Medical Image Generation with Limited Data

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A Survey on Generative Modeling with Limited Data, Few Shots, and Zero Shot

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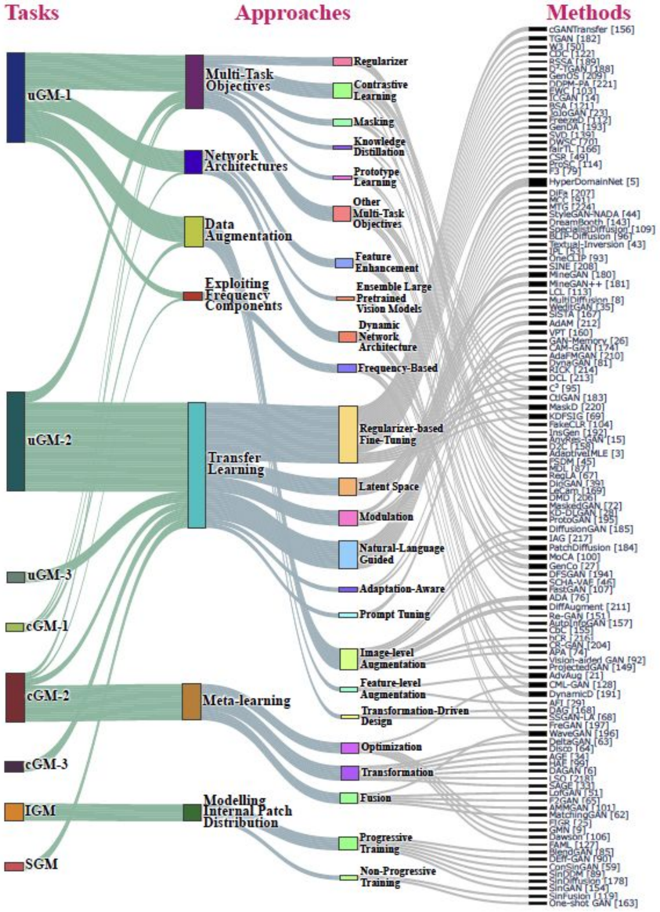

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arXiv Code Interactive Sankey

Outline

I. Background of Generative Models

II. Major Challenges of Training Generative Models with Limited Data

III. Approaches for Image Generation with Limited Data

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I. **Background of Generative Models**

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III. Approaches for Image Generation with Limited Data

Background of Generative Modeling

Definition of Domain and Generative Modeling

Unconditional vs Conditional Image Generation

Popular Image Generation Models

- **Variational AutoEncoder (VAE)**
- **Generative Adversarial Networks (GAN)**
- **Flow-based Models**
- **Diffusion Models (DM)**

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Background: **Definition of Domain**

Domain. a domain consists of two components:

$$\mathcal{D} = \{\mathcal{X}, P_{data}\}$$

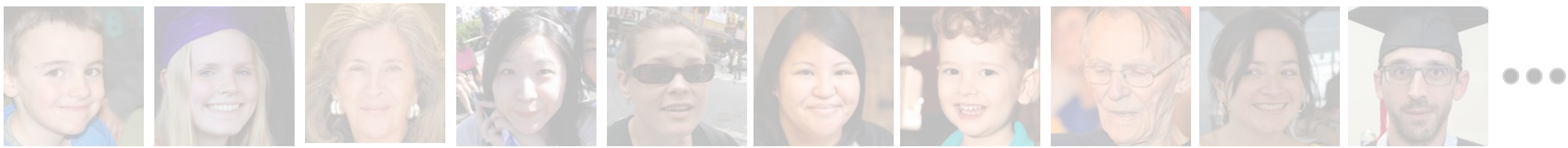
a sample space

a probability distribution

a sample from a domain

$$x \sim P_{data} \in \mathcal{X}$$

Example. Flickr-Faces-HQ (FFHQ) as the domain of image of human faces



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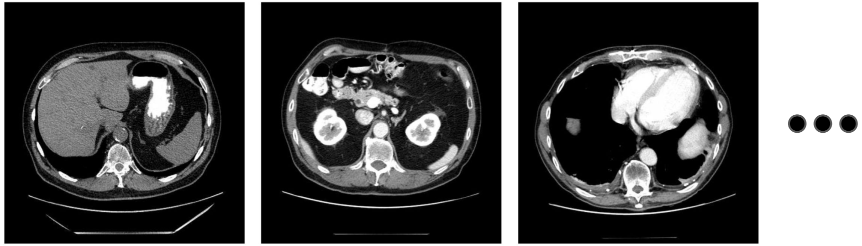

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Generative Models.
Given a set of training samples from a domain $\mathcal{D} = \{\mathcal{X}, P_{data}\}$, generative modeling aims to learn to capture the distribution of these samples, i.e., P_{data}.

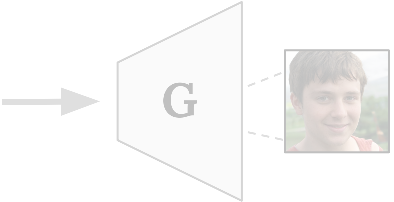
Result is a **generative model G**, encoding a probability distribution P_{model}.

Learning objective is to have P_{model} similar to P_{data} statistically.

After training, **G can generate samples** following P_{model}.

A set of training samples on human face dataset (P_{data})

Input noise



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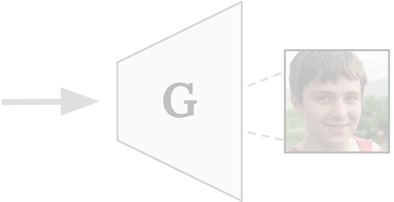

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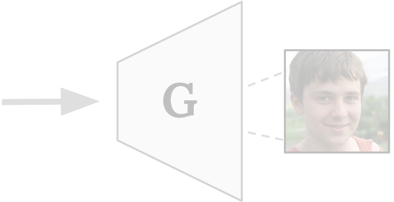

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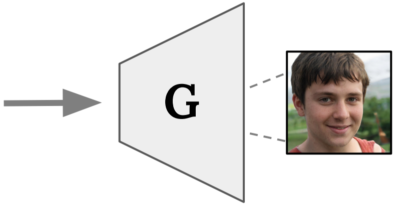

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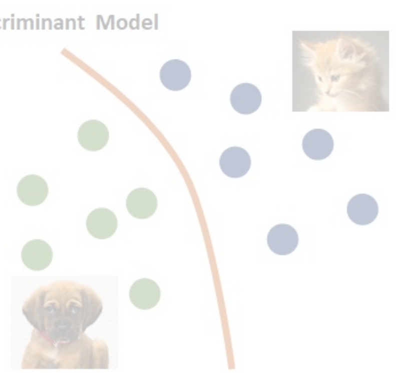
Generative vs Discriminative Modeling

Discriminative Models learn the boundary in data space to be able to discriminate samples from different classes (e.g., ResNet classifier).



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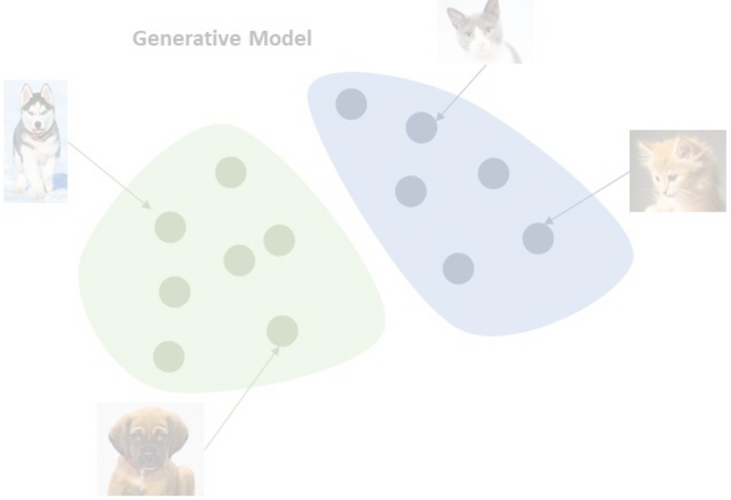
Later, by sampling from learned distribution, they can **generate new samples**.



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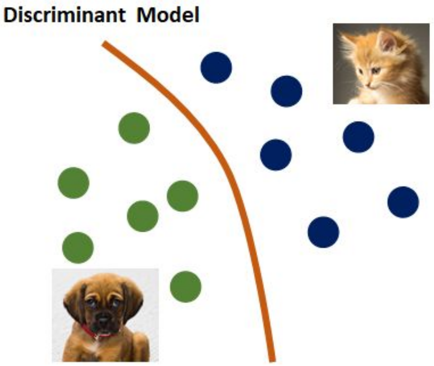

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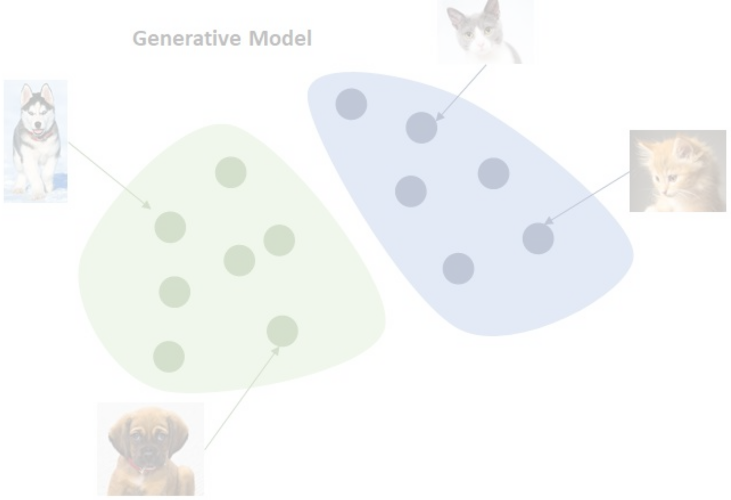

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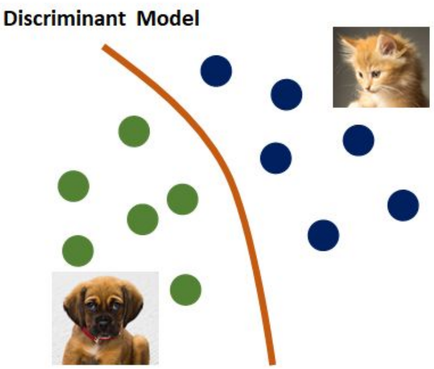

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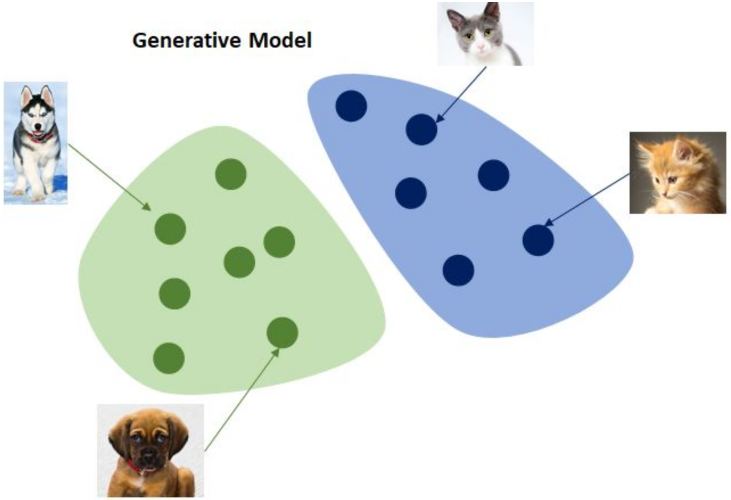

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Image Generation: after learning generative model, typically:

- image generation starts with sampling a random noise z (also called latent code) as input.
- This input as passed into generative model G which transforms it to a new sample G(z)

This is called **unconditional image generation** as there is no conditioning mechanism to restrict image generation.

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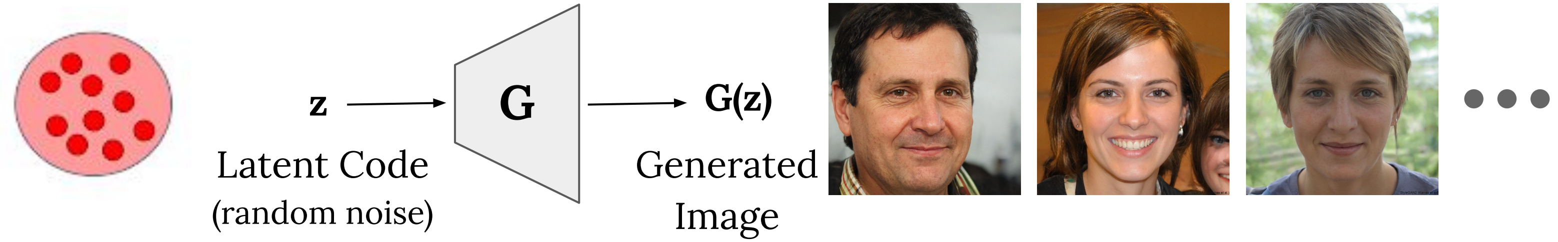

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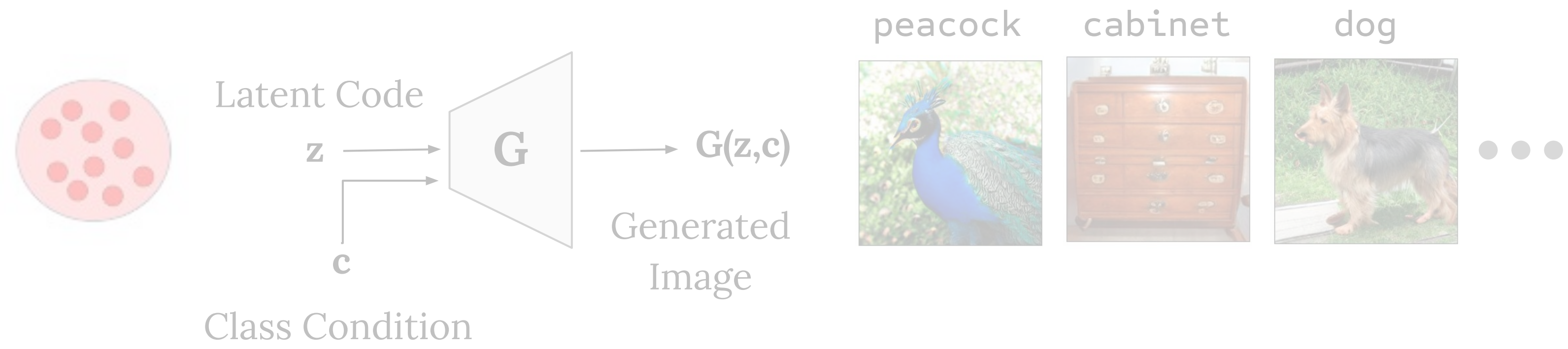
If **an additional condition c** (e.g., class label, ...) is used to steer sample generation towards c, the sample generation is called **conditional image generation**: G(z,c)

For example, **conditioning on class label**:



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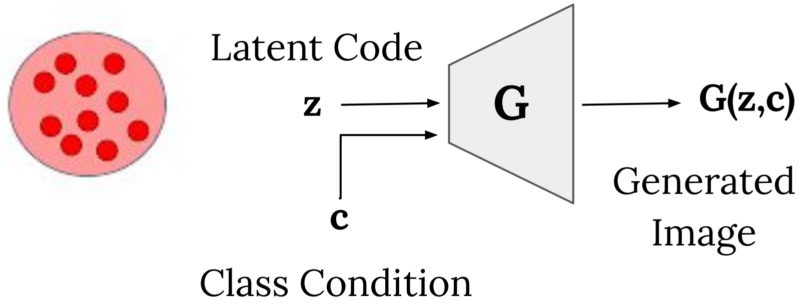

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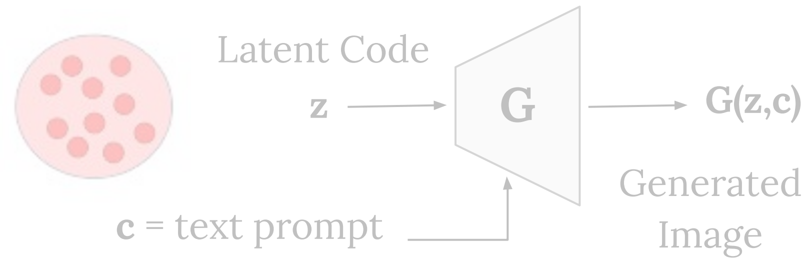


```
An art installation floats in the air, the
installation is a cute shark made of candy,
bright colors, light gray background,
studio, contemporary art, minimalism,
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Generator: Midjourney

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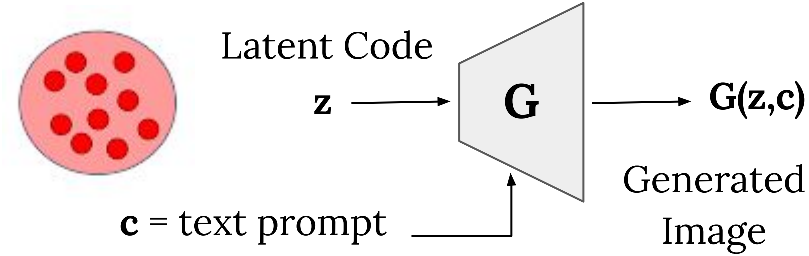


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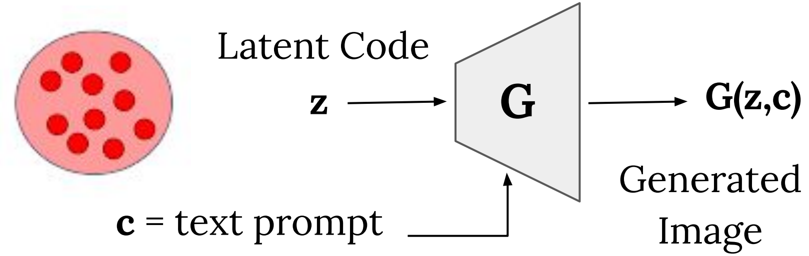


```
Fundoscopy image of the
left retina with no
Diabetic retinopathy
```

Generator:
[**MediSyn**] Text-Guided Diffusion Models for Broad Medical 2D and 3D Image Synthesis (Stanford Medicine)

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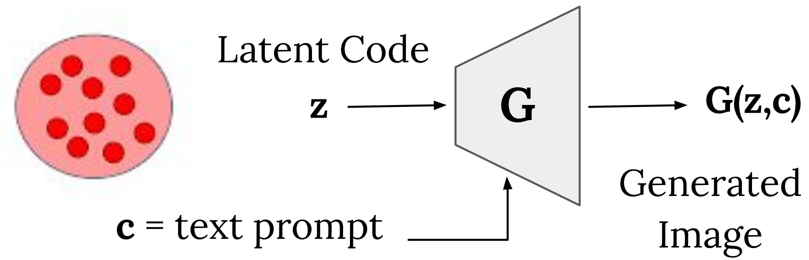
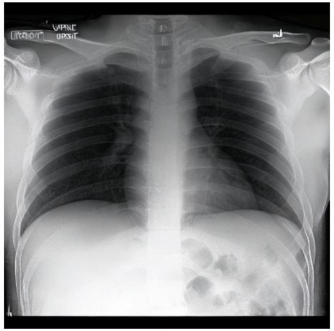



```
AP Frontal Chest X-ray
(CXR) of a male patient
```



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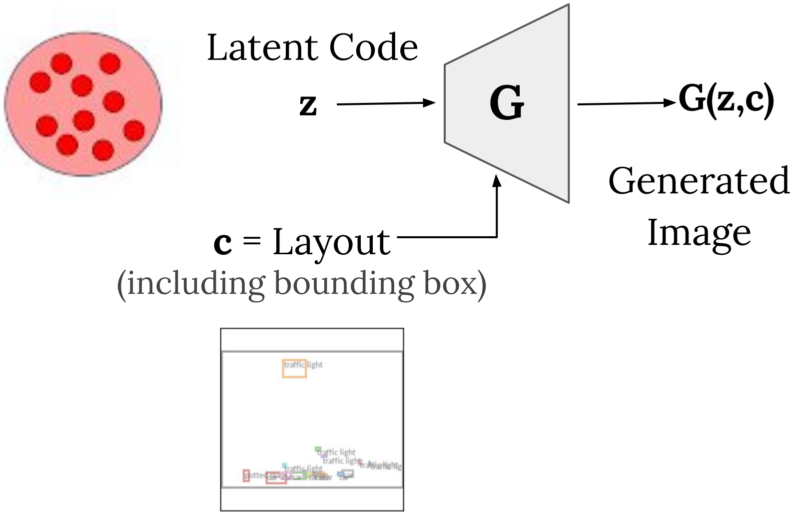

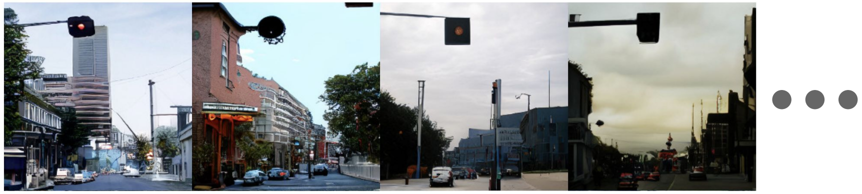

Generator: Stable Diffusion

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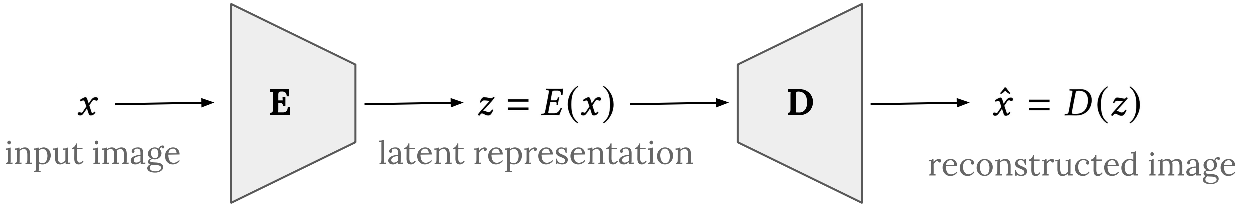
Generative Models: **Variational Auto-Encoder (VAE)**

Auto-Encoder (AE) consist of **two networks**:

- **Encoder (E)** learn to map input image to a low-dimensional latent representation
- **Decoder (D)** aims to reconstruct the image from that latent representation



Learning objective:

$$\mathcal{L}_{rec} = ||x - D(z)||_2$$

AEs focus on **dimensionality reduction**, and the **irregularity of their latent space** makes them improper for sample generation.

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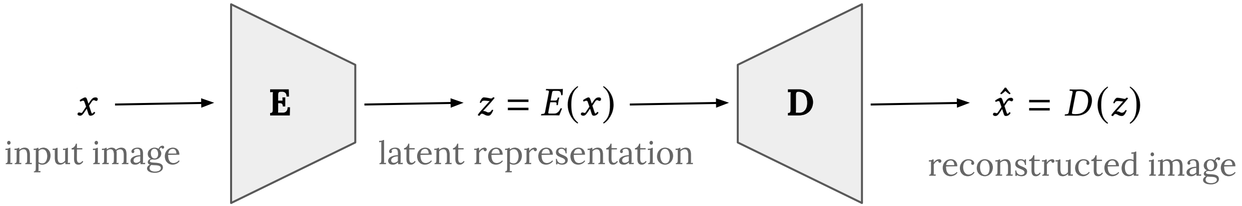

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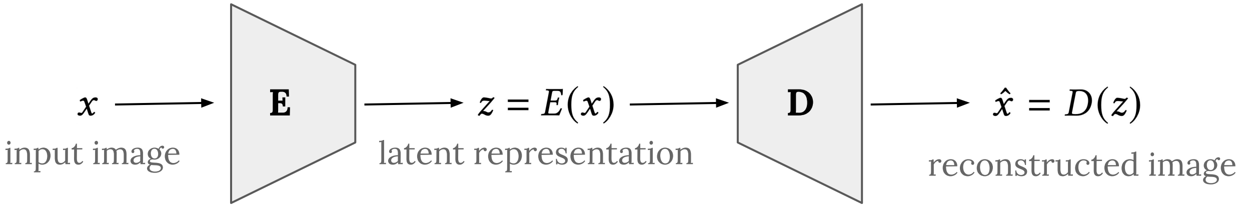

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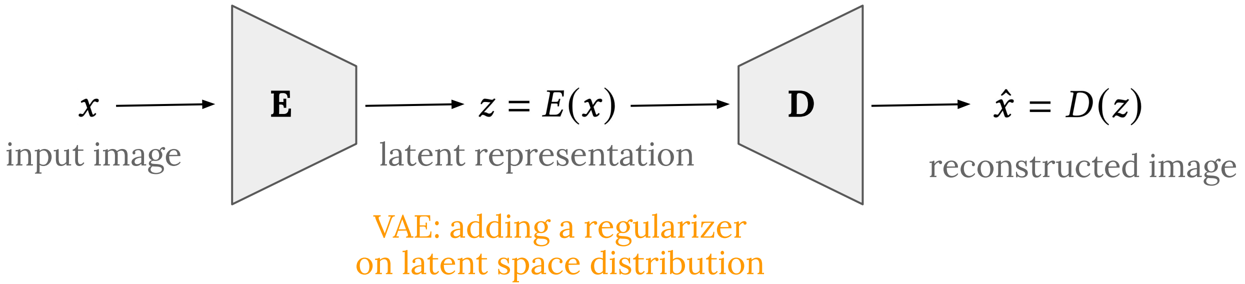

Learning objective:

$$\mathcal{L} = ||x - D(z)||_2 + KL(\mathcal{N}(\mu, \sigma^2), \mathcal{N}(0, I))$$

Vector-Quantized VAE (VQ-VAE) adds tokenization which quatizes the embedding into visual tokens for mitigating the challenge of direct maximization of likelihood in image space.

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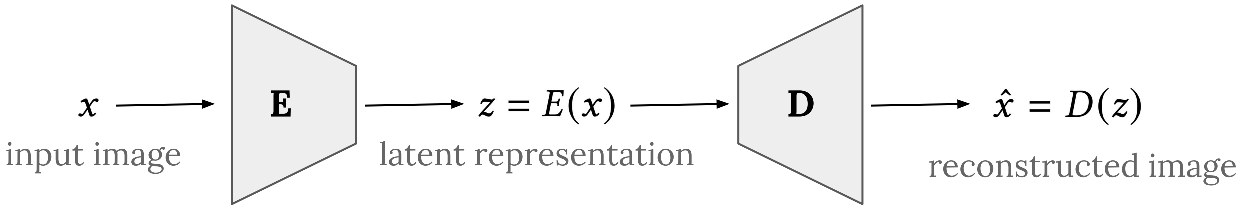

VAE: adding a regularizer
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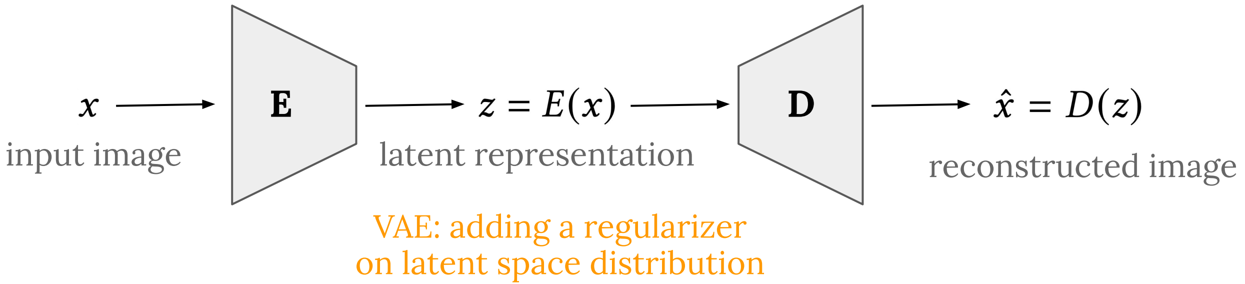

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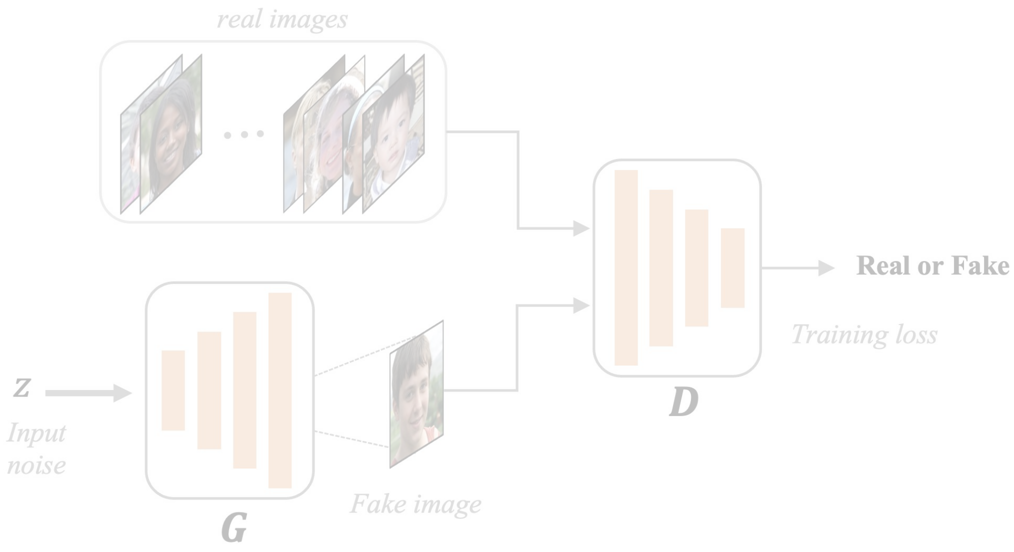
- **Discriminator (D)** learn to distinguish between **real** and **fake** images



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$$min_G \, max_D \, v(D, G) = \mathbb{E}_{x \sim p_{data}}[log(D(x)] + \mathbb{E}_{z \sim p_z}[log(1 - D(G(z))]$$

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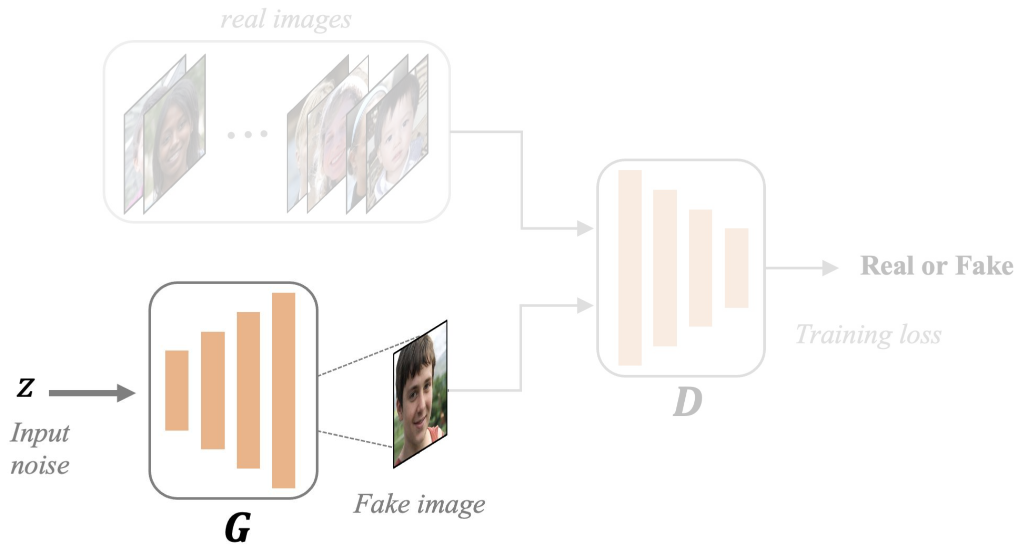

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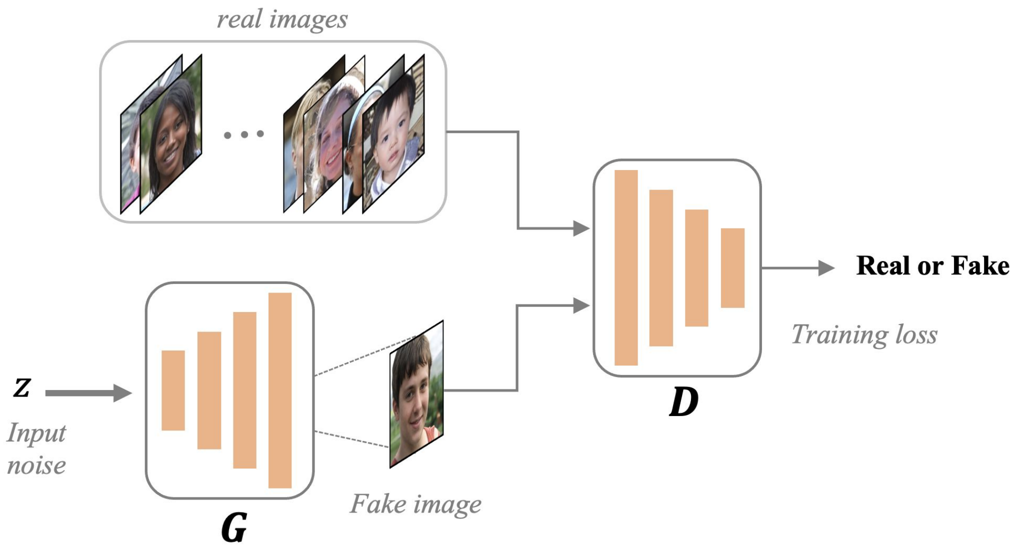

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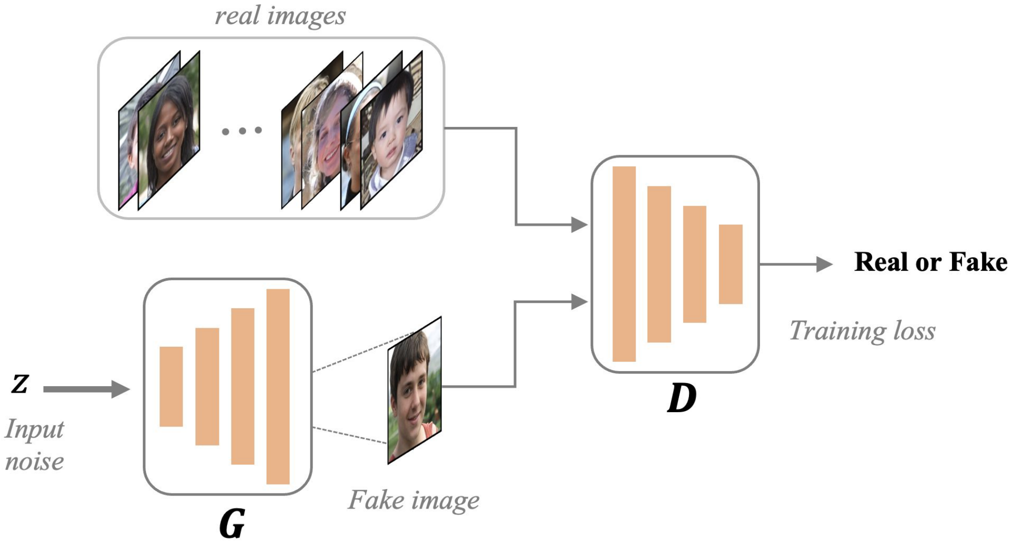

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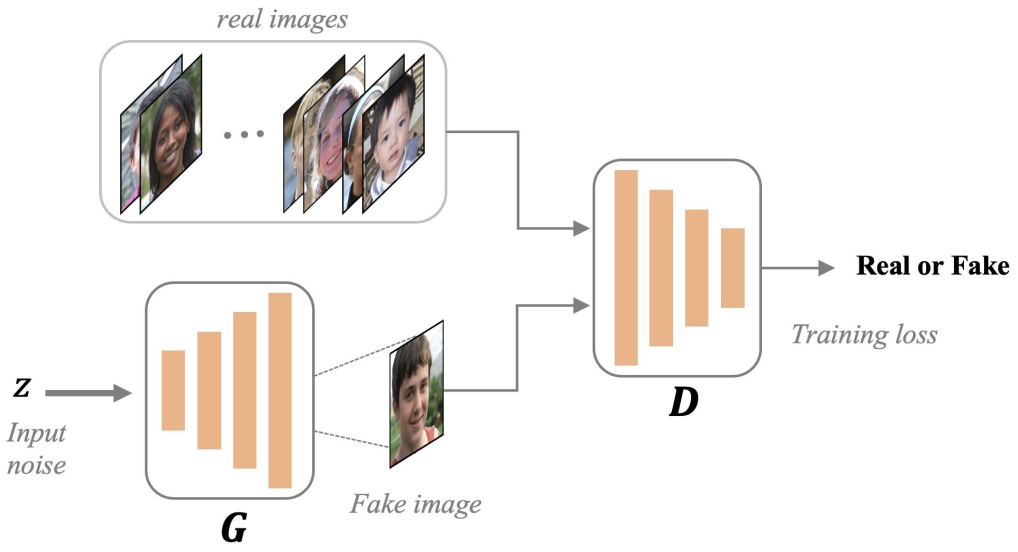

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Generative Models: **Diffusion Models (DMs)**

Diffusion Models (DMs) leverage the **concepts of the diffusion process** from stochastic calculus and consists of two main steps:

- **Forward Diffusion Process** consists of multiple steps in which low-level noise is added to each input image, where the scale of the noise varies at each step. The training data is progressively destroyed until it results in pure Gaussian noise.
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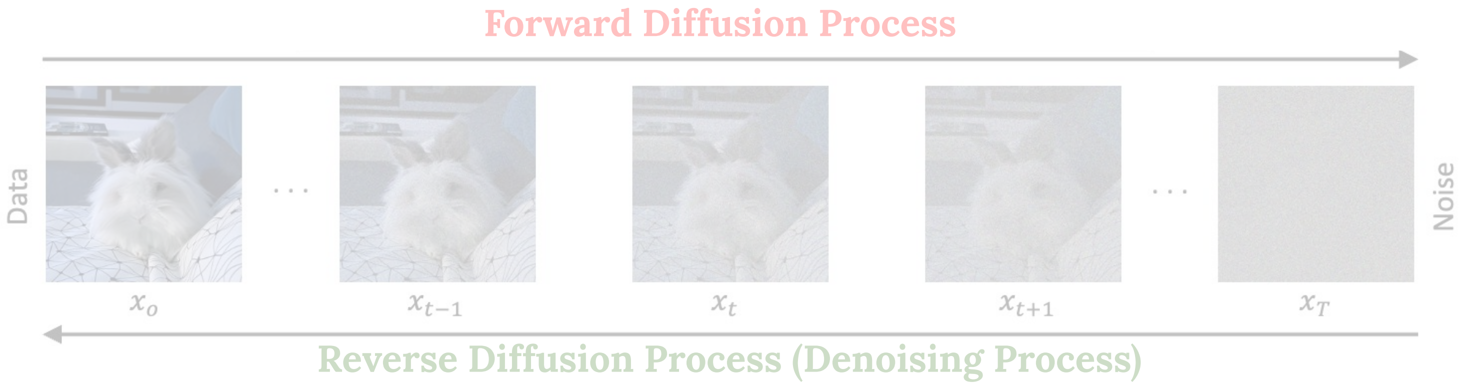

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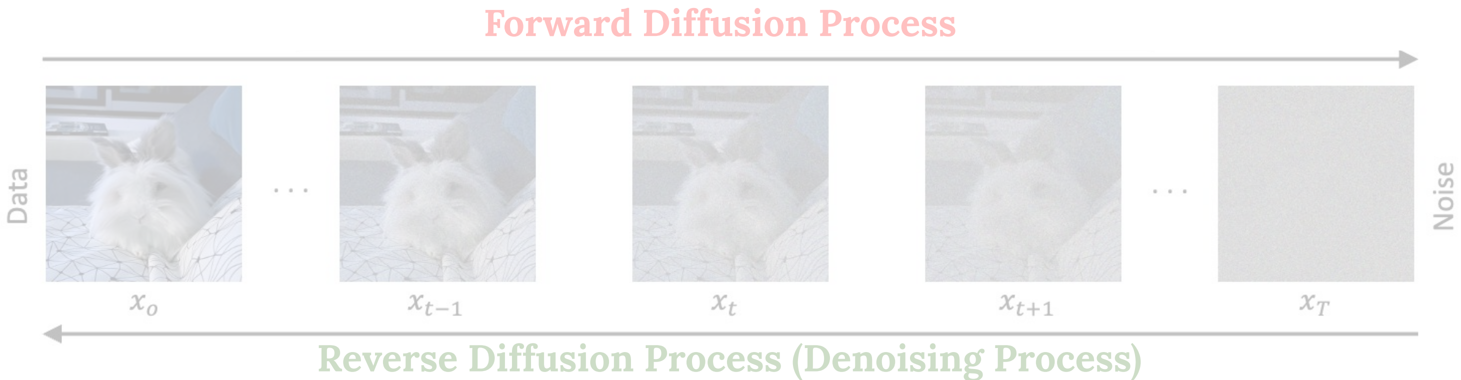

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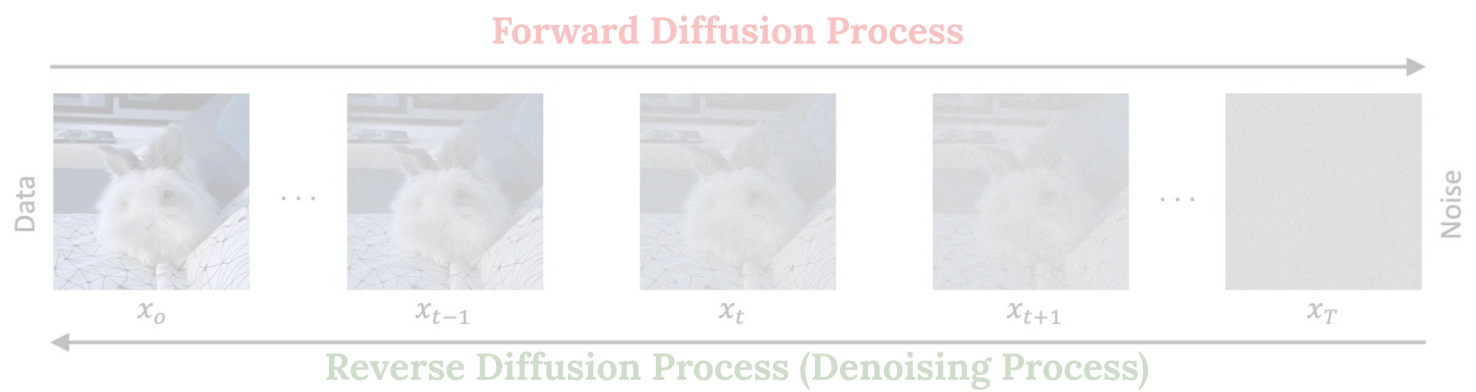

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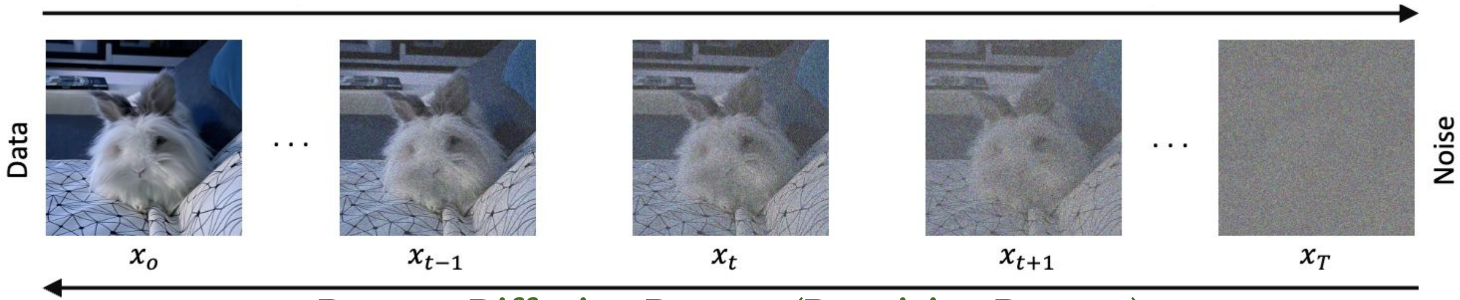

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Important property of this formulation is the possibility to directly sample at time step t:

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Popularity of DMs start from HERE!!

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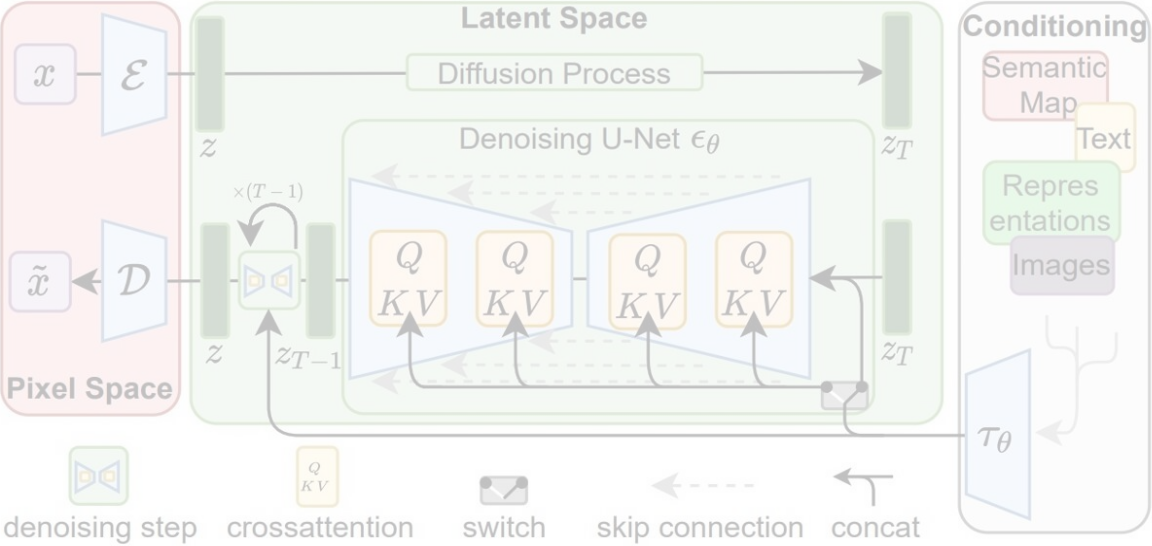
Latent Diffusion Model (LDM), and **Stable Diffusion Model** (SDM)

- trains the denoiser network (reverse diffusion) in the latent space instead of image space
- uses cross-attention mechanism for conditioning



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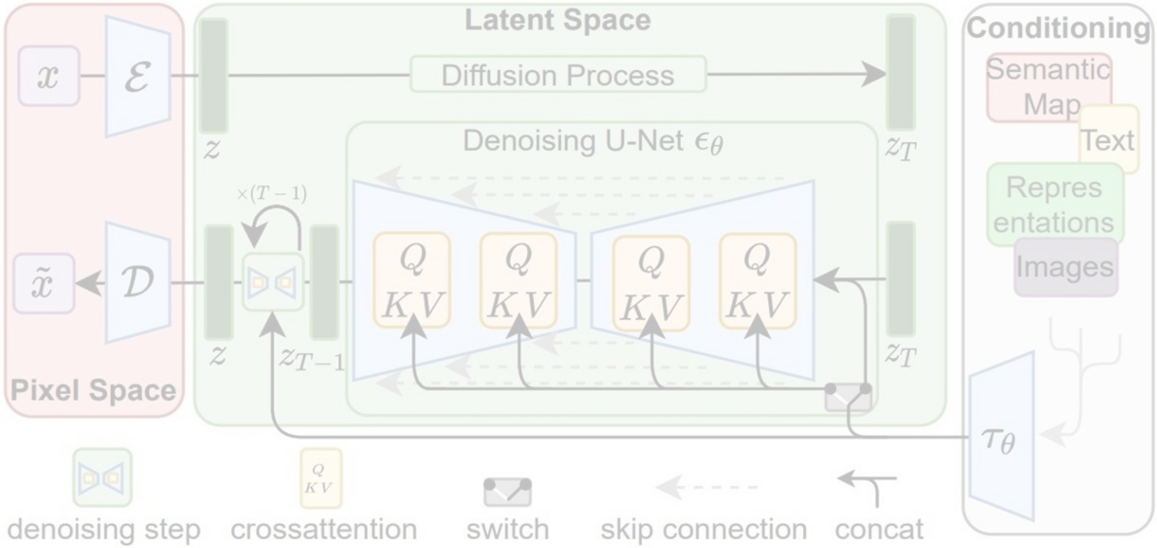

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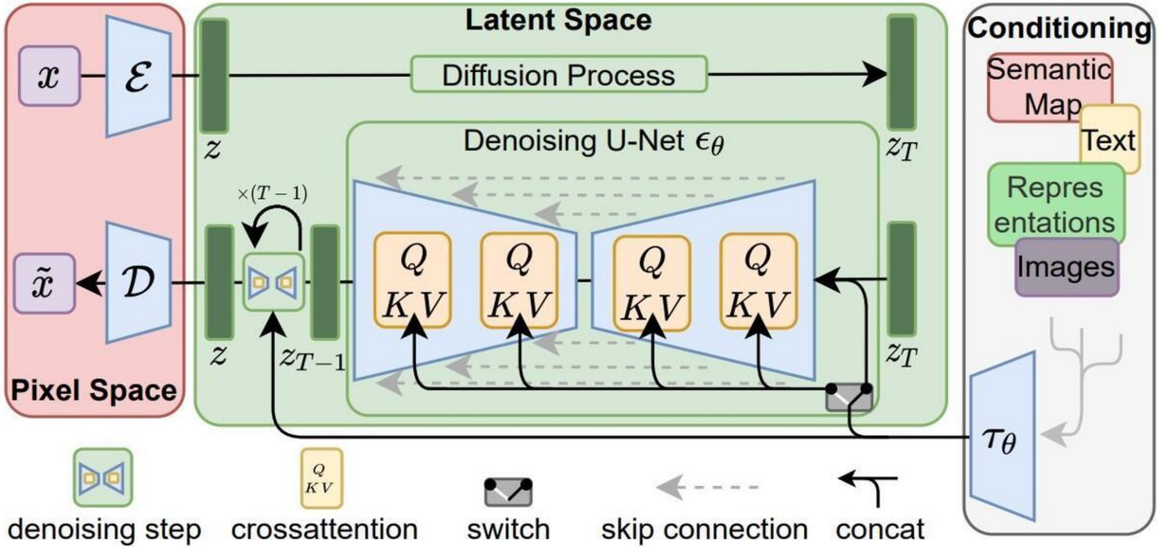

Outline

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II. Major Challenges of Training Generative Models with Limited Data

III. Approaches for Image Generation with Limited Data

Major Challenges

Challenges for Training Generative Models under Data Constraint

- **Overfitting**
- **Frequency Bias**

Major Challenges: **Training**

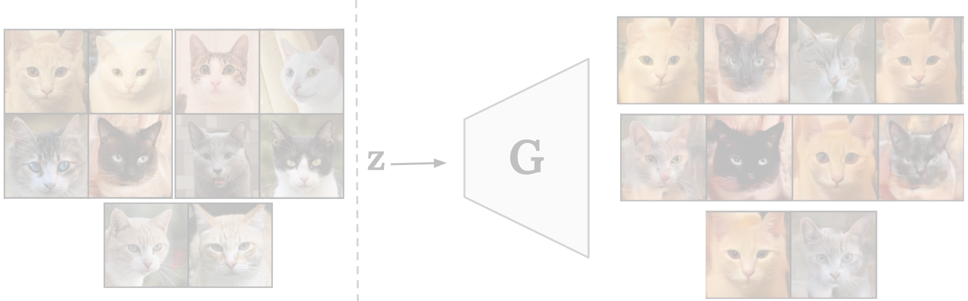
Overfitting to Training Data

Overfitting. a common issue in machine learning when powerful models start to memorize the training data instead of learning the generalizable semantics

Mode Collapse. Under data constraints generative models are more prone to mode collapse

Example of mode e collapse on MNIST handwritten digits

Replicate Training Data. Under extreme cases, the generator just learns to replicate the training data



10-shot training data

Generated images are extremely similar to training data

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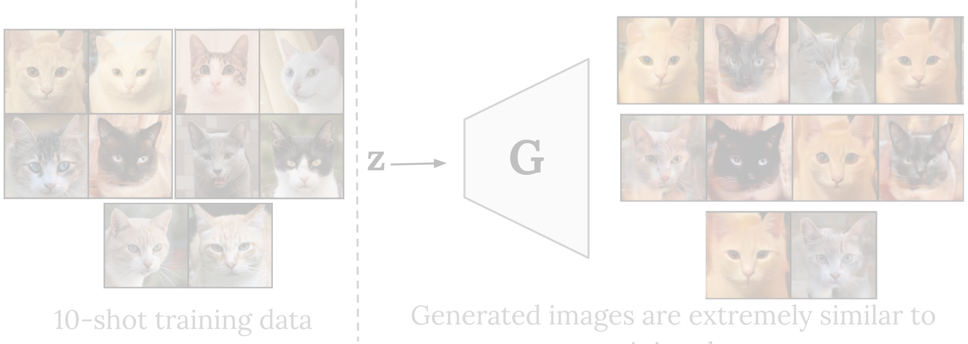

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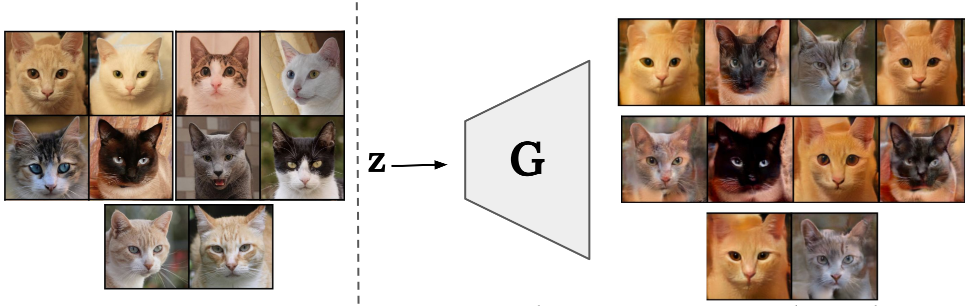

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Major Challenges: **Training**

Frequency Bias: Neural networks learn lower frequencies first

On the Spectral Bias of Neural Networks

Nasim Rahaman [*1 2] **Aristide Baratin** [*1] **Devansh Arpit** [1] **Felix Draxler** [2] **Min Lin** [1] **Fred A. Hamprecht** [2]
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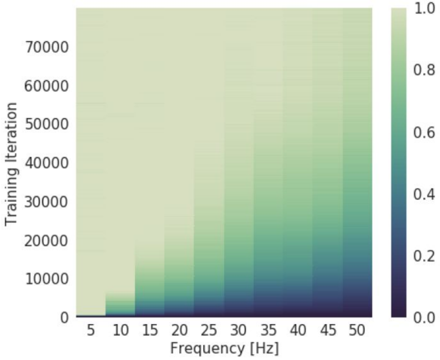
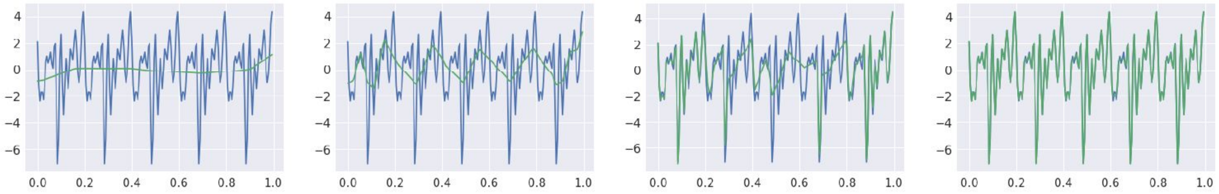
$$\lambda(z) = \sum_i A_i \sin(2\pi k_i z + \varphi_i)$$





(a) Iteration 100 (b) Iteration 1000 (c) Iteration 10000 (d) Iteration 80000

Figure 2. The learnt function (green) overlayed on the target function (blue) as the training progresses. The target function is a superposition of sinusoids of frequencies $\kappa = (5, 10, ..., 45, 50)$, equal amplitudes and randomly sampled phases.

Major Challenges: **Training**

Frequency Bias: generative models **prioritize fitting low-frequency** components while disregarding the high-frequency components

Spatial Frequency Bias in Convolutional Generative Adversarial Networks

Mahyar Khayatkhoei, Ahmed Elgammal
Department of Computer Science, Rutgers University
New Brunswick, New Jersey
{m.khayatkhoei, elgammal}@cs.rutgers.edu

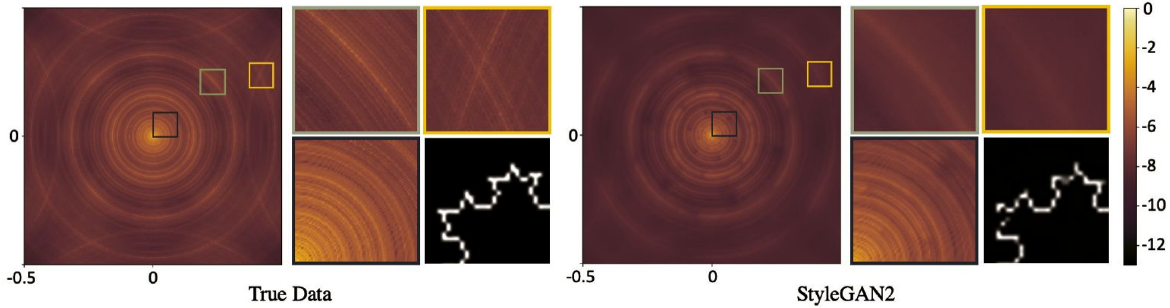


Figure 1: Average power spectrum of a large-scale GAN trained on a fractal-based dataset clearly reveals how the low frequencies (closer to center) are matched much more accurately than the high frequencies (closer to corners). (Left) Average power spectrum of randomly rotated Koch snowflakes of level 5 and size 1024×1024. (Right) Average power spectrum of StyleGAN2 trained on the latter. A representative patch from the perimeter of true and generated fractals are also displayed.

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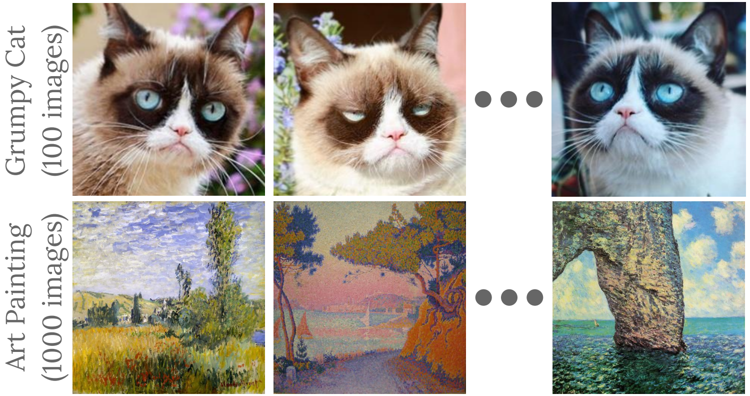
This bias **worsens** when data for training is limited.

Exclusion of these high-frequency components which encode intricate image details significantly impacts the quality of generated samples



Training data

Generated images by FastGAN showing loss of high-frequency details.

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Approaches for Image Generation with Limited Data (Training Generative Models with Limited Data):

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Transfer the knowledge of a pre-trained generator (on a large and diverse dataset) to a target domain with limited data

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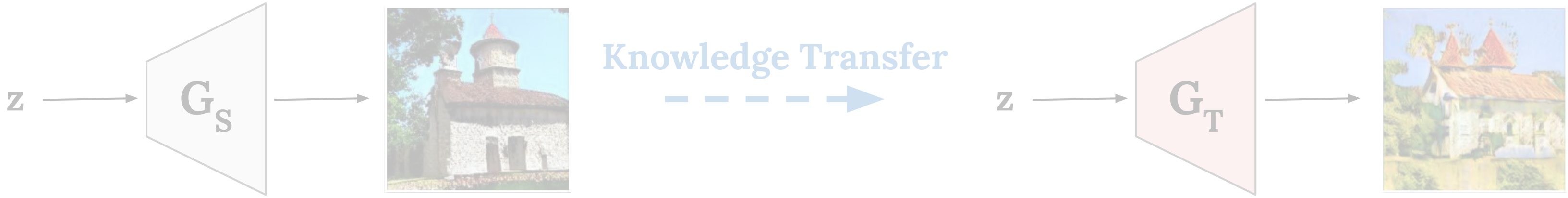

Pre-trained generator on **"LSUN-Church"** domain

Adapted generator to **"Van Gogh's House"** using limited data

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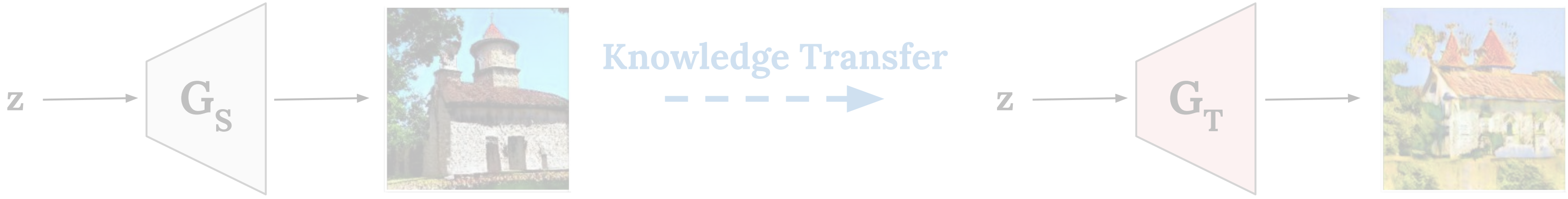

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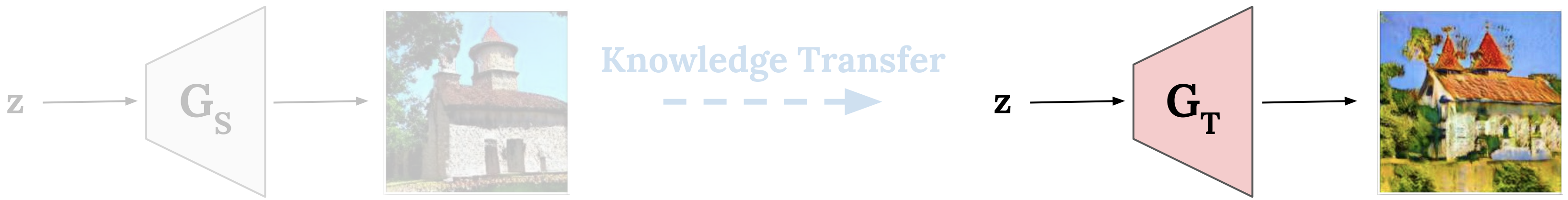

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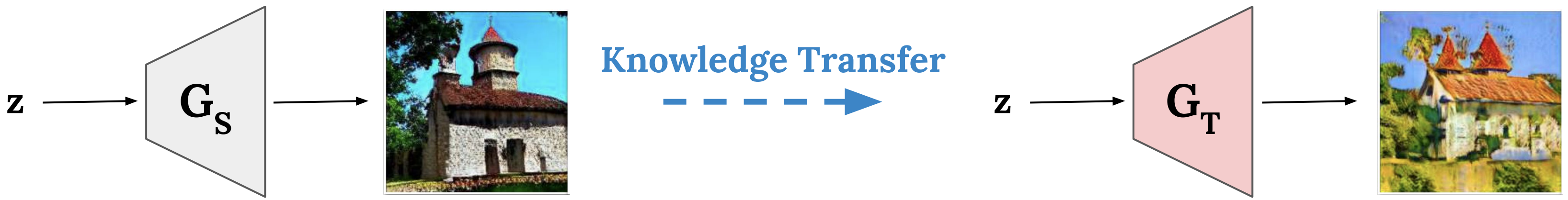
Transfer the knowledge of a pre-trained generator (on a large and diverse dataset) to a target domain with limited data

➠ Initialize the generator $\mathbf{G_T}$ with weights of pre-trained generator $\mathbf{G_S}$
➠ Fine-tune $\mathbf{G_T}$ using limited data from target domain
➠ General knowledge (domain-agnostic) from $\mathbf{G_S}$ is useful for target domain, and the domain-specific knowledge needs to be acquired using limited data from target domain



Pre-trained generator on **"LSUN-Church"** domain

Adapted generator to **"Van Gogh's House"** using limited data

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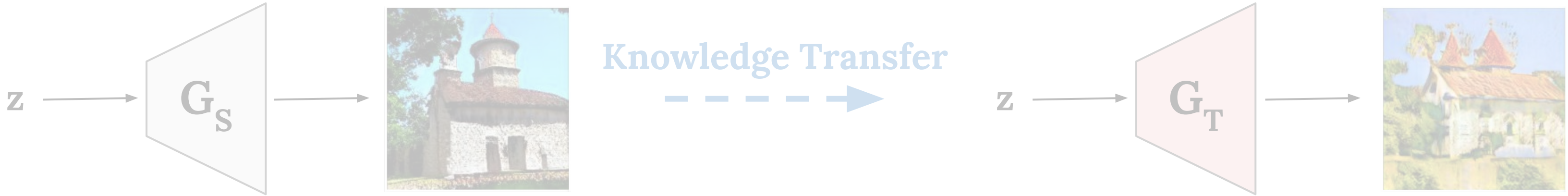
Similar approach can be applied to Medical Image Generation conditioned on having a powerful source model trained on medical data!



Pre-trained generator on **“LSUN-Church”** domain

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Approaches: **Transfer Learning**

Major Limitation

Because of data constraints on target domain, the **general knowledge can be degraded** during fine-tuning generator on target data (acquiring the domain-specific knowledge)

Example. Adapting a generator trained on human faces (FFHQ) to painting of human faces (e.g., Fernand Léger):

- **Shared (general) knowledge:** face structure, diversity in pose, hairstyle, ...
- **Domain-specific knowledge:** the style of the paining with Fernand Léger

Result. Conventional transfer learning results in missing general knowledge: losing diversity and only containing the target style

Training examples

Generated images by adapting a pre-trained StyleGAN on FFHQ to Fernand Léger Painting

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Li, Yijun, et al. "Few-shot image generation with elastic weight consolidation." NeurIPS'20.

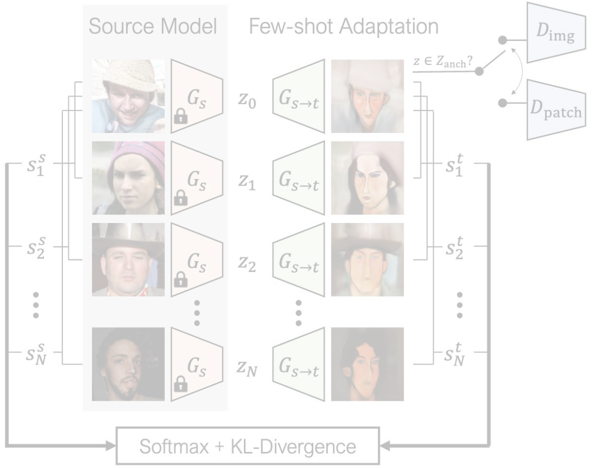
Approaches: **Transfer Learning**

Regularizer-based Fine-Tuning: These approaches add a regularizer term to the main objective to preserve the knowledge in the pre-trained generator

Cross-Domain Correspondence (CDC)

Key Observation. Overfitting in transfer learning, leads to the **loss of correspondence** between images generated by source and target domain

Objective. Add a regularizer to **preserve the correspondence between generated images before and after adapting** the generator to target domain



Ojha, Utkarsh, et al. "Few-shot image generation via cross-domain correspondence." CVPR'21.

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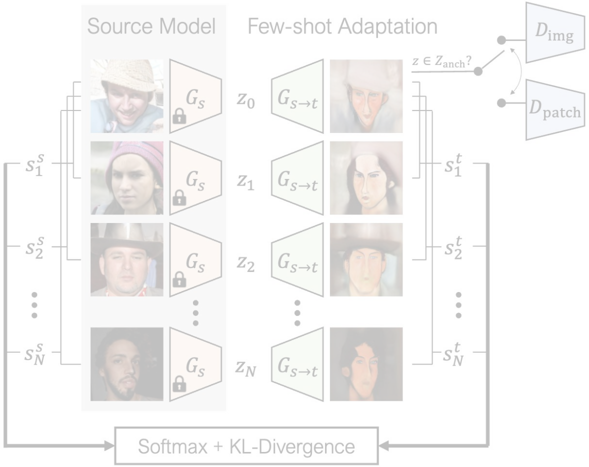

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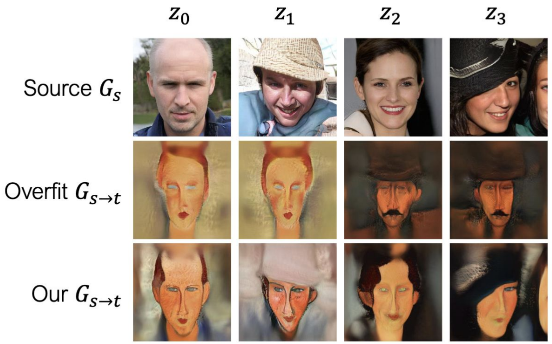

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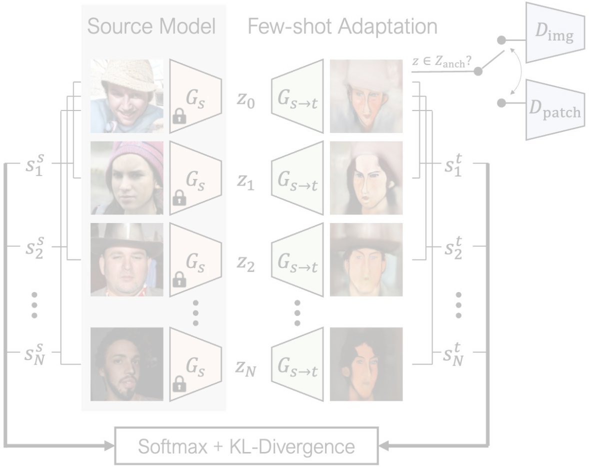

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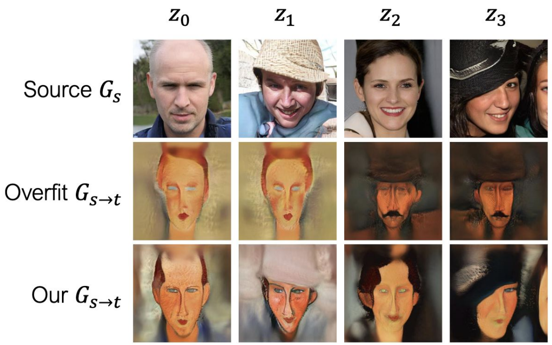

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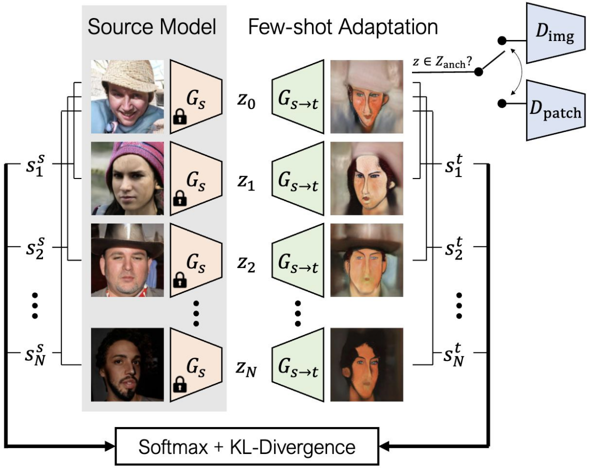

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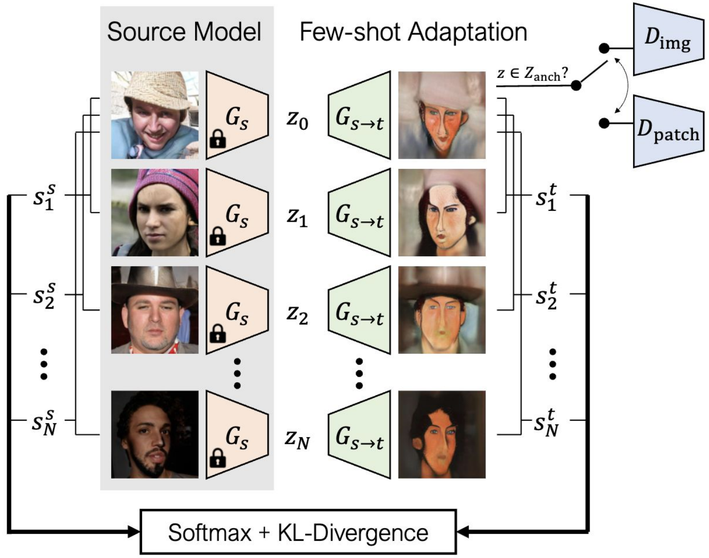

Approach:

- Sample N+1 noise vectors
- Compute **pairwise similarity scores s_i** between images generated by these noise vectors
- Construct **N-way probability distribution** by applying softmax on similarity scores

$$y_i^{s,l} = \text{Softmax}\left(\{\text{sim}(G_s^l(z_i), G_s^l(z_j))\}_{\forall i \neq j}\right)$$
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- Enforce adapted model to have similar distributions to the source

$$\mathcal{L}_{\text{dist}}(G_{s\to t}, G_s) = \mathbb{E}_{\{z_i \sim p_z(z)\}} \sum_{l,i} D_{KL}\left(y_i^{s\to t,l} || y_i^{s,l}\right)$$

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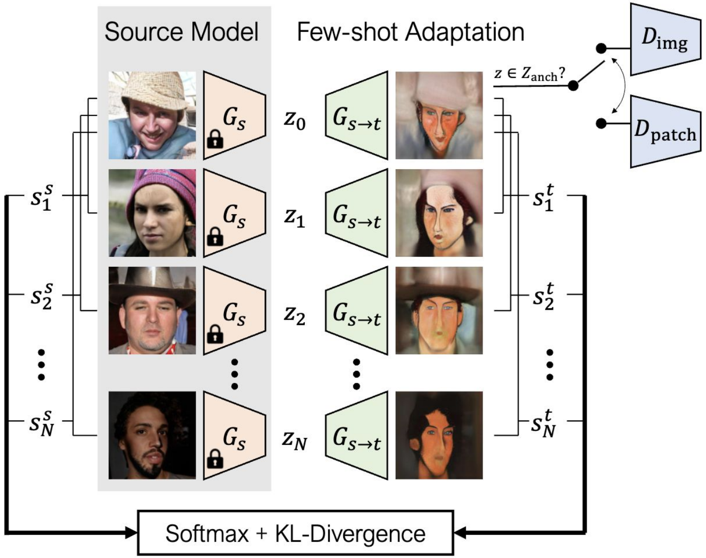

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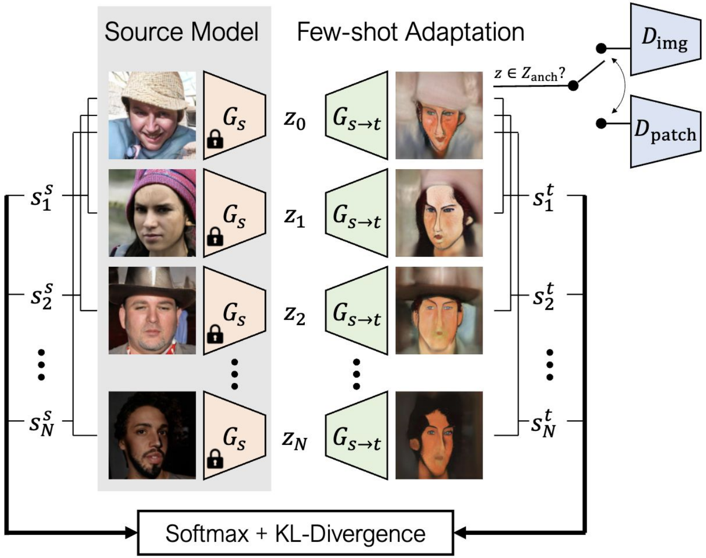

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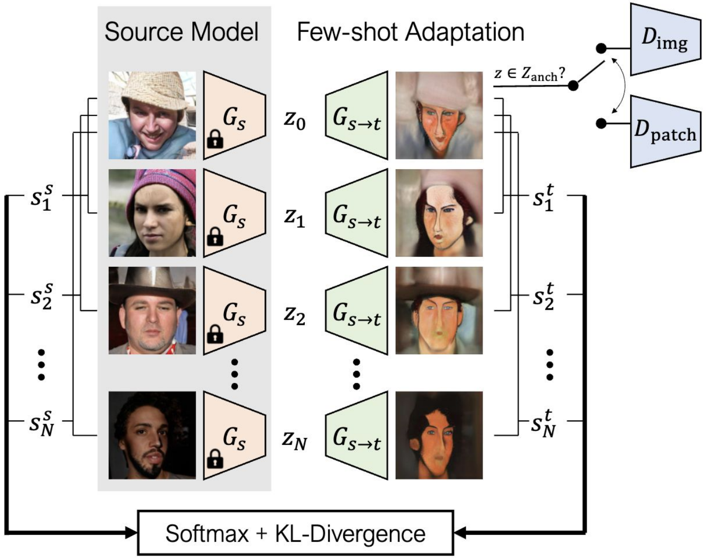

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Cross-Domain Correspondence (CDC)

Qualitative Results.
10-shot adaptation
(FFHQ⇒ Sketches)

Ojha, Utkarsh, et al. "Few-shot image generation via cross-domain correspondence." CVPR'21.

Approaches

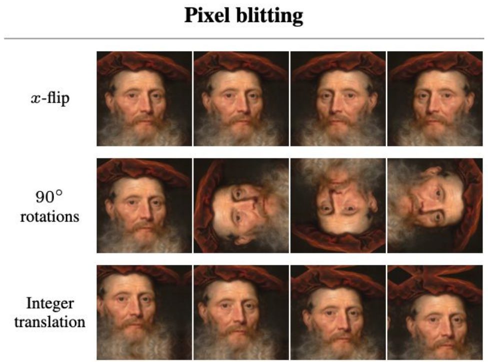
Approaches for Image Generation with Limited Data (Training Generative Models with Limited Data):

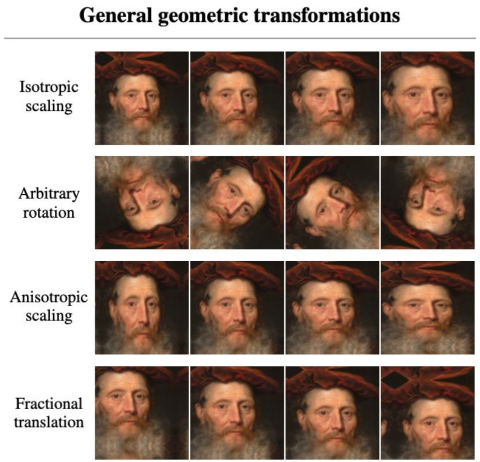
1. Transfer Learning
2. **Data Augmentation**
3. Network Architecture

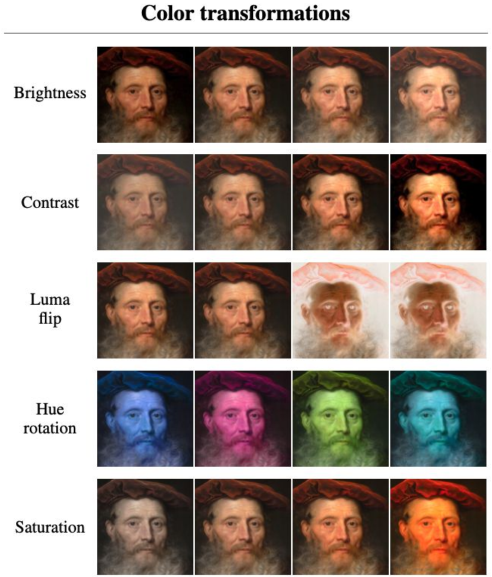
Approaches: **Data Augmentation**

Data Augmentation in Generative Modeling

- Data augmentation aims to **increase the quantity and diversity of the training data** by applying some transformations in real data, e.g., adding noise, rotating images, …
- Increased quantity can **prevent overfitting** of the generative model



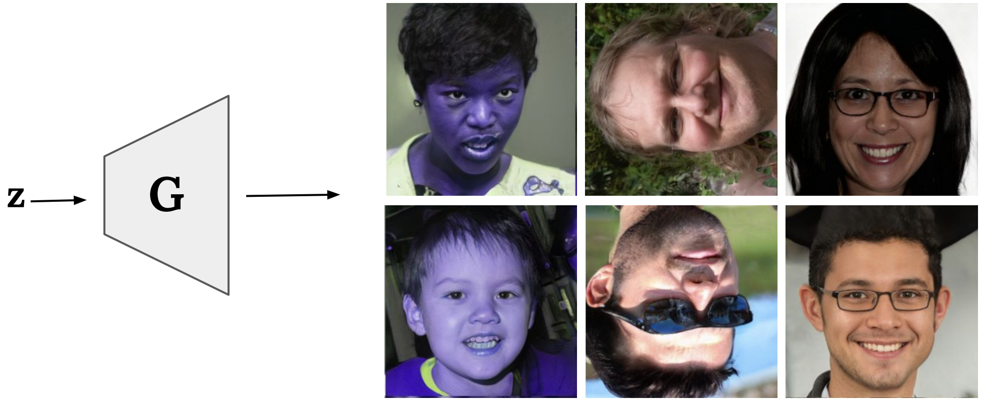




Approaches: **Data Augmentation**

Major Limitation of Classical Data Augmentation in Generative Learning

Generator **learns the augmented data distribution** instead of the real distribution and generate image with same transformations



Approaches: **Data Augmentation**

Image-Level Augmentation: Apply data transformation on image space.

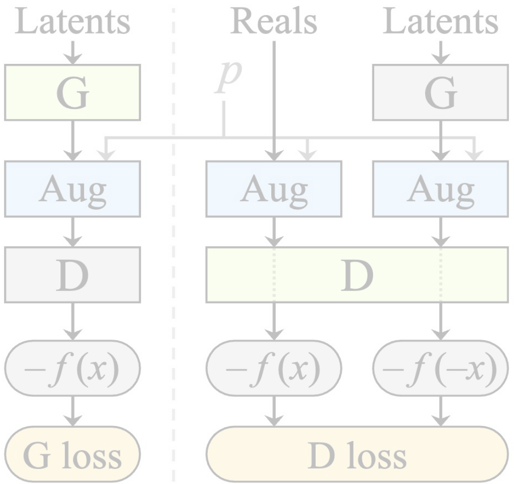
Adaptive Data Augmentation (ADA): apply augmentation to the both real and fake images with an adjustable probability based on the training dynamics

Approach. ADA includes following components:

- Augmentation is applied to **both real and fake images** (in training both D and G)
- The augmentation is applied **with a probability p<1** to enable the occurrence of the real distribution
- The **strength of the augmentation (p)** is adjusted based on the **degree of overfitting**
- Two heuristics are proposed to monitor the overfitting

$$r_v = \frac{\mathbb{E}[D_{\text{train}}] - \mathbb{E}[D_{\text{validation}}]}{\mathbb{E}[D_{\text{train}}] - \mathbb{E}[D_{\text{generated}}]} \qquad r_t = \mathbb{E}[\text{sign}(D_{\text{train}})]$$

r=0 means no overfitting, and r=1 indicates complete overfitting



Karras, Tero, et al. "Training generative adversarial networks with limited data." NeurIPS'20.

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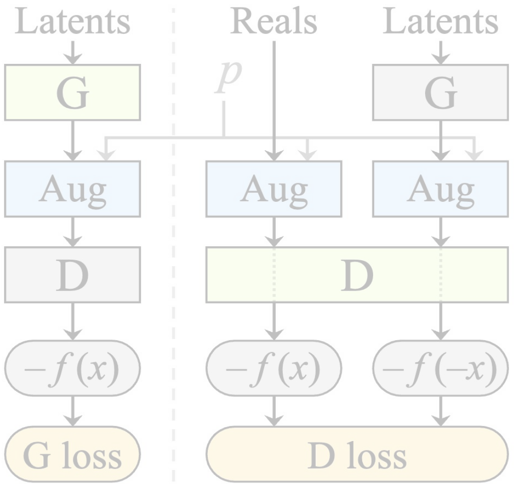

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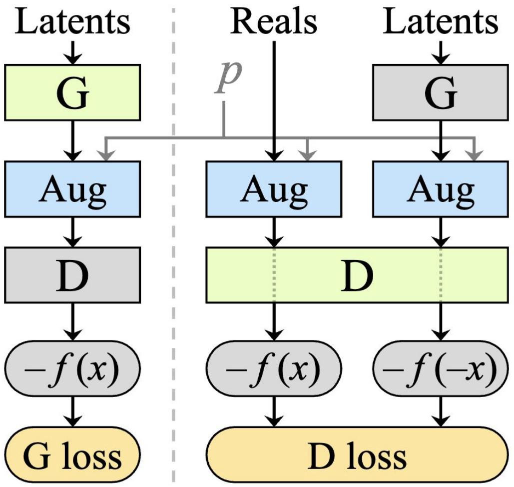

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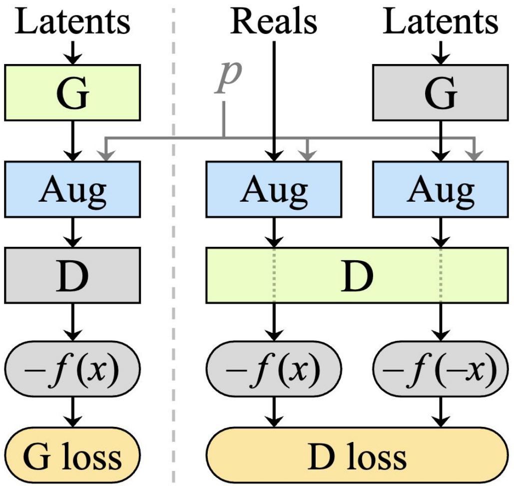

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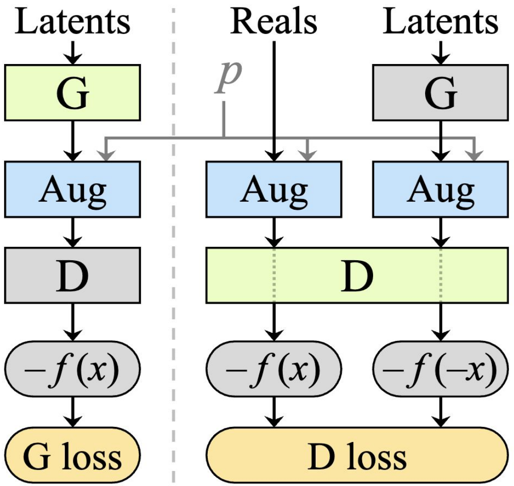

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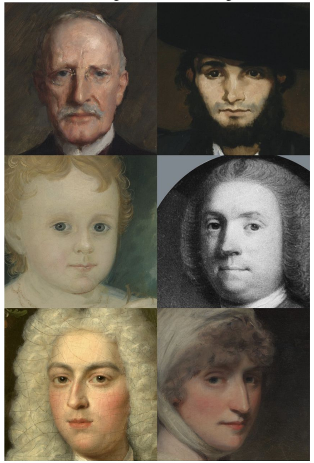
Results

MetFaces dataset (1336 images) of art paintings

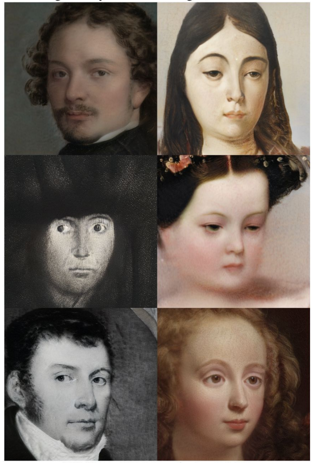
Real images from the training set



ADA (Ours), untruncated

FID **15.34** – KID **0.81**$\times 10^3$ – Recall 0.261

Original StyleGAN2 config F, untruncated



FID 19.47 – KID 3.16$\times 10^3$ – Recall **0.350**

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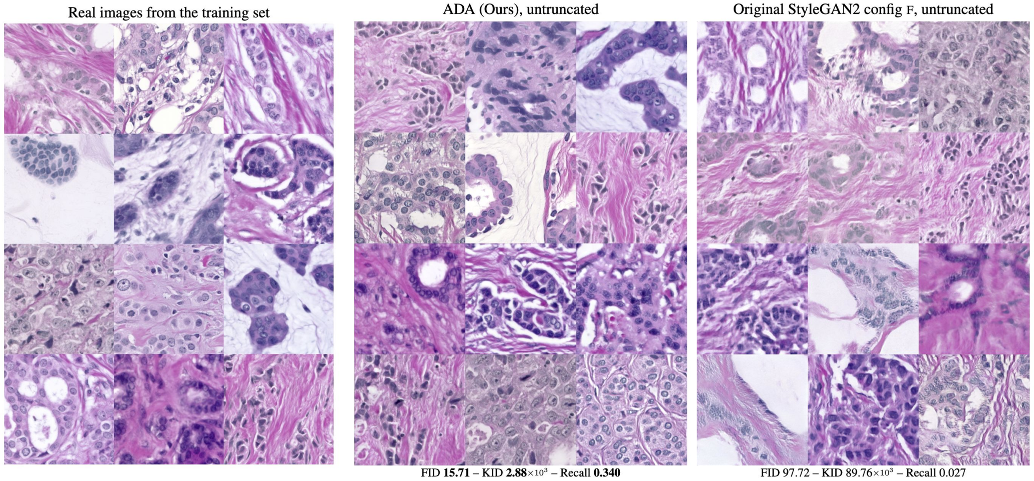
Results

BreCaHAD dataset (1944 images) for breast cancer annotation



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Adaptive Data Augmentation (ADA)

Evaluating the Performance of StyleGAN2-ADA on Medical Images

McKell Woodland[1,2], John Wood[1], Brian M. Anderson[1,4], Suprateek Kundu[1]
Ethan Lin[1], Eugene Koay[1], Bruno Odisio[1], Caroline Chung[1], Hyunseon
Christine Kang[1], Aradhana M. Venkatesan[1], Sireesha Yedururi[1], Brian De[1],
Yuan-Mao Lin[1], Ankit B. Patel[2,3], and Kristy K. Brock[1]

[1] The University of Texas MD Anderson Cancer Center, Houston TX 77030, USA
MEWoodland@mdanderson.org
[2] Rice University, Houston TX 77005, USA
[3] Baylor College of Medicine, Houston TX 77030, USA
[4] University of California San Diego, La Jolla CA 92093, USA

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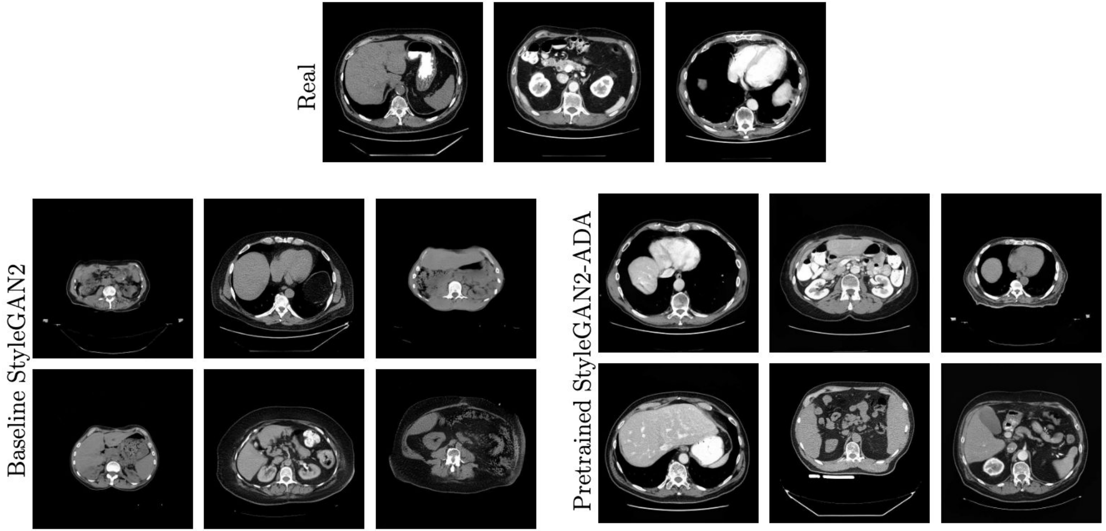

Start from a pre-trained StyleGAN2-ADA on FFHQ and fine-tune on the SLIVER07 dataset

Karras, Tero, et al. "Training generative adversarial networks with limited data." NeurIPS'20.

Approaches

Approaches for Image Generation with Limited Data (Training Generative Models with Limited Data):

1. Transfer Learning
2. Data Augmentation
3. **Network Architecture**

Comprehensive Review: **Network Architecture**

Network Architecture

Design specific architectures for the generators to improve their training performance under data constraints. Like designing shallow/sparse architectures to **prevent over-parameterization**.

Primary Challenge/Limitation

- When aiming to design a new architecture, the process of discovering optimal hyperparameters can be laborious
- Designing new architecture prevents leveraging the powerful pre-trained generators

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Comprehensive Review: **Network Architecture**

Feature Enhancement: Design additional modules to enhance/retain the features of the generator

FastGAN has **three major design** choices:

i) Using a **compact size network** for both G and D in GAN
ii) introducing **Skip-layer excitation** for G for better gradient flow
iii) adding **self-supervised** task for D

Results of training FastGAN **from scratch** on **1024^2 resolution** using **single RTX 2080-Ti GPU** with only 1000 images. Left: **20 hours** on Nature photos; Right: **10 hours** on FFHQ.

Liu, Bingchen, et al. "Towards faster and stabilized gan training for high-fidelity few-shot image synthesis." ICLR'20.

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Results of training FastGAN **from scratch** on 1024^2 **resolution** using **single RTX 2080-Ti GPU** with only 1000 images. Left: **20 hours** on Nature photos; Right: **10 hours** on FFHQ.

Liu, Bingchen, et al. "Towards faster and stabilized gan training for high-fidelity few-shot image synthesis." ICLR'20.

Comprehensive Review: **Network Architecture**

Feature Enhancement: Design additional modules to enhance/retain the features of the generator

FastGAN has **three major design** choices:

i) Using a **compact size network** for both G and D in GAN

ii) introducing **Skip-layer excitation** for G for better gradient flow

iii) adding **self-supervised** task for D

Results of training FastGAN **from scratch** on **1024^2 resolution** using **single RTX 2080-Ti GPU** with only 1000 images. Left: **20 hours** on Nature photos; Right: **10 hours** on FFHQ.

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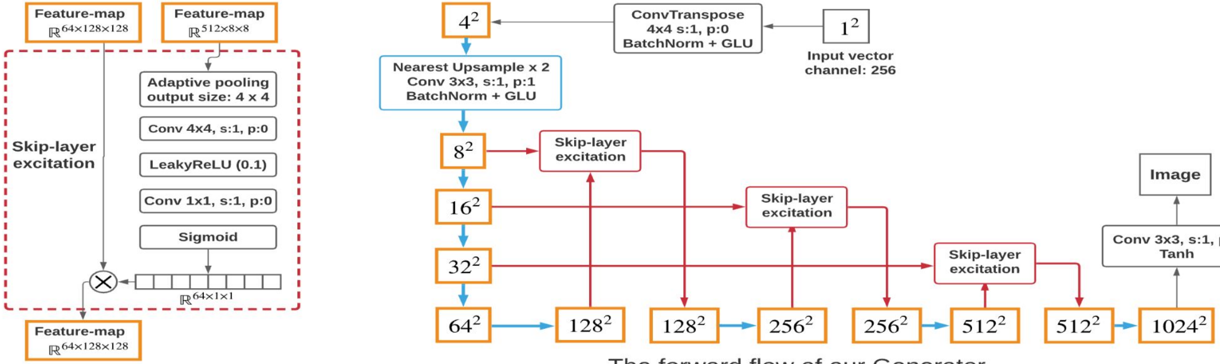
Comprehensive Review: **Network Architecture**

Feature Enhancement: Design additional modules to enhance/retain the features of the generator

FastGAN

Design of Generator (G):

- Use a **single Conv-layer** for each resolution
- Use **skip-layer excitation** including skip connection and connection between different resolutions for **better gradient flow during training G**



The forward flow of our Generator

Liu, Bingchen, et al. "Towards faster and stabilized gan training for high-fidelity few-shot image synthesis." ICLR'20.

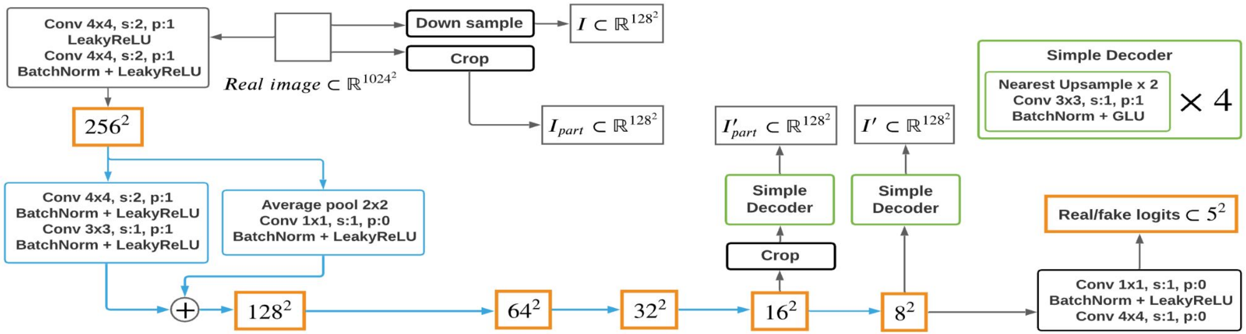
Comprehensive Review: **Network Architecture**

Feature Enhancement: Design additional modules to enhance/retain the features of the generator

FastGAN

Design of Discriminator (D):

- Use a **compact design** for D
- Add reconstruction loss in two different resolution (additional task as auto-encoder) to improve learning of D using **additional supervisory signal**

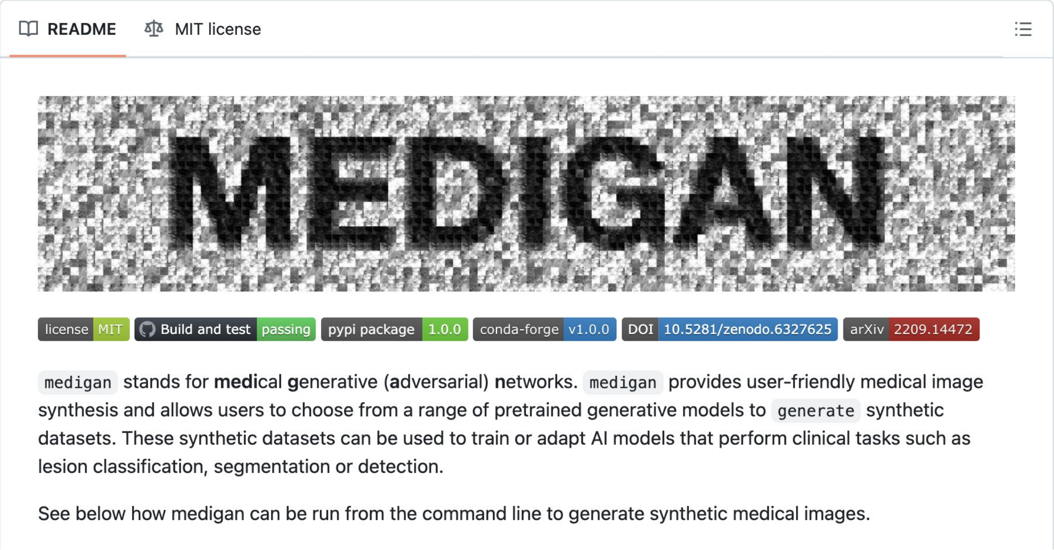


Liu, Bingchen, et al. "Towards faster and stabilized gan training for high-fidelity few-shot image synthesis." ICLR'20.

Comprehensive Review: **Network Architecture**

Feature Enhancement: Design additional modules to enhance/retain the features of the generator

FastGAN



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MEDIGAN

license MIT | Build and test passing | pypi package 1.0.0 | conda-forge v1.0.0 | DOI 10.5281/zenodo.6327625 | arXiv 2209.14472

`medigan` stands for **medi**cal **g**enerative (**a**dversarial) **n**etworks. `medigan` provides user-friendly medical image synthesis and allows users to choose from a range of pretrained generative models to `generate` synthetic datasets. These synthetic datasets can be used to train or adapt AI models that perform clinical tasks such as lesion classification, segmentation or detection.

See below how medigan can be run from the command line to generate synthetic medical images.

https://github.com/RichardObi/medigan

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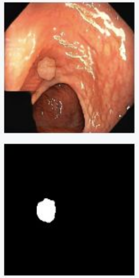
Comprehensive Review: **Network Architecture**

Feature Enhancement: Design additional modules to enhance/retain the features of the generator

FastGAN

Output type	Modality	Model type	Output size	Base dataset	Output examples	`model_id`
Polyp with Mask	endoscopy	fastgan	256x256	HyperKvasir		`00010_FASTGAN_POLYP_PATCHES_W_MASKS`

Liu, Bingchen, et al. "Towards faster and stabilized gan training for high-fidelity few-shot image synthesis." ICLR'20.

Q&A