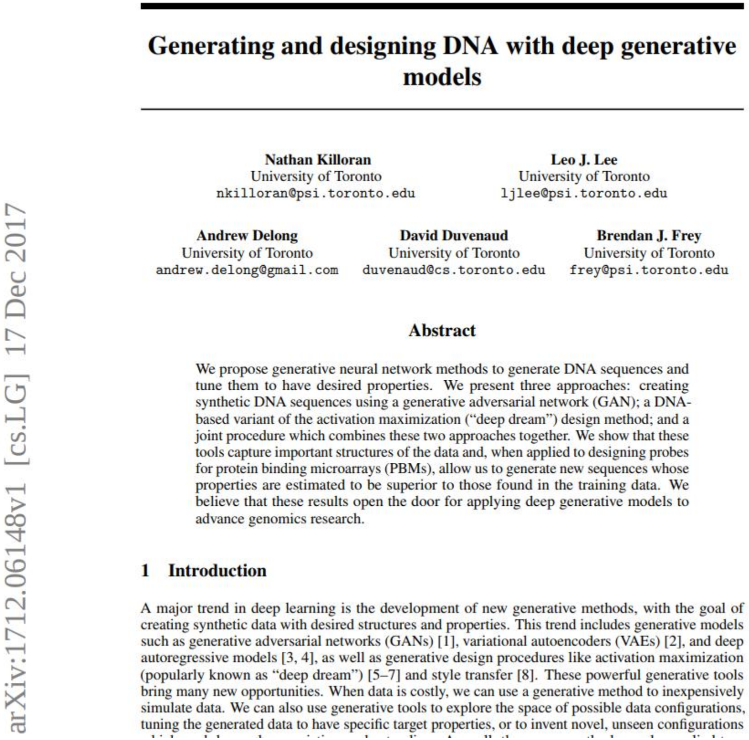
Text -> Image Synthesis

Reed et al. 2017.

Many GAN applications

Pix2pix. Isola 2017. Many examples at https://phillipi.github.io/pix2pix/

Generative Adversarial Nets in Genomics



arXiv:1712.06148v1 [cs.LG] 17 Dec 2017

Generating and designing DNA with deep generative models

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Abstract

We propose generative neural network methods to generate DNA sequences and tune them to have desired properties. We present three approaches: creating synthetic DNA sequences using a generative adversarial network (GAN); a DNA-based variant of the activation maximization ("deep dream") design method; and a joint procedure which combines these two approaches together. We show that these tools capture important structures of the data and, when applied to designing probes for protein binding microarrays (PBMs), allow us to generate new sequences whose properties are estimated to be superior to those found in the training data. We believe that these results open the door for applying deep generative models to advance genomics research.

1 Introduction

A major trend in deep learning is the development of new generative methods, with the goal of creating synthetic data with desired structures and properties. This trend includes generative models such as generative adversarial networks (GANs) [1], variational autoencoders (VAEs) [2], and deep autoregressive models [3, 4], as well as generative design procedures like activation maximization (popularly known as "deep dream") [5–7] and style transfer [8]. These powerful generative tools bring many new opportunities. When data is costly, we can use a generative method to inexpensively simulate data. We can also use generative tools to explore the space of possible data configurations, tuning the generated data to have specific target properties, or to invent novel, unseen configurations

Figure 7: Motif-matching experiment: a) Sequence logo for the PWM detected by the predictor. Letter heights reflect their relative frequency at each position. Sequences which have a strong match with this motif will score highly. b) Sample sequences tuned to have a high predictor score. The boxes indicate strong motif matches for each sequence.

Generative Adversarial Nets in Genomics

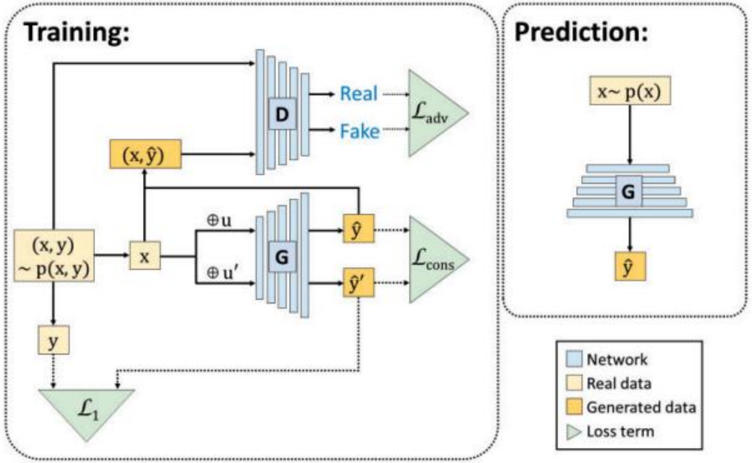

Fig. 1. Illustration of GGAN architecture and its loss functions. We use $(\mathbf{x}, \mathbf{y}) \in \mathbb{R}^{l+t}$ to denote a gene expression profile, where $\mathbf{x} \in \mathbb{R}^l$ corresponds to the landmark genes and $\mathbf{y} \in \mathbb{R}^t$ represents the target genes. Our goal is to learn a generator function *G* which takes *x* as the input and output $\hat{y}$ as the prediction of the target gene expression. To construct an appropriate prediction function *G*, we consider three loss terms in our model: $\mathcal{L}_{cons}$, $\mathcal{L}_{adv}$ and $\mathcal{L}_1$. $\mathcal{L}_{cons}$ measures the consistency of the prediction from *G* when the input *x* is perturbed by random noise u and u′. $\mathcal{L}_1$ measures the difference between the prediction vector $\hat{y}$ and the ground truth **y**. For the term $\mathcal{L}_{adv}$, we construct a discriminator *D* which takes both $(\mathbf{x}, \mathbf{y})$ and $(\mathbf{x}, \hat{\mathbf{y}})$ as the input. The discriminator *D* tries to distinguish the 'real' sample $(\mathbf{x}, \mathbf{y})$ from the 'fake' sample $(\mathbf{x}, \hat{\mathbf{y}})$ while the *G* tries to predict the realistic $\hat{y}$ vector to fool the discriminator. $\mathcal{L}_{adv}$ measures the adversarial loss in the game between the generator *G* and discriminator *D*

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ECCB 2018
OXFORD

Conditional generative adversarial network for gene expression inference

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[†]The authors wish it to be known that, in their opinion, the first two authors should be regarded as Joint First Authors.

Abstract

Motivation: The rapid progress of gene expression profiling has facilitated the prosperity of recent biological studies in various fields, where gene expression data characterizes various cell conditions and regulatory mechanisms under different experimental circumstances. Despite the widespread application of gene expression profiling and advances in high-throughput technologies, profiling in genome-wide level is still expensive and difficult. Previous studies found that high correlation exists in the expression pattern of different genes, such that a small subset of genes can be informative to approximately describe the entire transcriptome. In the Library of Integrated Network-based Cell-Signature program, a set of ~1000 landmark genes have been identified that contain ~80% information of the whole genome and can be used to predict the expression of remaining genes. For a cost-effective profiling strategy, traditional methods measure the profiles of landmark genes and then infer the expression of other target genes via linear models. However, linear models do not have the capacity to capture the non-linear associations in gene regulatory networks.

Results: As a flexible model with high representative power, deep learning models provide an alternate to interpret the complex relation among genes. In this paper, we propose a deep learning architecture for the inference of target gene expression profiles. We construct a novel conditional generative adversarial network by incorporating both the adversarial and ℓ_1-norm loss terms in our model. Unlike the smooth and blurry predictions resulted by mean squared error objective, the coupled adversarial and ℓ_1-norm loss function leads to more accurate and sharp predictions. We validate our method under two different settings and find consistent and significant improvements over all the comparing methods.

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“The GAN Zoo”

- GAN - Generative Adversarial Networks
- 3D-GAN - Learning a Probabilistic Latent Space of Object Shapes via 3D Generative-Adversarial Modeling
- acGAN - Face Aging With Conditional Generative Adversarial Networks
- AC-GAN - Conditional Image Synthesis With Auxiliary Classifier GANs
- AdaGAN - AdaGAN: Boosting Generative Models
- AEGAN - Learning Inverse Mapping by Autoencoder based Generative Adversarial Nets
- AffGAN - Amortised MAP Inference for Image Super-resolution
- AL-CGAN - Learning to Generate Images of Outdoor Scenes from Attributes and Semantic Layouts
- ALI - Adversarially Learned Inference
- AM-GAN - Generative Adversarial Nets with Labeled Data by Activation Maximization
- AnoGAN - Unsupervised Anomaly Detection with Generative Adversarial Networks to Guide Marker Discovery
- ArtGAN - ArtGAN: Artwork Synthesis with Conditional Categorial GANs
- b-GAN - b-GAN: Unified Framework of Generative Adversarial Networks
- Bayesian GAN - Deep and Hierarchical Implicit Models
- BEGAN - BEGAN: Boundary Equilibrium Generative Adversarial Networks
- BiGAN - Adversarial Feature Learning
- BS-GAN - Boundary-Seeking Generative Adversarial Networks
- CGAN - Conditional Generative Adversarial Nets
- CaloGAN - CaloGAN: Simulating 3D High Energy Particle Showers in Multi-Layer Electromagnetic Calorimeters with Generative Adversarial Networks
- CCGAN - Semi-Supervised Learning with Context-Conditional Generative Adversarial Networks
- CatGAN - Unsupervised and Semi-supervised Learning with Categorical Generative Adversarial Networks
- CoGAN - Coupled Generative Adversarial Networks
- Context-RNN-GAN - Contextual RNN-GANs for Abstract Reasoning Diagram Generation
- C-RNN-GAN - C-RNN-GAN: Continuous recurrent neural networks with adversarial training
- CS-GAN - Improving Neural Machine Translation with Conditional Sequence Generative Adversarial Nets
- CVAE-GAN - CVAE-GAN: Fine-Grained Image Generation through Asymmetric Training
- CycleGAN - Unpaired Image-to-Image Translation using Cycle-Consistent Adversarial Networks
- DTN - Unsupervised Cross-Domain Image Generation
- DCGAN - Unsupervised Representation Learning with Deep Convolutional Generative Adversarial Networks
- DiscoGAN - Learning to Discover Cross-Domain Relations with Generative Adversarial Networks
- DR-GAN - Disentangled Representation Learning GAN for Pose-Invariant Face Recognition
- DualGAN - DualGAN: Unsupervised Dual Learning for Image-to-Image Translation
- EBGAN - Energy-based Generative Adversarial Network
- f-GAN - f-GAN: Training Generative Neural Samplers using Variational Divergence Minimization
- FF-GAN - Towards Large-Pose Face Frontalization in the Wild
- GAWWN - Learning What and Where to Draw
- GeneGAN - GeneGAN: Learning Object Transfiguration and Attribute Subspace from Unpaired Data
- Geometric GAN - Geometric GAN
- GoGAN - Gang of GANs: Generative Adversarial Networks with Maximum Margin Ranking
- GP-GAN - GP-GAN: Towards Realistic High-Resolution Image Blending
- IAN - Neural Photo Editing with Introspective Adversarial Networks
- iGAN - Generative Visual Manipulation on the Natural Image Manifold
- IcGAN - Invertible Conditional GANs for image editing
- ID-CGAN - Image De-raining Using a Conditional Generative Adversarial Network
- Improved GAN - Improved Techniques for Training GANs
- InfoGAN - InfoGAN: Interpretable Representation Learning by Information Maximizing Generative Adversarial Nets
- LAGAN - Learning Particle Physics by Example: Location-Aware Generative Adversarial Networks for Physics Synthesis
- LAPGAN - Deep Generative Image Models using a Laplacian Pyramid of Adversarial Networks

https://github.com/hindupuravinash/the-gan-zoo

Now, it’s time to practice...