

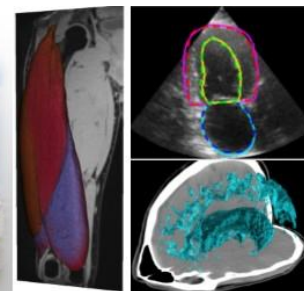
# Generative Adversarial Networks (GANs)

Anirban Mukhopadhyay  
TU Darmstadt, Germany



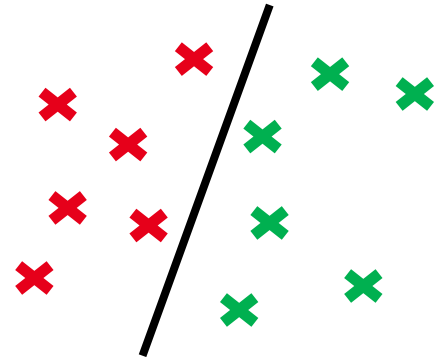
**Deep learning for medical imaging school**

**April 15—19 2019, Campus de la Doua, Lyon**



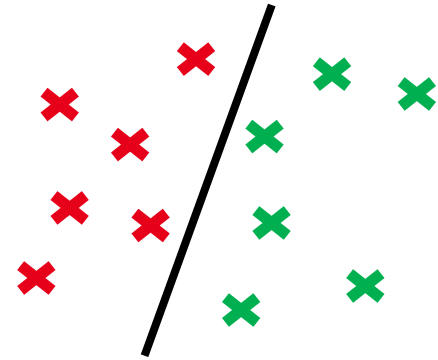
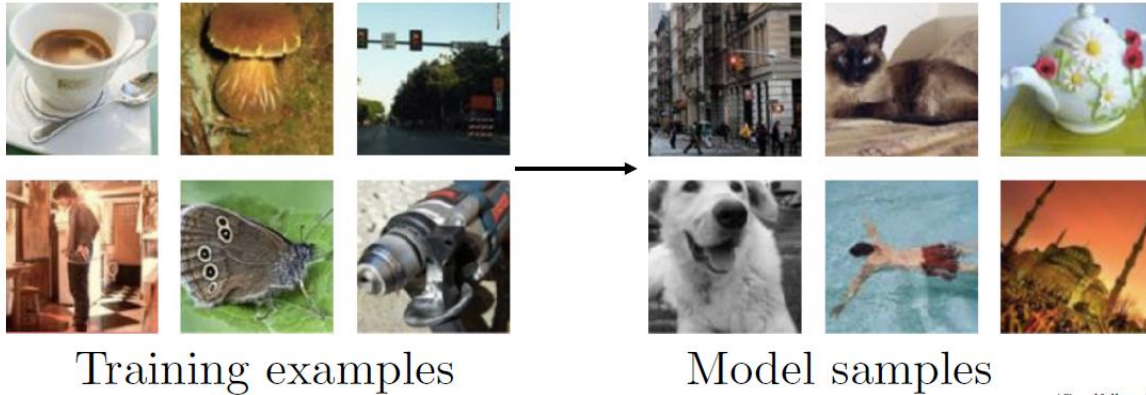
# Introduction

- Generative vs. Discriminative



# Introduction

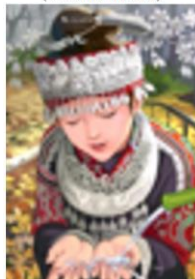
- Generative vs. Discriminative
  - Generating “realistic-looking” images – one step closer to understanding it



(Goodfellow 2016)

# GAN Results

bicubic  
(21.59dB/0.6423)



SRResNet  
(23.53dB/0.7832)



SRGAN  
(21.15dB/0.6868)



original



© SRGAN



© Karras2018

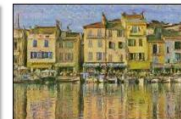
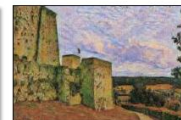
Input



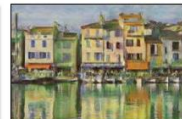
Monet



Van Gogh



Cezanne



Ukiyo-e

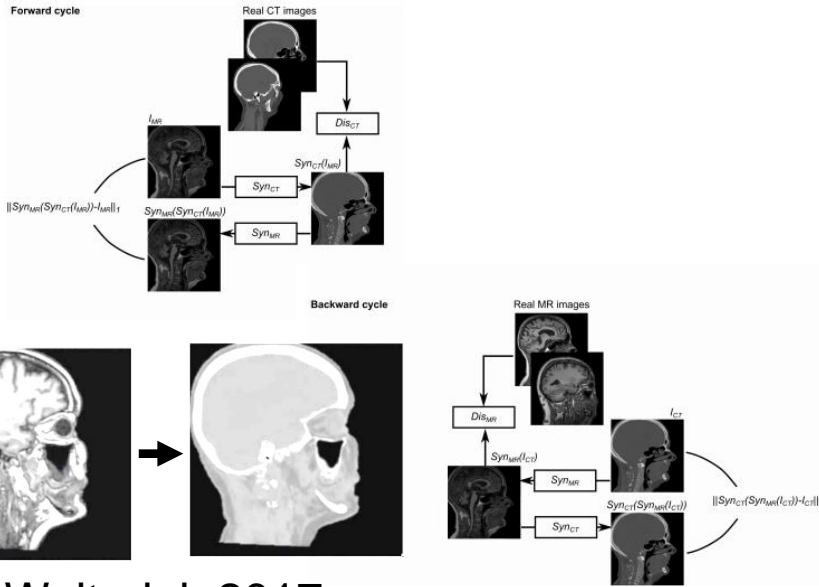


© CycleGAN

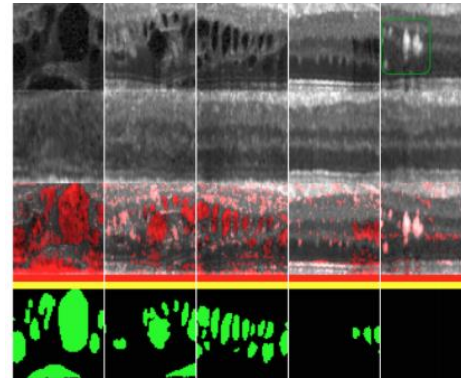
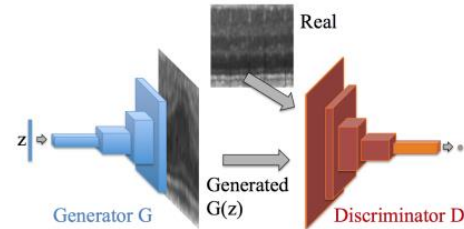
# What is in it for me?

## MR to CT Reconstruction

## Anomaly Detection



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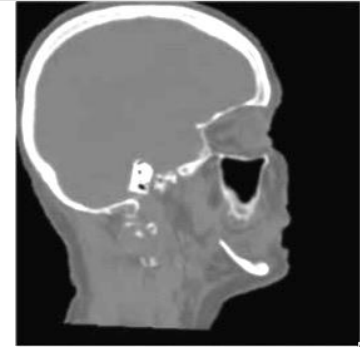
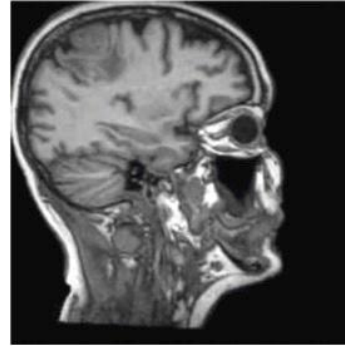


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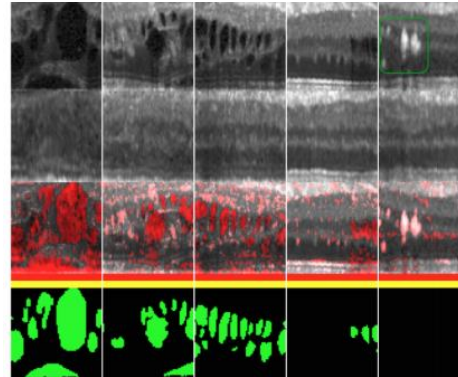


# What is in it for me?

- Proxy for training data
  - Costly annotation
  - Imbalance



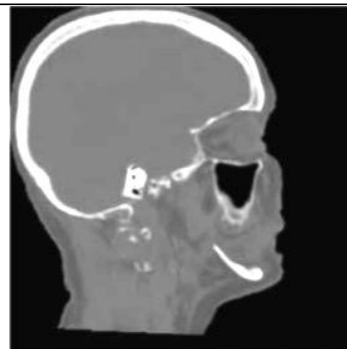
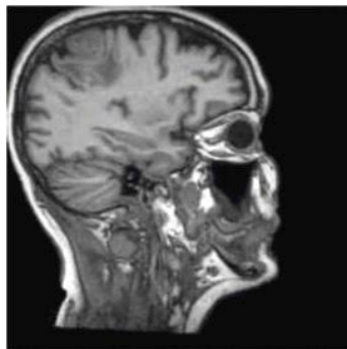
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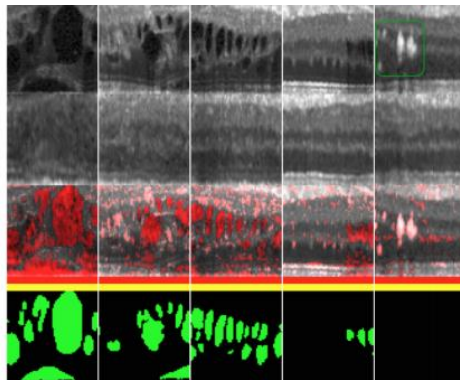
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# What is in it for me?

- Proxy for training data
  - Costly annotation
  - Imbalance
- Similarity metric
  - Discriminator



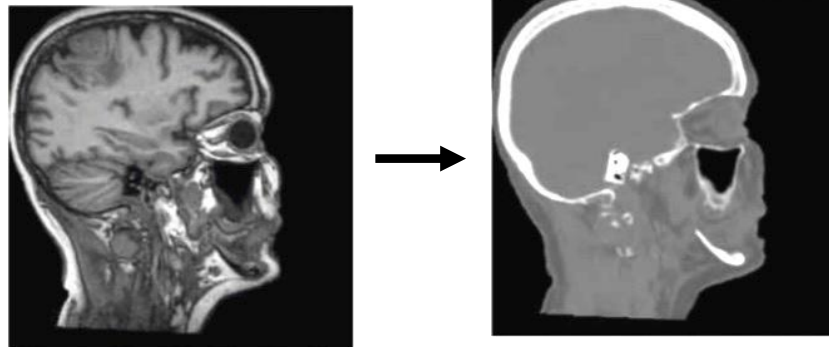
©Wolterink 2017



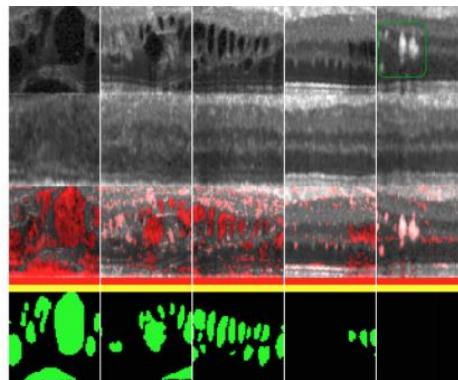
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# What is in it for me?

- Proxy for training data
  - Costly annotation
  - Imbalance
- Similarity metric
  - Discriminator
- Domain Shift
  - Adversarial training



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- Theory
- Key GANs
  
- Medical Applications
- Adversarial Learning
  
- Limitations of GAN
- Summary



***Tidying Up GAN – the Marie Kondo way***

Closet

- Theory
- Key GANs

Kitchen

- Medical Applications
- Adversarial Learning

Emotional

- Limitations of GAN
- Summary



***Tidying Up GAN – the Marie Kondo way***

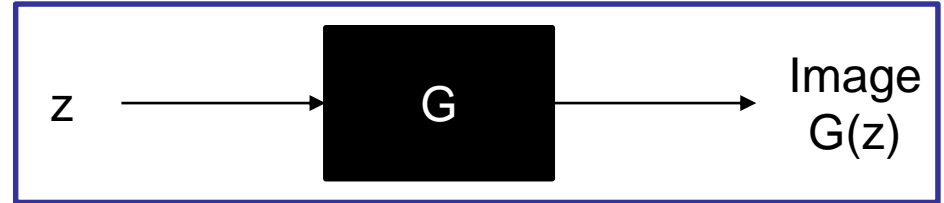
# Theory



- UNSUPERVISED Learning



- UNSUPERVISED Learning
- Perplexity
  - pdf for the generated distribution



Critique  $G$  – Calculating Perplexity

- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets
- **Idea 2:** Gradient feedback from discriminator
- **Idea 3:** Game of many moves



- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets



Similarity of  $P_{\text{real}}$  and  $P_{\text{synth}}$

- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets



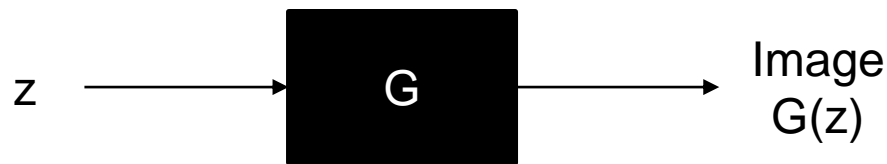
Similarity of  $P_{\text{real}}$  and  $P_{\text{synth}}$   
Deep Net D – maps images to  $[0,1]$

- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets



Similarity of  $P_{\text{real}}$  and  $P_{\text{synth}}$   
Deep Net  $D$  – maps images to  $[0,1]$   
 $E_x[D(x)]$  is high if  $x \in P_{\text{real}}$   
 $E_x[D(x)]$  is low if  $x \in P_{\text{synth}}$

- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets



Similarity of  $P_{\text{real}}$  and  $P_{\text{synth}}$   
Deep Net  $D$  – maps images to  $[0,1]$   
 $E_x[D(x)]$  is high if  $x \in P_{\text{real}}$   
 $E_x[D(x)]$  is low if  $x \in P_{\text{synth}}$   
Train using **Backpropagation**

- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets
- **Idea 2:** Gradient feedback from discriminator



Goal of generator G:  
 $E_z[D(G(z))]$  is as high as possible

- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets
- **Idea 2:** Gradient feedback from discriminator



Goal of generator  $G$ :  
 $E_z[D(G(z))]$  is as high as possible  
**Fooling** Discriminator

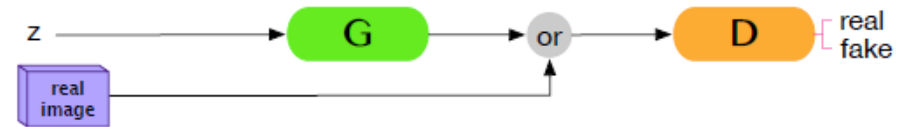


- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets
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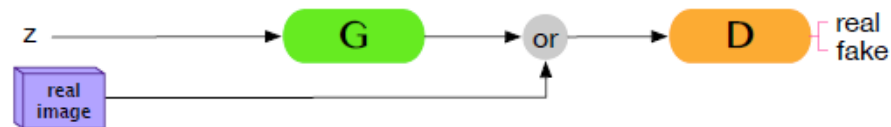
Goal of generator G:  
 $E_z[D(G(z))]$  is as high as possible  
**Fooling** Discriminator  
Backpropagation through  $D(G(.))$

- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets
- **Idea 2:** Gradient feedback from discriminator
- **Idea 3:** Game of many moves



- Generative vs. Discriminative
- UNSUPERVISED Learning
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- **Idea 1:** Sidestep perplexity with deep nets
- **Idea 2:** Gradient feedback from discriminator
- **Idea 3:** Game of many moves

$$\min_G \max_D E_{x \sim P_{real}} [f(D(x))] + E_{z \sim P_{synth}} [1 - f(D(G(z)))]$$

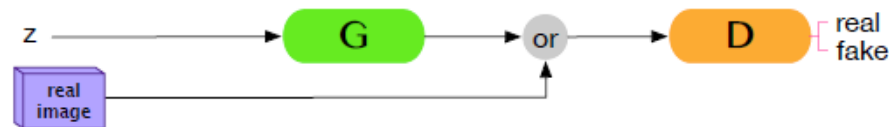


- Generative vs. Discriminative
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$$\min_G \max_D E_{x \sim P_{real}} [f(D(x))] + E_{z \sim P_{synth}} [1 - f(D(G(z)))]$$

For Goodfellow 2014

$f(x) = \log(x)$



- Generative vs. Discriminative
- UNSUPERVISED Learning
- Perplexity
- **Idea 1:** Sidestep perplexity with deep nets
- **Idea 2:** Gradient feedback from discriminator
- **Idea 3:** Game of many moves

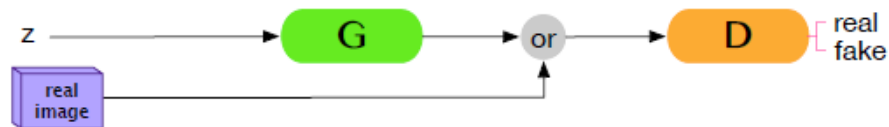
$$\min_G \max_D E_{x \sim P_{real}} [f(D(x))] + E_{z \sim P_{synth}} [1 - f(D(G(z)))]$$

For Goodfellow 2014

$f(x) = \log(x)$

Derivative of  $\log(x) = 1/x$

Training **sensitive** to instances  
that D finds **awful**

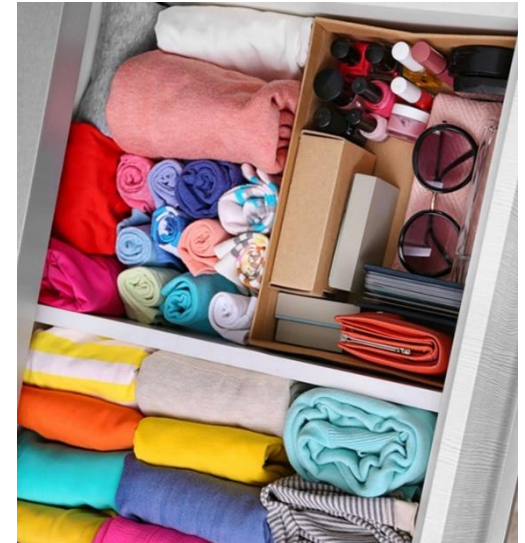


# Understanding Key GANs

Theory

Engineering Recipe

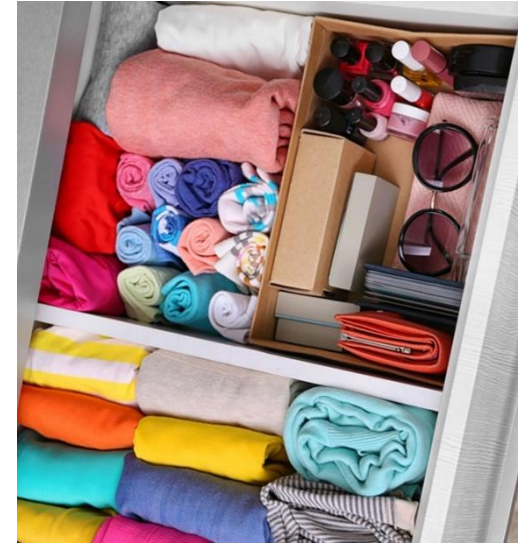
Tidy GANs



© giphy.com



- Engineering Recipe
  - I/P, O/P
  - Architecture
  - Loss Function



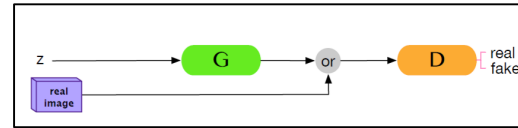
# Understanding Key GANs

## ■ Engineering Recipe

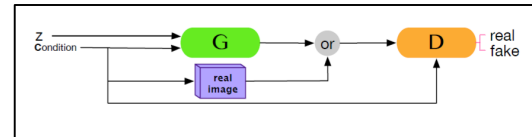
■ I/P, O/P

■ Architecture

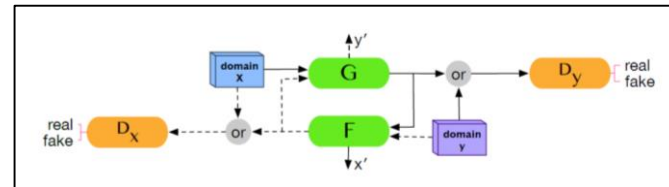
■ Loss Function



DC-GAN



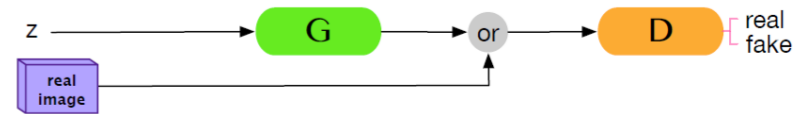
C-GAN



Cycle-GAN

# Deep Convolutional GAN (DC-GAN)

- Unsupervised
- Representation Learning



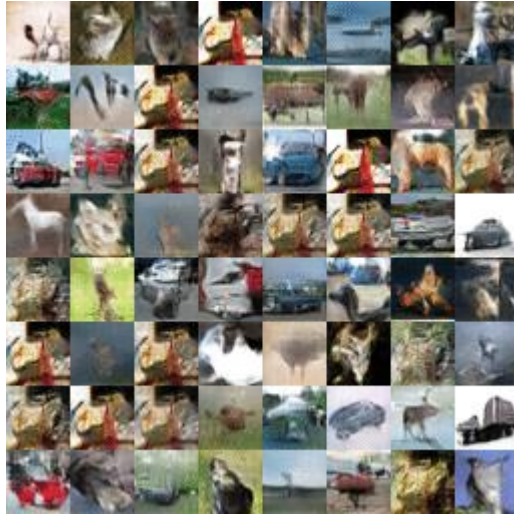
# Deep Convolutional GAN (DC-GAN)

- Unsupervised
- Representation Learning
- Latent space Interpolation



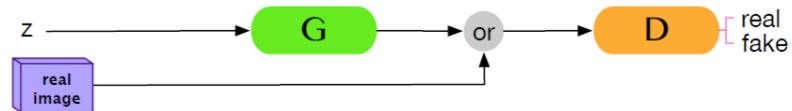
# Deep Convolutional GAN

- I/P:  $Z$  (100-D multivariate Gaussian)
- O/P: Image



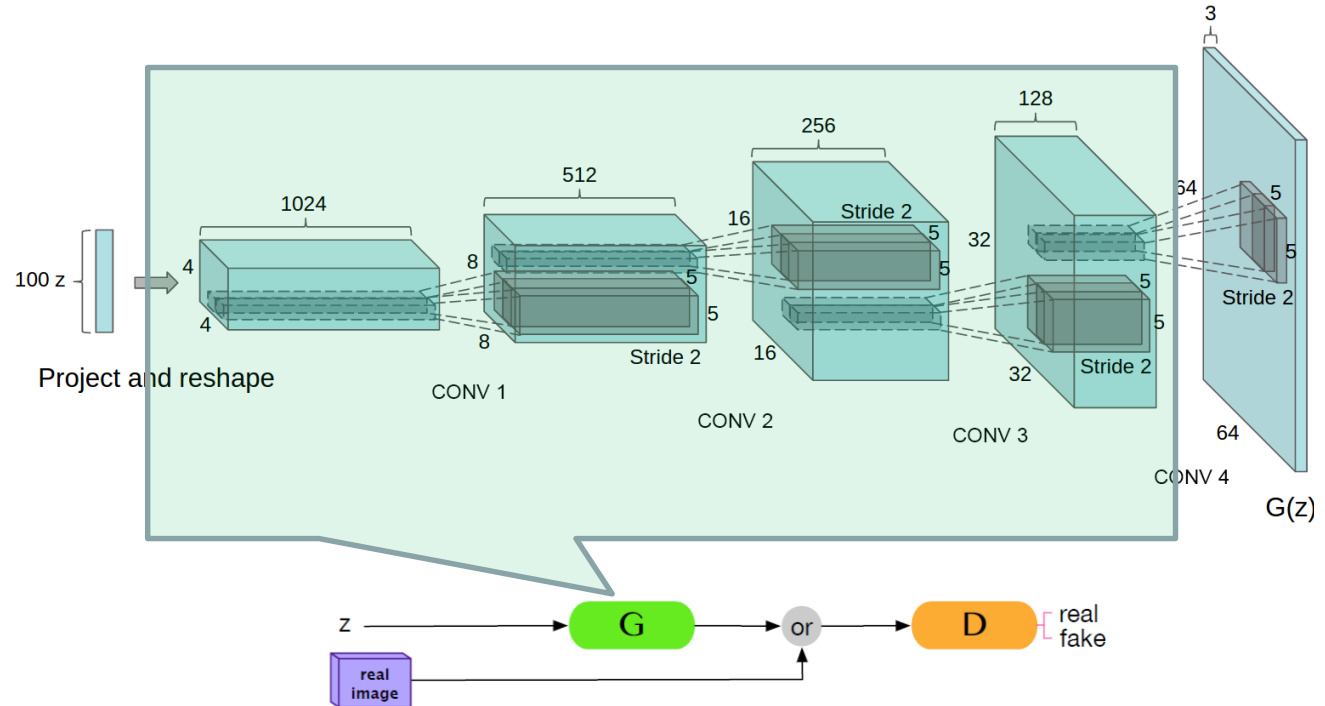
# DC-GAN

- I/P:  $Z$  (100-D multivariate Gaussian)
- O/P: Image
  
- Architecture:



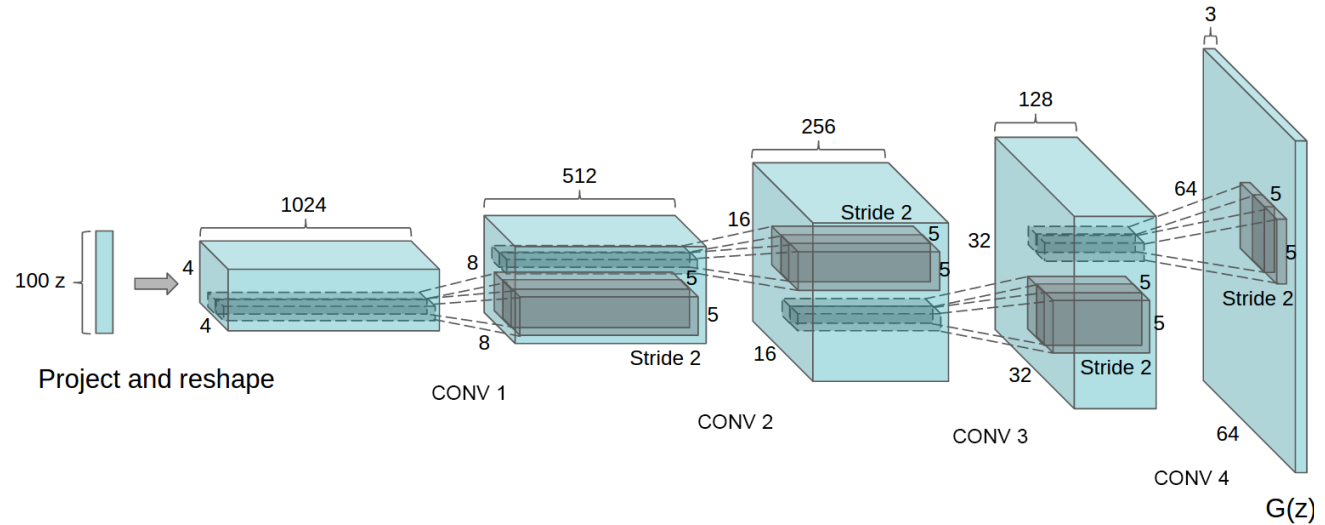
- I/P:  $Z$
- O/P: Image

- Architecture:



- I/P:  $Z$
- O/P: Image

- Architecture:

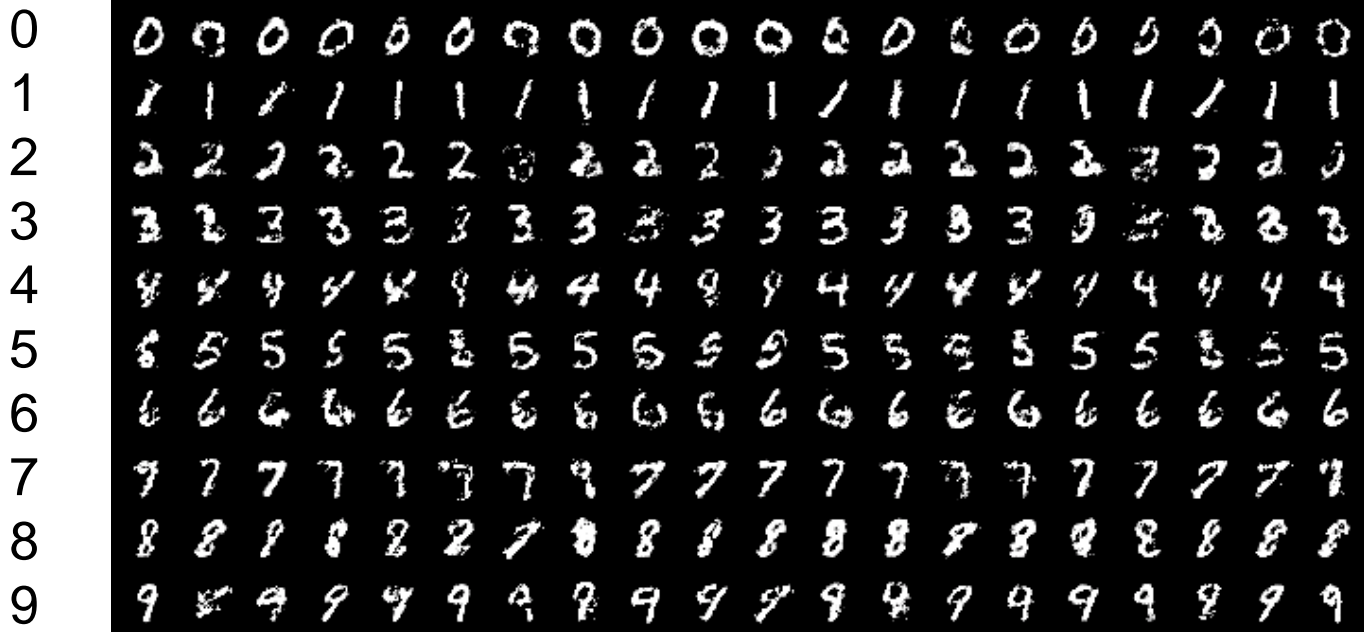


- Loss Function: Same as Goodfellow 2014



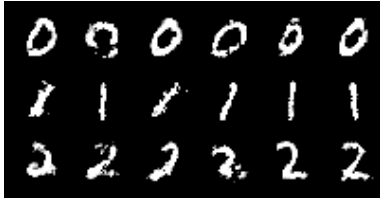
# Conditional GAN (C-GAN)

- How to bring in some supervision?

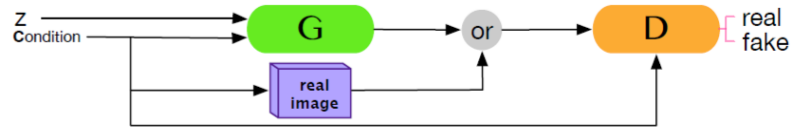


# Conditional GAN (C-GAN)

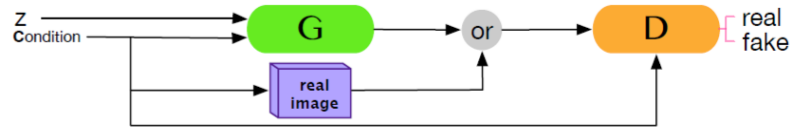
- I/P: Z, Condition 0,1,2,...
- O/P: Image



- I/P: Z, Condition
- O/P: Image
  
- Architecture:



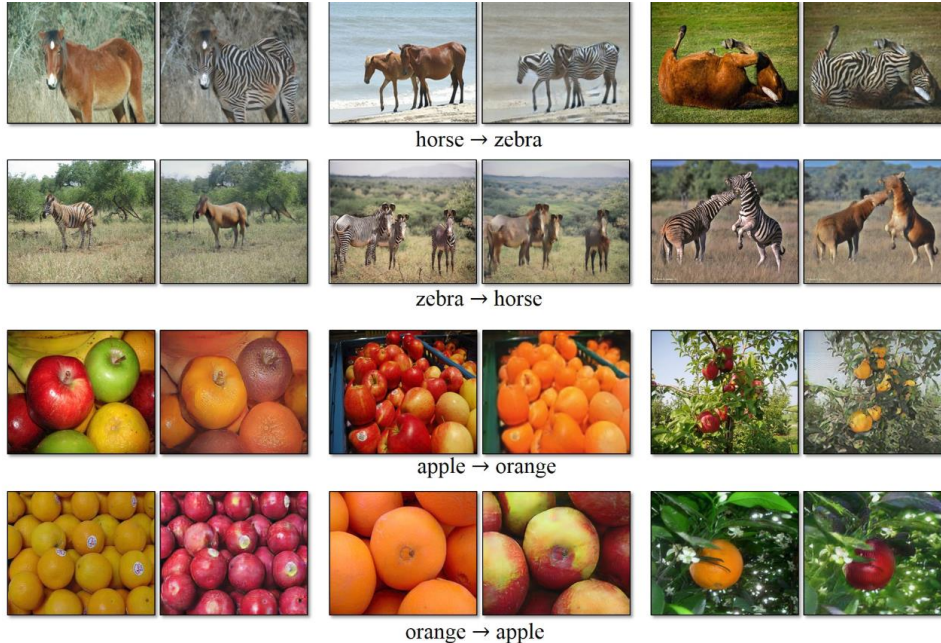
- I/P: Z, Condition(c)
- O/P: Image
  
- Architecture:



- Loss Function:

$$\min_G \max_D E_{x \sim P_{real}} [f(D(x|c))] + E_{z \sim P_{synth}} [1 - f(D(G(z|c)))]$$

- How to incorporate **unpaired** images for style/ domain transfer?

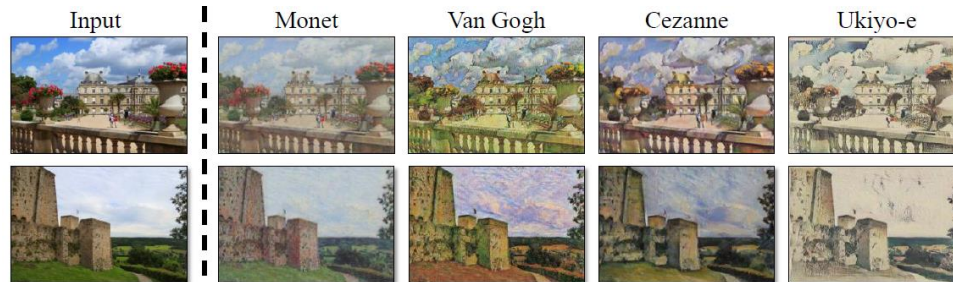


©Cycle-GAN

# Cycle-GAN

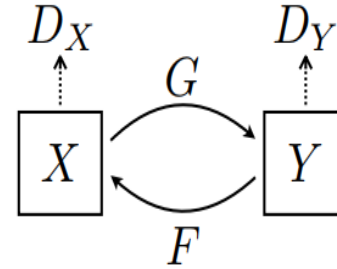
- I/P: Image (Domain X)
- O/P: Image (Domain Y)

UN-PAIRED



# Cycle-GAN

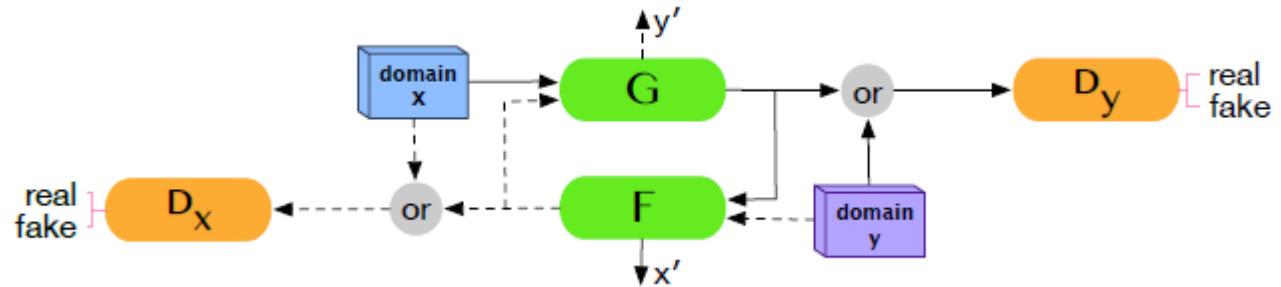
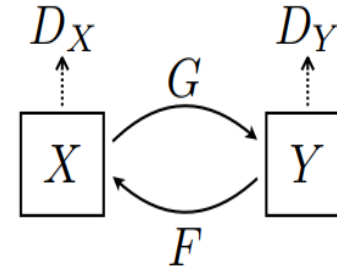
- I/P: Image (Domain X)
  - O/P: Image (Domain Y)
- 
- Architecture:



# Cycle-GAN

- I/P: Image (Domain X)
- O/P: Image (Domain Y)

- Architecture:

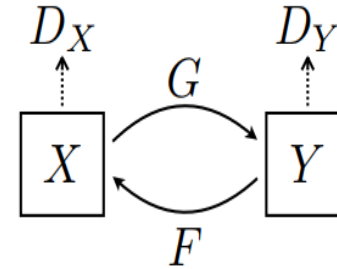




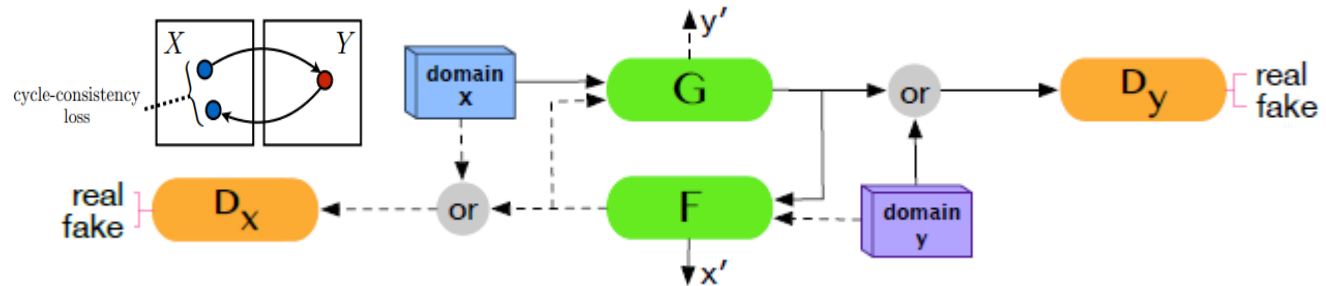
# Cycle-GAN

- I/P: Image (Domain X)
- O/P: Image (Domain Y)

- Architecture:



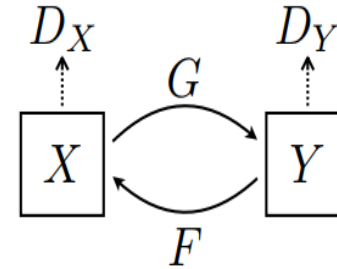
- Loss Function



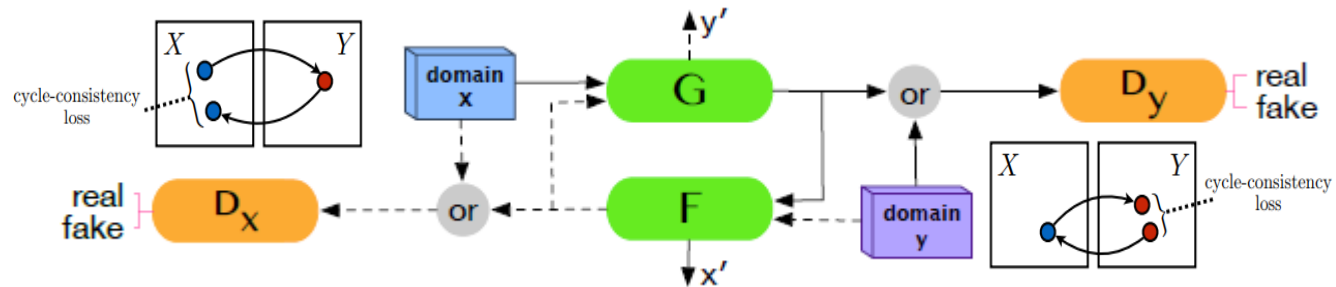
# Cycle-GAN

- I/P: Image (Domain X)
- O/P: Image (Domain Y)

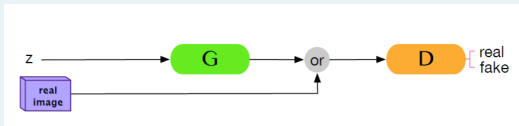
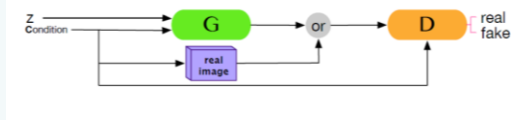
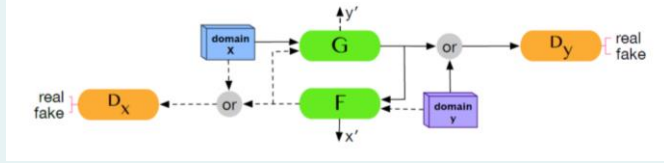
- Architecture:



- Loss Function



# Engineering Recipe Summary

GANs	I/P	O/P	Architect.	Loss	Note
DC-GAN	z	Img		GAN	Unsup.
C-GAN	z,c	Img		Modif. GAN	Cond. Supervis.
Cycle-GAN	Img (X)	Img (Y)		Cycle Loss	Style Transfer

# Medical Applications

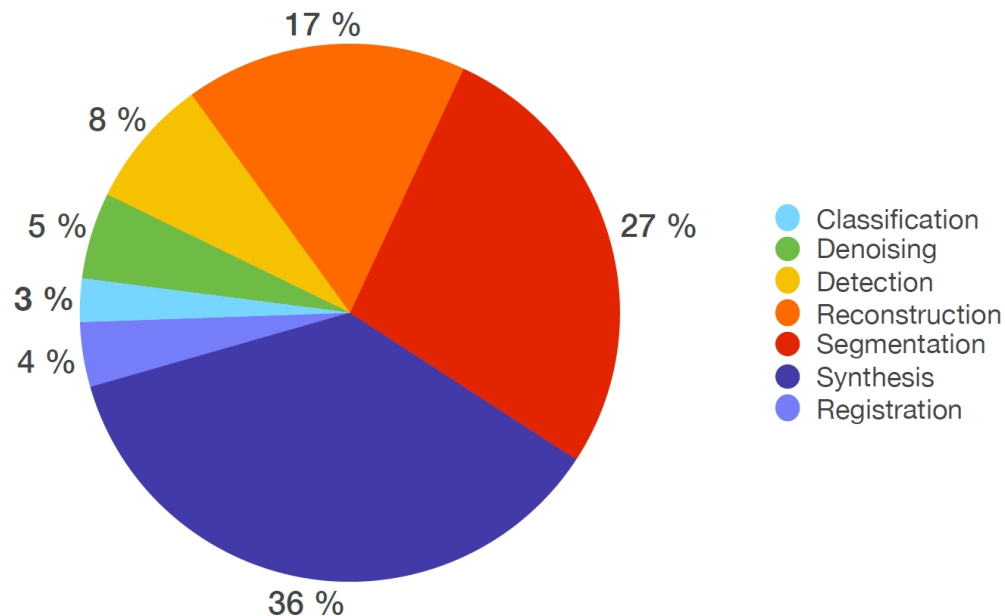


© popsugar

- Review article
  - 77 papers are reviewed
  - Till end of 2018
  - Incl. MICCAI, MiDL, ISBI, TMI, MedIA etc.

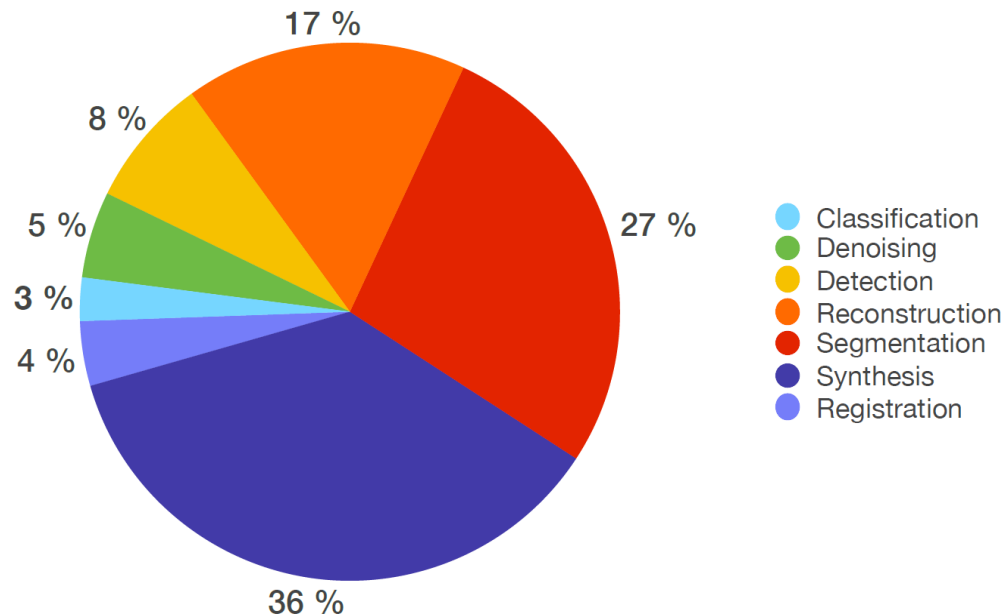
# Medical Applications

- Review article
  - 77 papers are reviewed
  - Till end of 2018
  - Incl. MICCAI, MiDL, ISBI, TMI, MedIA etc.
- Mostly applied in
  - Synthesis
  - Segmentation



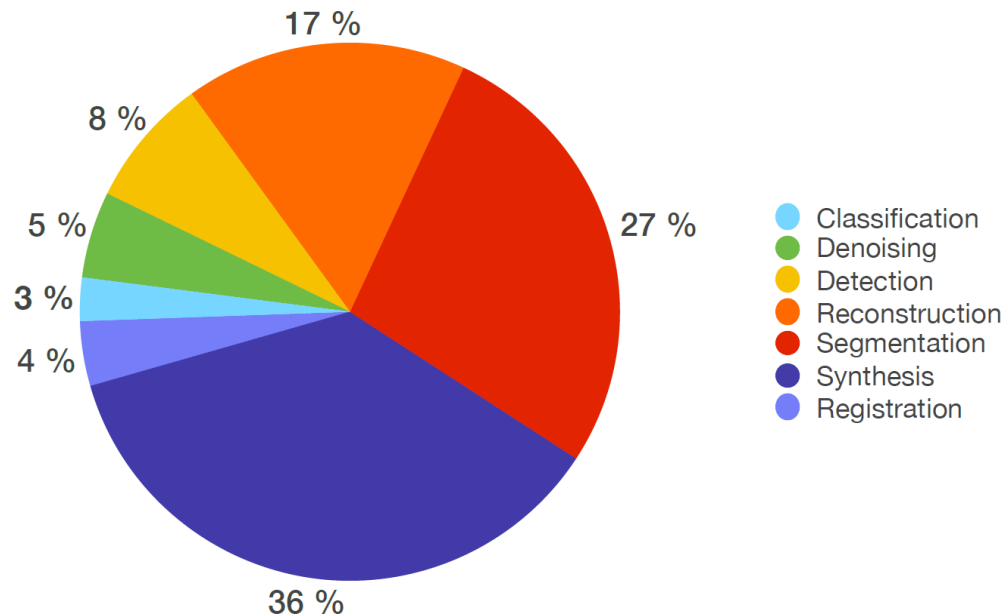
<https://arxiv.org/abs/1809.06222>

- Review article
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  - Incl. MICCAI, MiDL, ISBI, TMI, MedIA etc.
- Mostly applied in
  - Synthesis
  - Segmentation
- **Pattern**
  - Modify Architecture
  - Modify Loss



<https://arxiv.org/abs/1809.06222>

- Review article
  - 77 papers are reviewed
  - Till end of 2018
  - Incl. MICCAI, MiDL, ISBI, TMI, MedIA etc.
- Mostly applied in
  - Synthesis
  - Segmentation
- **Pattern**
  - Modify Architecture
  - Modify Loss
- Re-apply the recipe



<https://arxiv.org/abs/1809.06222>

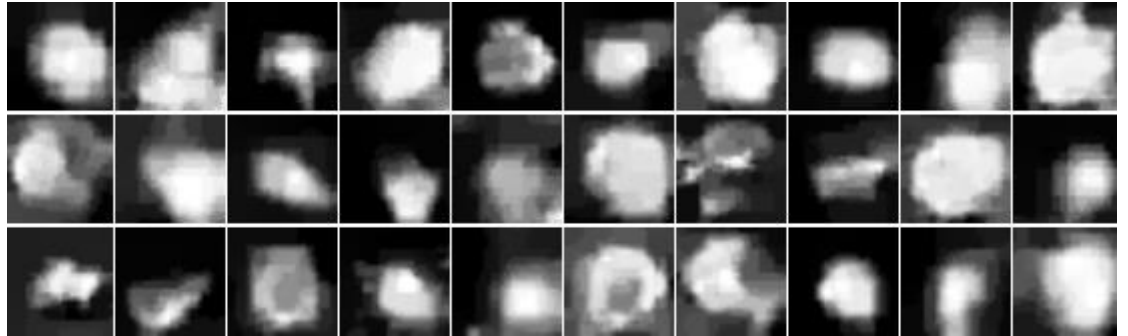


# Synthesis - Unsupervised

- Discriminating Lung Nodules
  - Benign
  - Malign

# Synthesis - Unsupervised

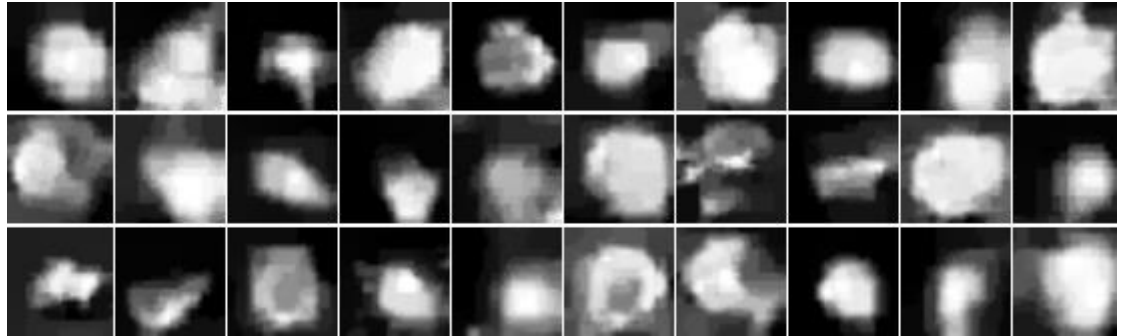
- Discriminating Lung Nodules
  - Benign
  - Malign
- Unsupervised synthesis
  - Modify DC-GAN



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# Synthesis - Unsupervised

- Discriminating Lung Nodules
  - Benign
  - Malign
- Unsupervised synthesis
  - Modify DC-GAN
- Visual Turing Test
  - 2 radiologists

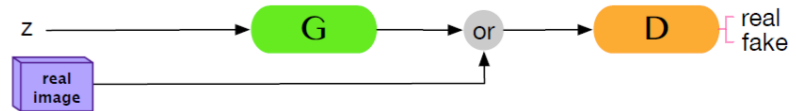


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# Synthesis - Unsupervised

- I/P: Z
- O/P: Image (64X64X3)

- Architecture:

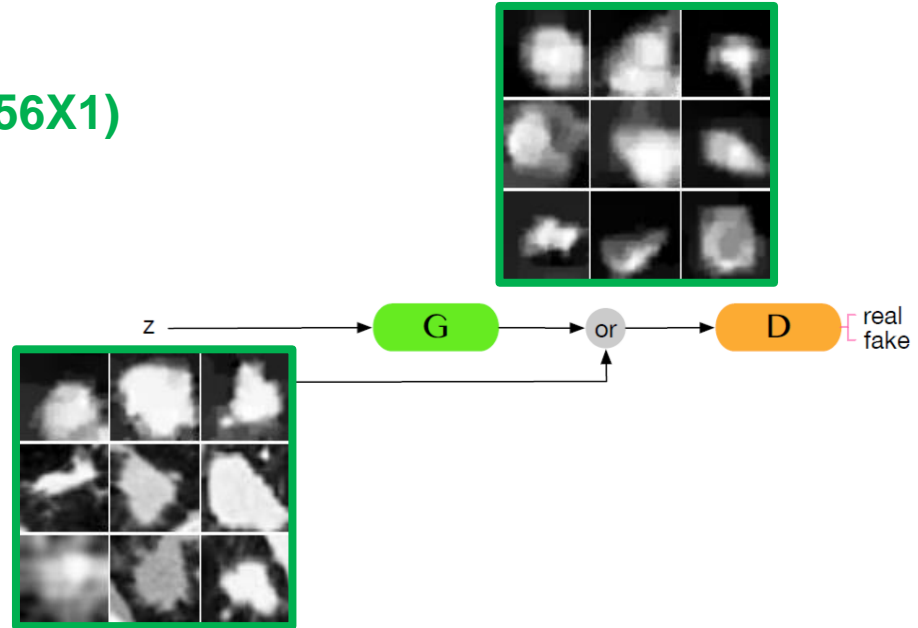


- Loss Function: Same as Goodfellow 2014

# Synthesis - Unsupervised

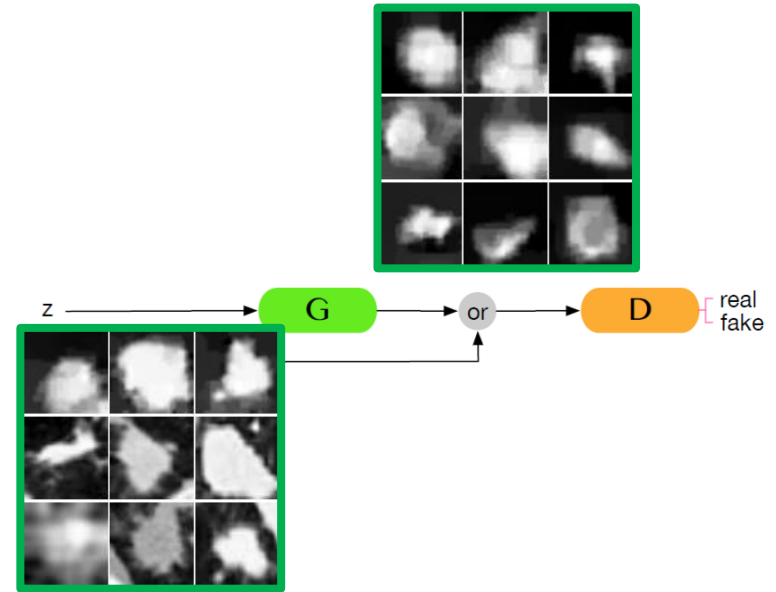
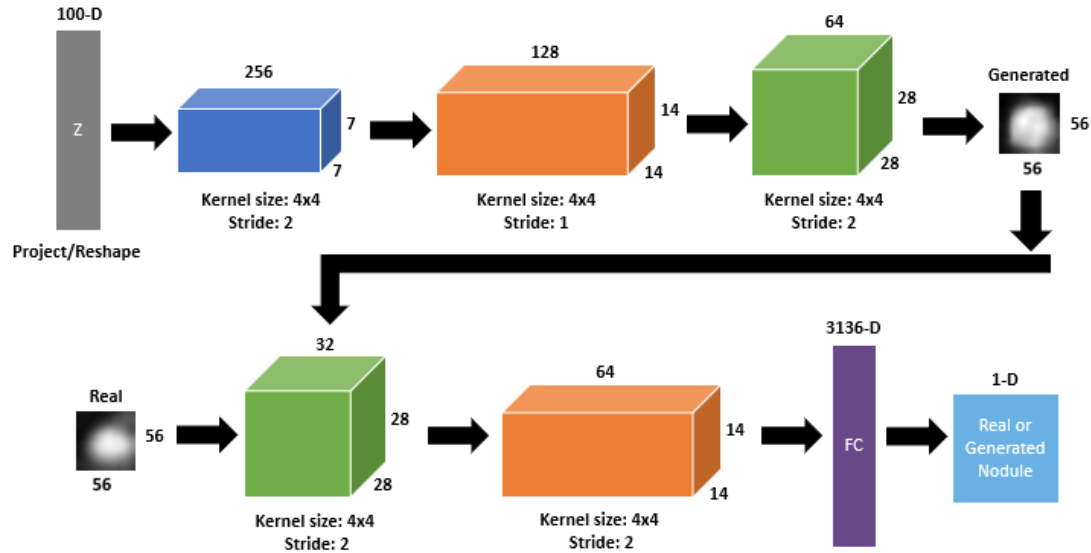
- I/P:  $Z$
- O/P: Lung Nodule image (56X56X1)

- Architecture:



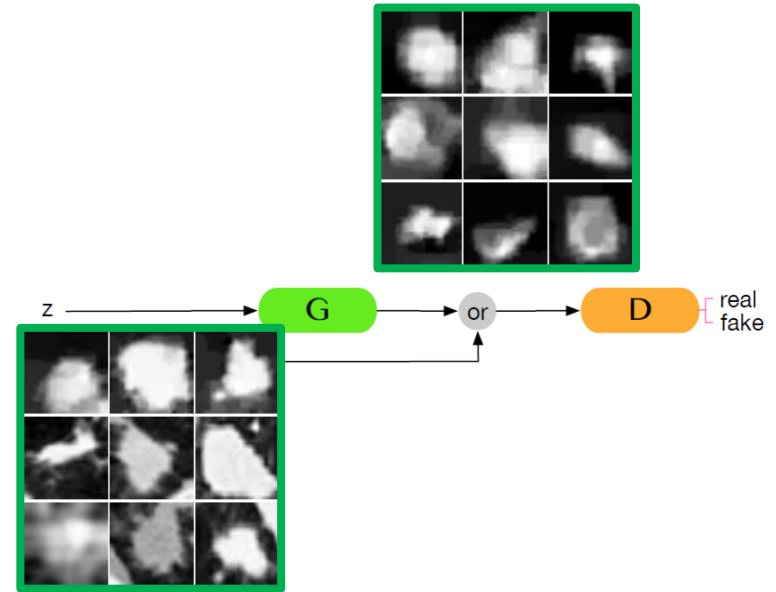
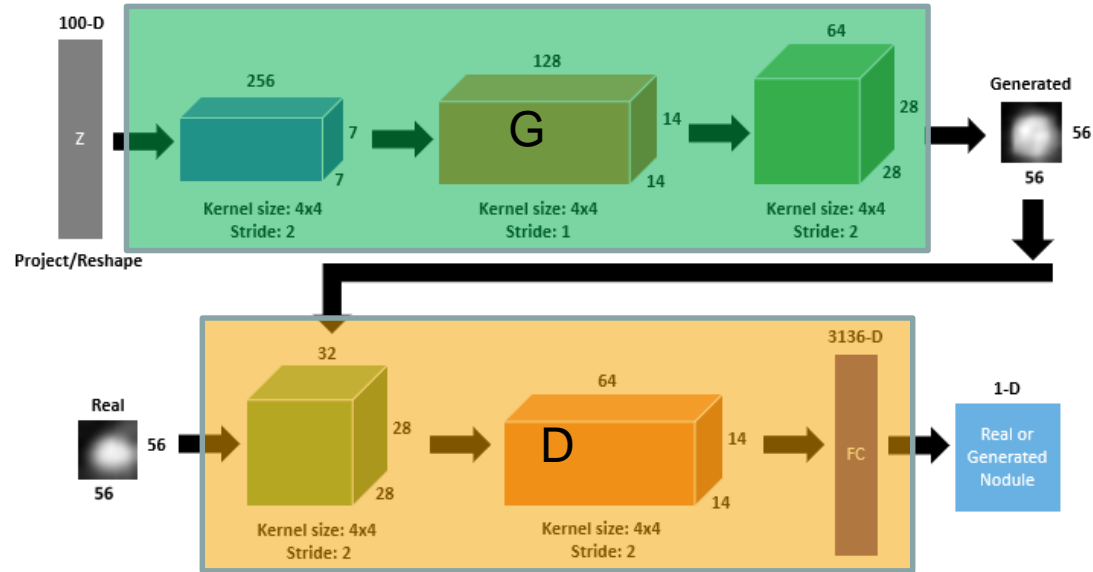
- Loss Function: Same as Goodfellow 2014

# Synthesis - Unsupervised



©Chuquicusma 2018

# Synthesis - Unsupervised



©Chuquicusma 2018

# Synthesis - Supervised

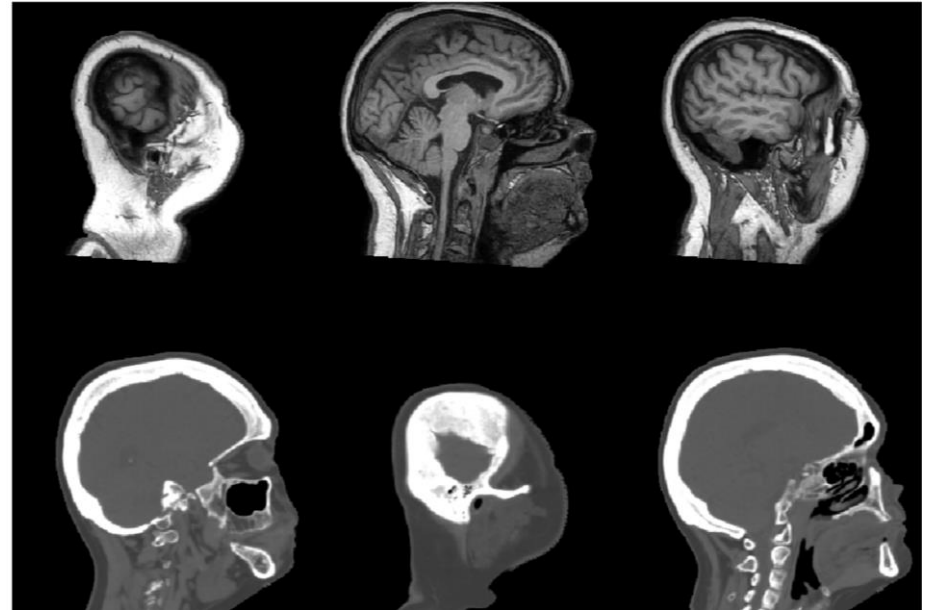
- Radiotherapy treatment planning
  - MR: Segmentation of tumor and organs
  - CT: Dose planning



# Synthesis - Supervised

- Radiotherapy treatment planning
  - MR: Segmentation of tumor and organs
  - CT: Dose planning
  
- MR-only radiotherapy treatment planning
  - Synthesize CT

Unpaired data

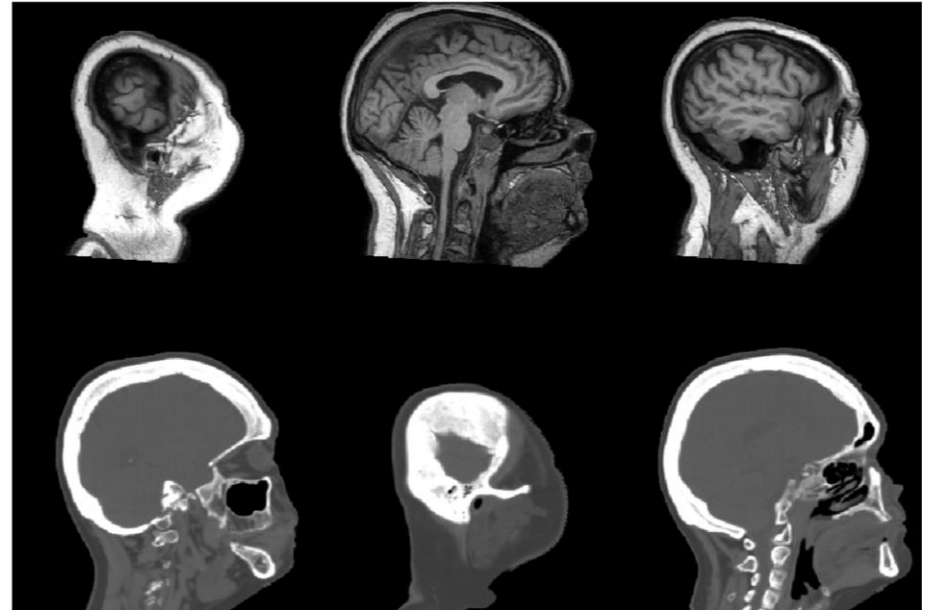


©Wolterink 2017

# Synthesis - Supervised

- Radiotherapy treatment planning
  - MR: Segmentation of tumor and organs
  - CT: Dose planning
  
- MR-only radiotherapy treatment planning
  - Synthesize CT
  
- Re-purpose Cycle-GAN

Unpaired data

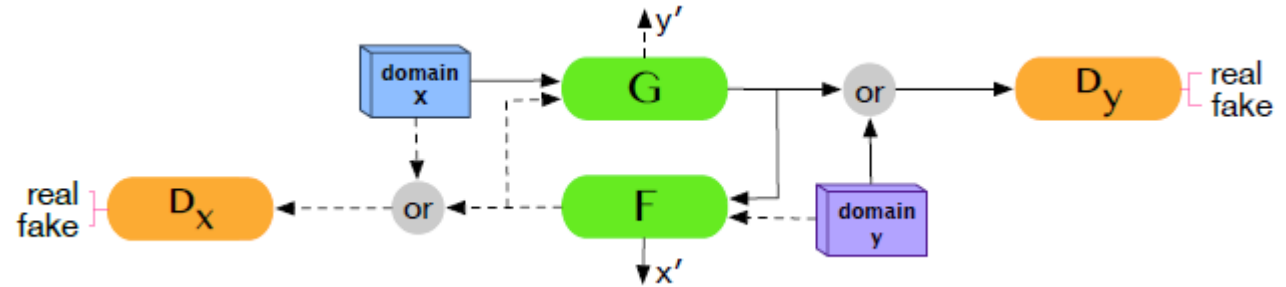


©Wolterink 2017

# Synthesis - Supervised

- I/P: Image (Domain X)
- O/P: Image (Domain Y)

- Architecture:

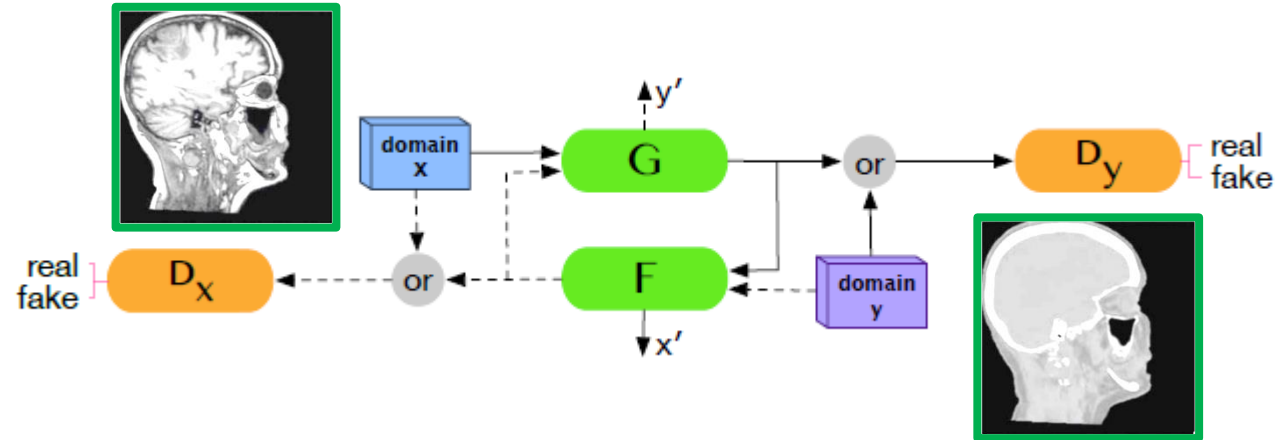


- Loss Function: Cycle Loss

# Synthesis - Supervised

- I/P: MR
- O/P: CT

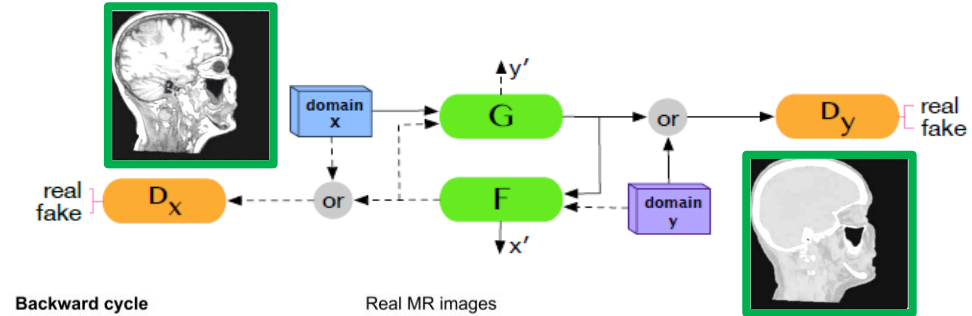
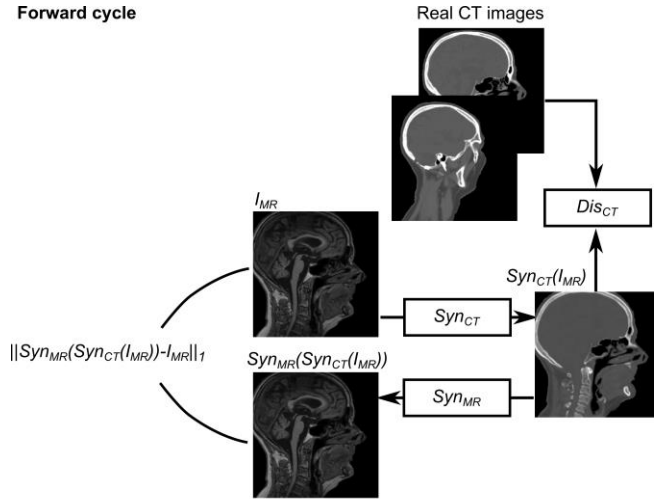
- Architecture:



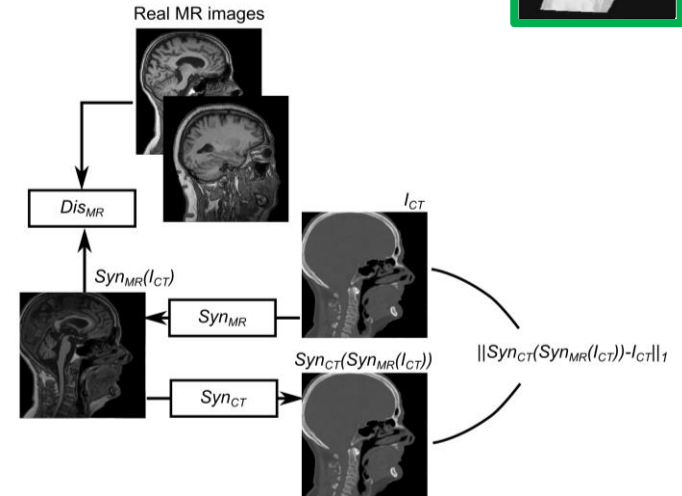
- Loss Function: Cycle Loss (Sum of L1 norms at MR and CT)

# Synthesis - Supervised

Forward cycle



Backward cycle



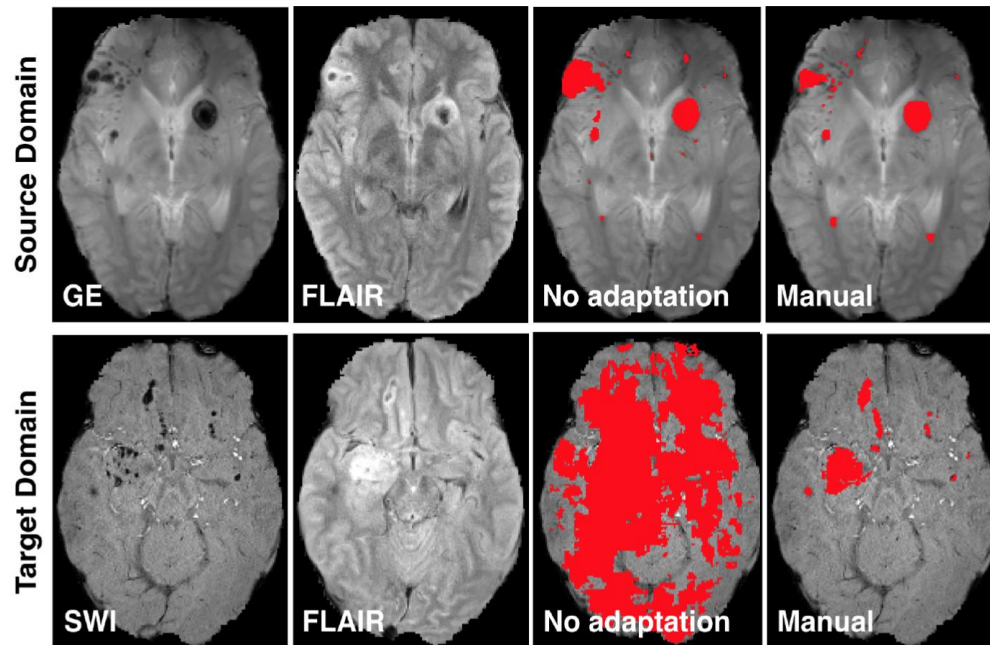
©Wolterink 2017

# Domain Adaptation - Adversarial Learning

- Deep Learning Segmentation
  - Performs well in same domain
  - Degrades with new domain

# Domain Adaptation - Adversarial Learning

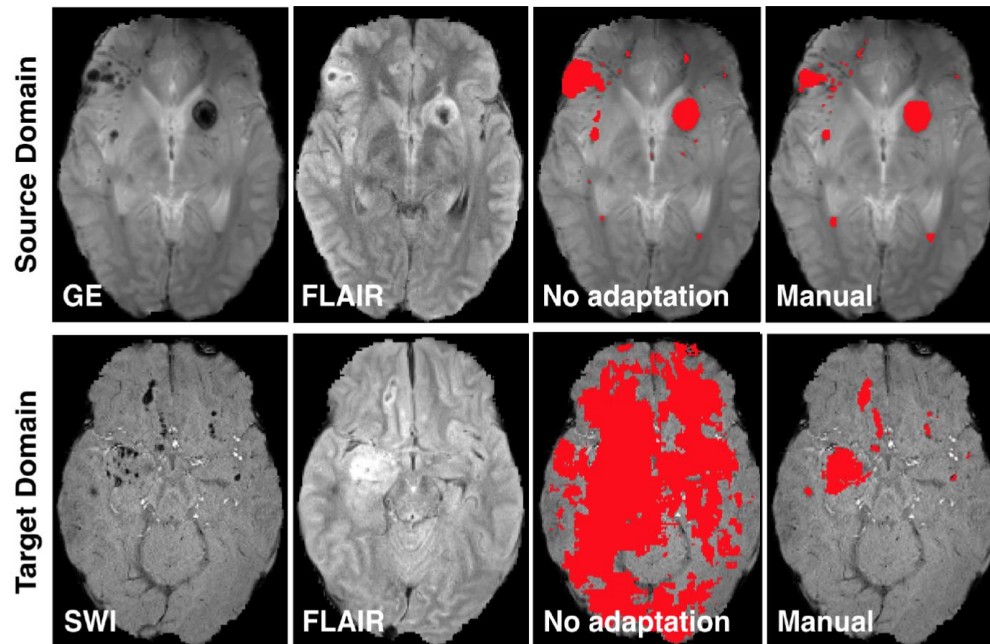
- Deep Learning Segmentation
  - Performs well in same domain
  - Degrades with new domain
- Traumatic Brain Injury
  - Segment bleeding



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# Domain Adaptation - Adversarial Learning

- Deep Learning Segmentation
  - Performs well in same domain
  - Degrades with new domain
- Traumatic Brain Injury
  - Segment bleeding
- Learn domain invariant features
  - Auxiliary task - Adversarial

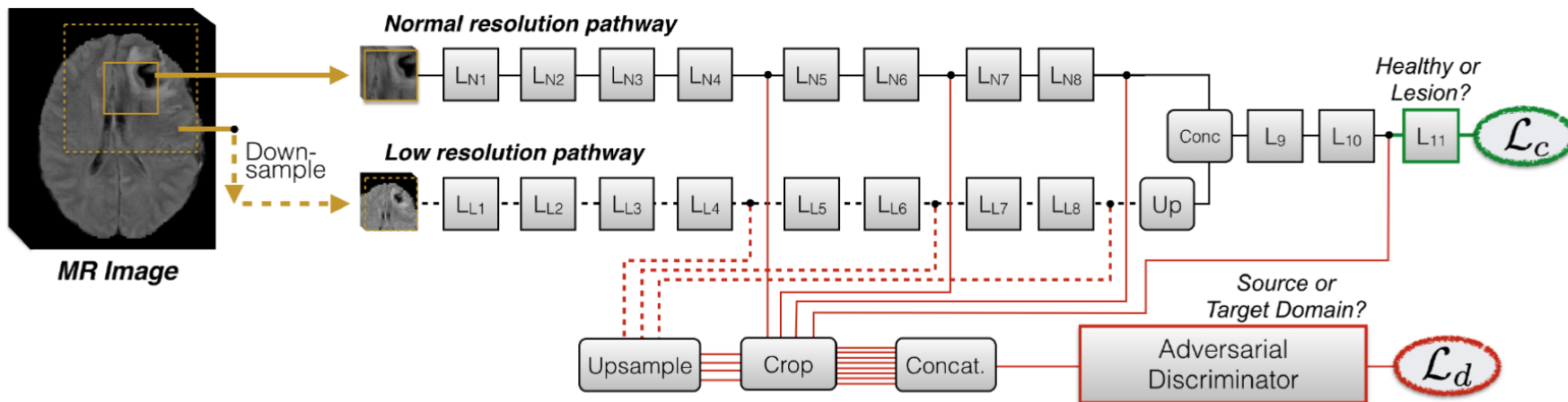


©Kamnitsas 2017



# Domain Adaptation - Adversarial Learning

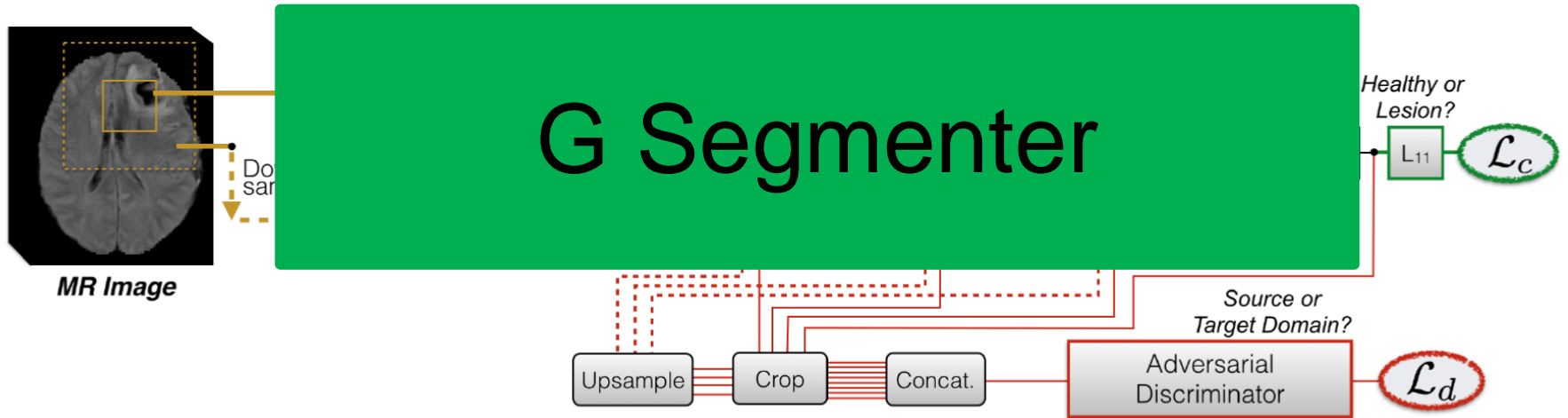
- Different MR sequences



©Kamnitsas 2017

# Domain Adaptation - Adversarial Learning

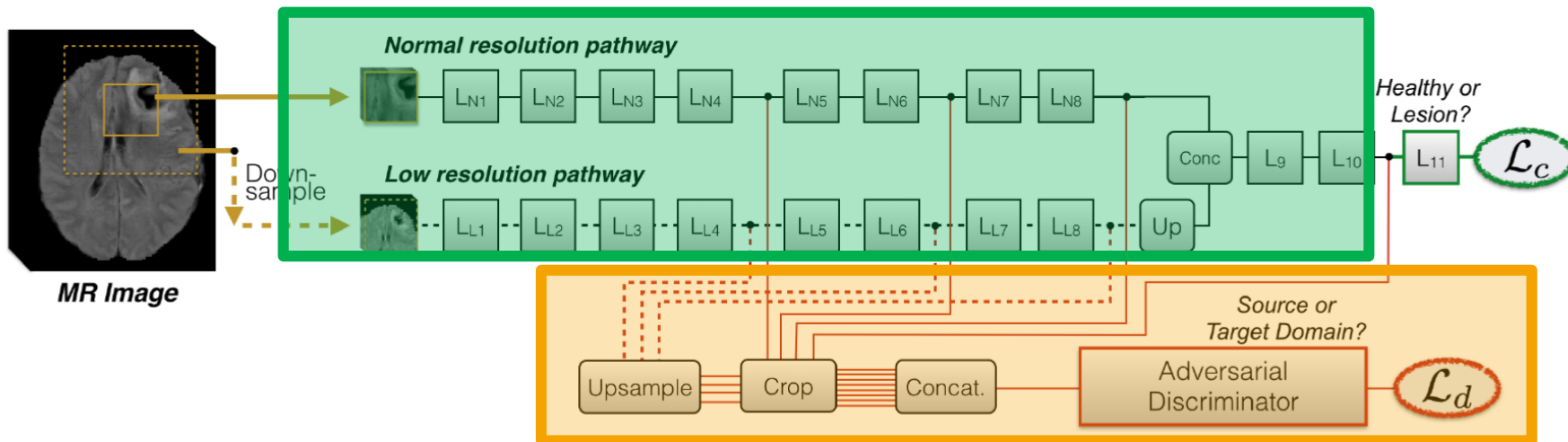
- Different MR sequences



©Kamnitsas 2017

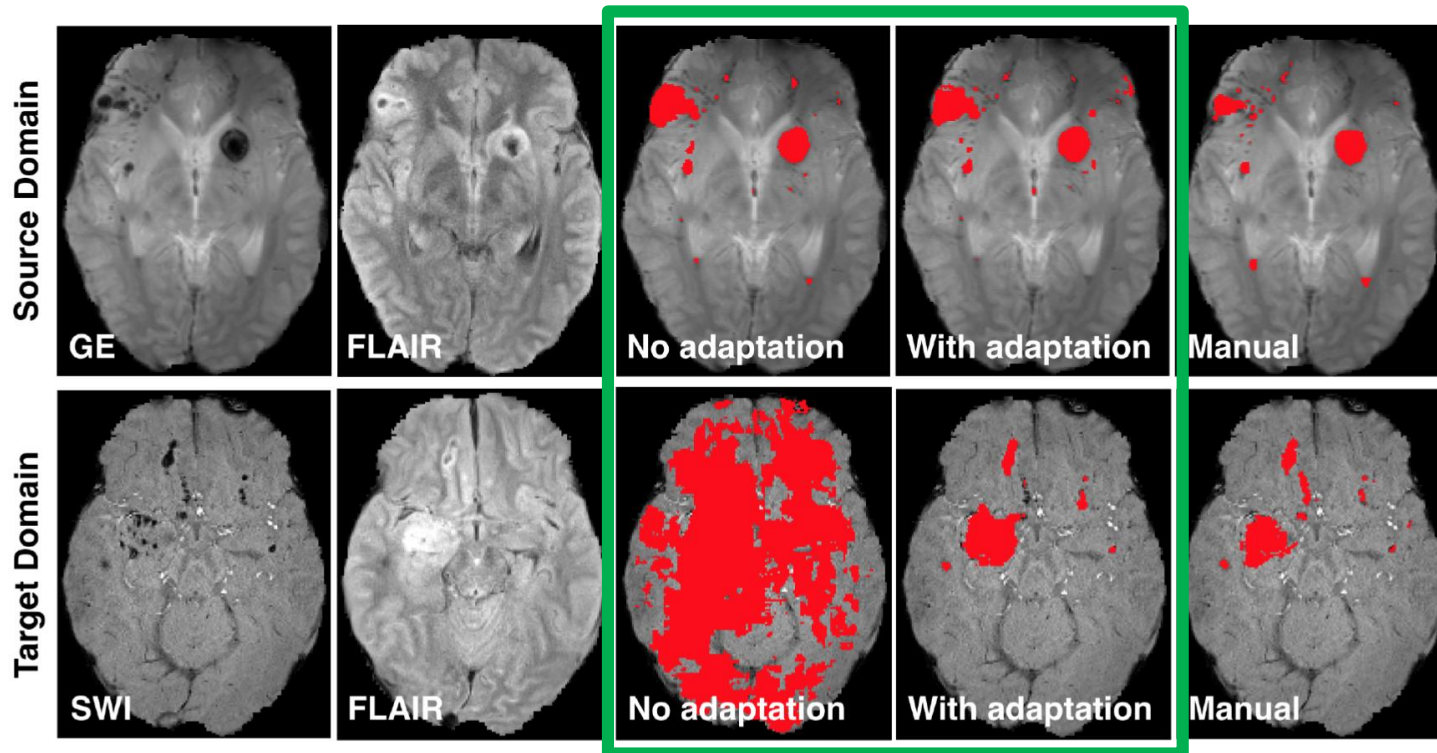
# Domain Adaptation - Adversarial Learning

- Different MR sequences



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# Domain Adaptation - Adversarial Learning



# Limitations of GAN



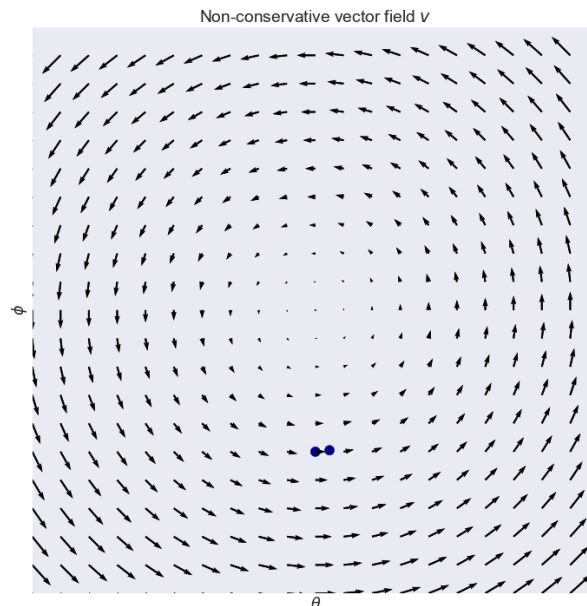
© slate.com

# Limitations of GAN

- Numerical Instability
  - Mode Collapse

# Extreme example

- Constant curl vector
  - Non-conservative
- Arises **naturally in zero-sum game**
  - Follow arrow like simultaneous gradient ascent
  - Though has equilibrium at  $(0,0)$
- Initial Solution
  - Numerics of GAN (Reading List)



© inFERENCe

# Limitations of GAN

- Numerical Instability
  - Mode Collapse
- Evaluation
  - Metrics



# Limitations of GAN - Practical

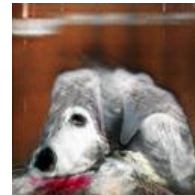
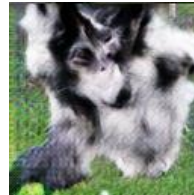


Counting

Medical Equivalent

Cell Images

# Limitations of GAN - Practical



Counting

Medical Equivalent  
Cell Images

Perspective

Medical Equivalent  
Cross domain synthesis

# Limitations of GAN - Practical



Counting

Medical Equivalent  
Cell Images



Perspective

Medical Equivalent  
Cross domain synthesis

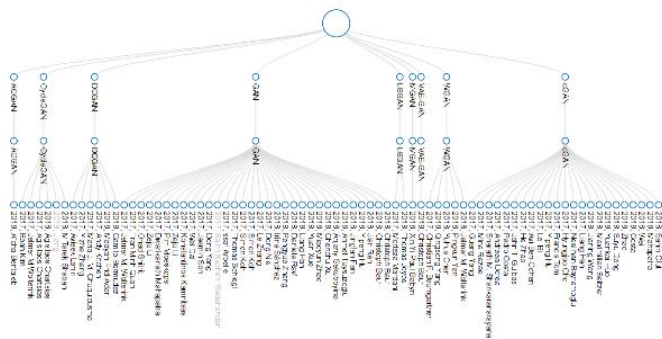


Global Structure

Medical Equivalent  
Reconstruction

## Review: GANs for Medical Image Analysis

- Engineering
  - [DC-GAN](#)
  - [C-GAN](#)
  - [CycleGAN](#)
- GAN applications
  - [Living Review](#)
  - [Wolterink 2017](#)
  - [Kamnitsas 2017](#)
  - [Chuquicusma 2018](#)



- Theory
  - [Numerics of GANs](#)
  - [Are GANs Created Equal?](#)
  - [f-GANs](#)
- Blogs
  - [Off the convex Path](#)
  - [GAN Open Problems](#)
- **MICCAI 2019 Tutorial**
  - Lecturers: Me, J. Wolterink, K. Kamnitsas

# Summary

- GANs – Unsupervised generative models with adversarial twist
- When done correctly
  - Realistic-looking images of unprecedented quality
- Medical Imaging
  - Synthesis - proxy for training data
  - Domain shift
- Issues
  - Numerical Instability
  - Evaluation metric

<https://arxiv.org/abs/1809.06222>

GANs for Medical Image Analysis

Salome Kazemina<sup>a,1</sup>, Christoph Baur<sup>b,1</sup>, Arjan Kuijper<sup>c</sup>, Bram van Ginneken<sup>d</sup>, Nassir Navab<sup>b</sup>, Shadi Albarqouni<sup>b</sup>, Anirban Mukhopadhyay<sup>a</sup>

<sup>a</sup>Department of Computer Science, TU Darmstadt, Germany

<sup>b</sup>Computer Aided Medical Procedures (CAMP), TU Munich, Germany

<sup>c</sup>Fraunhofer IGD, Darmstadt, Germany

<sup>d</sup>Radboud University Medical Center, Nijmegen, The Netherlands

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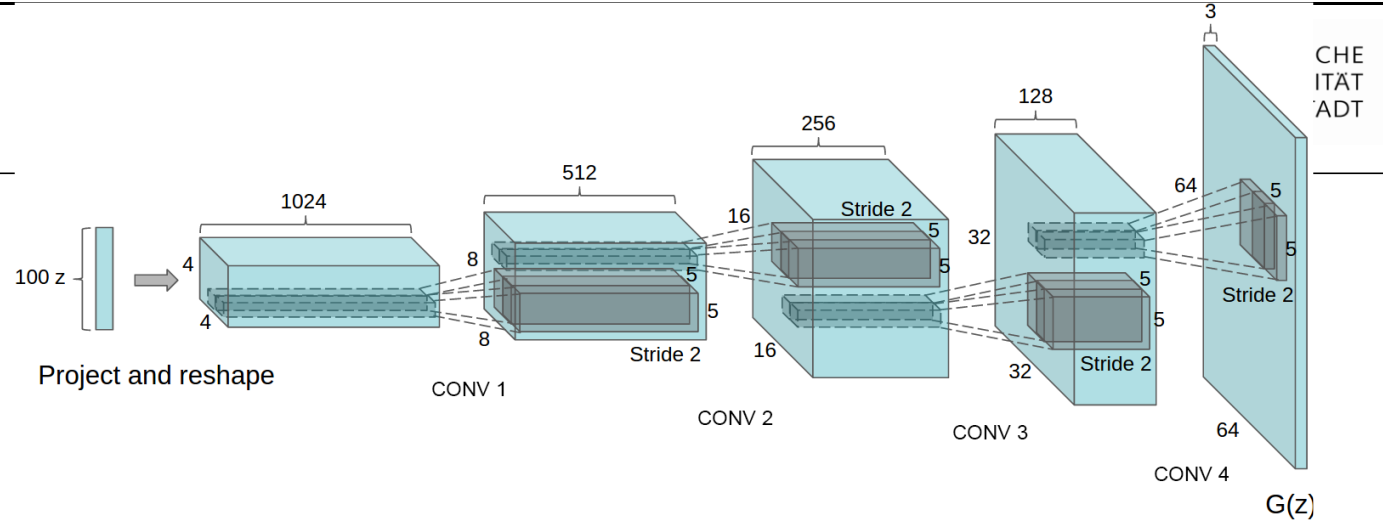
# Thank You!

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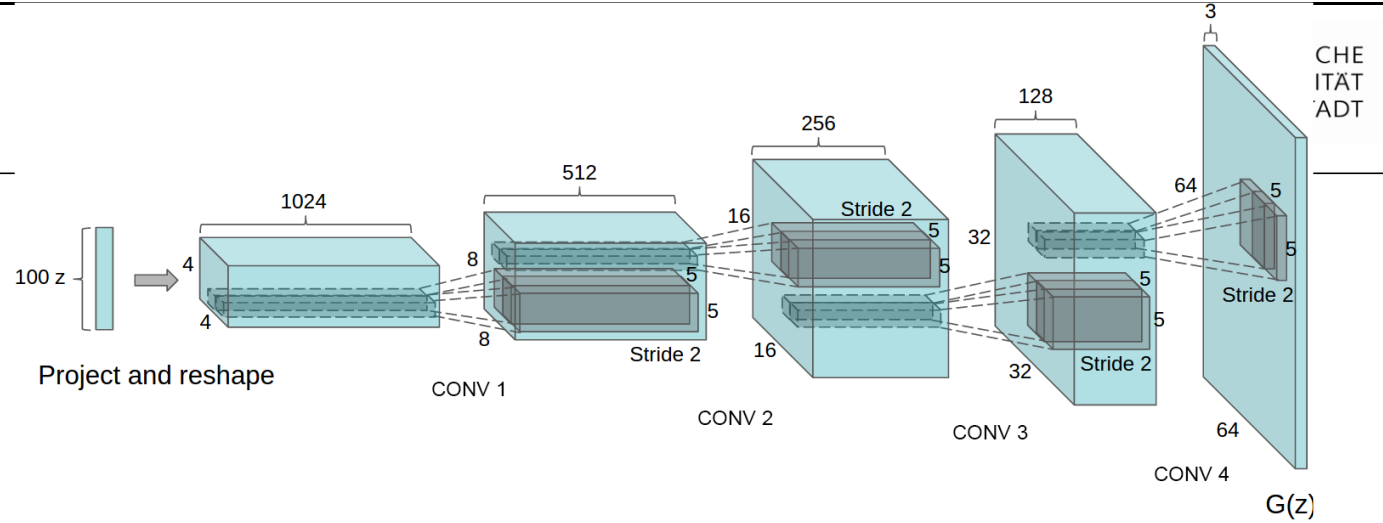
# Backup Slides

# DC-GAN





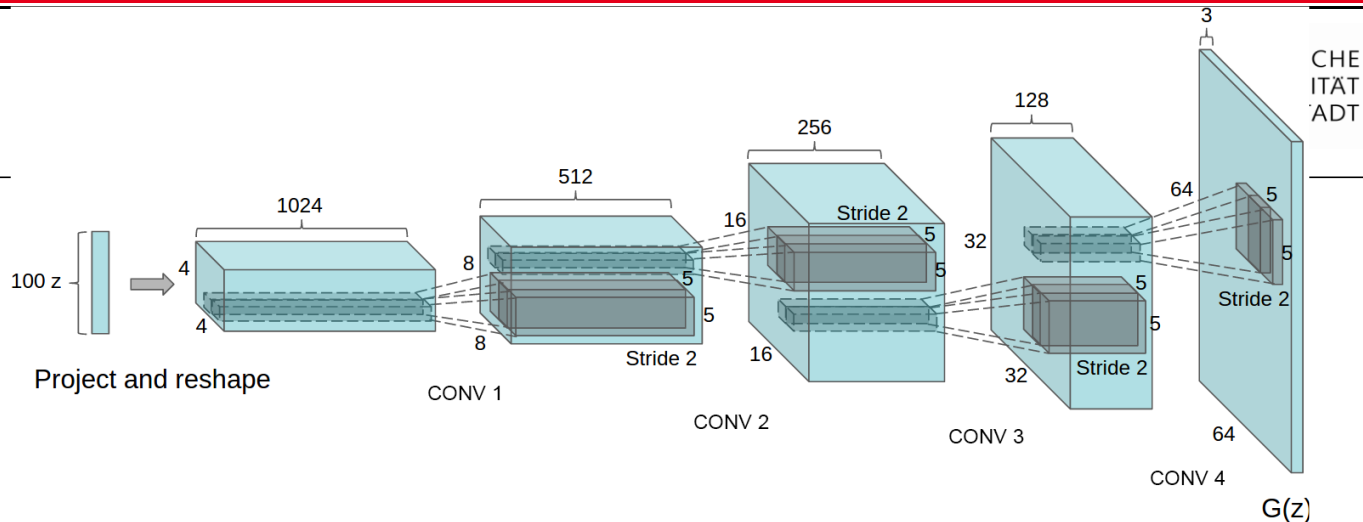
# DC-GAN



## Recipe

- Replace pooling layers with strided convolutions (discriminator) and fractional-strided convolutions (generator).

# DC-GAN



## Recipe

- Replace pooling layers with strided convolutions (discriminator) and fractional-strided convolutions (generator).
- Use batchnorm
- Use LeakyReLU in discriminator

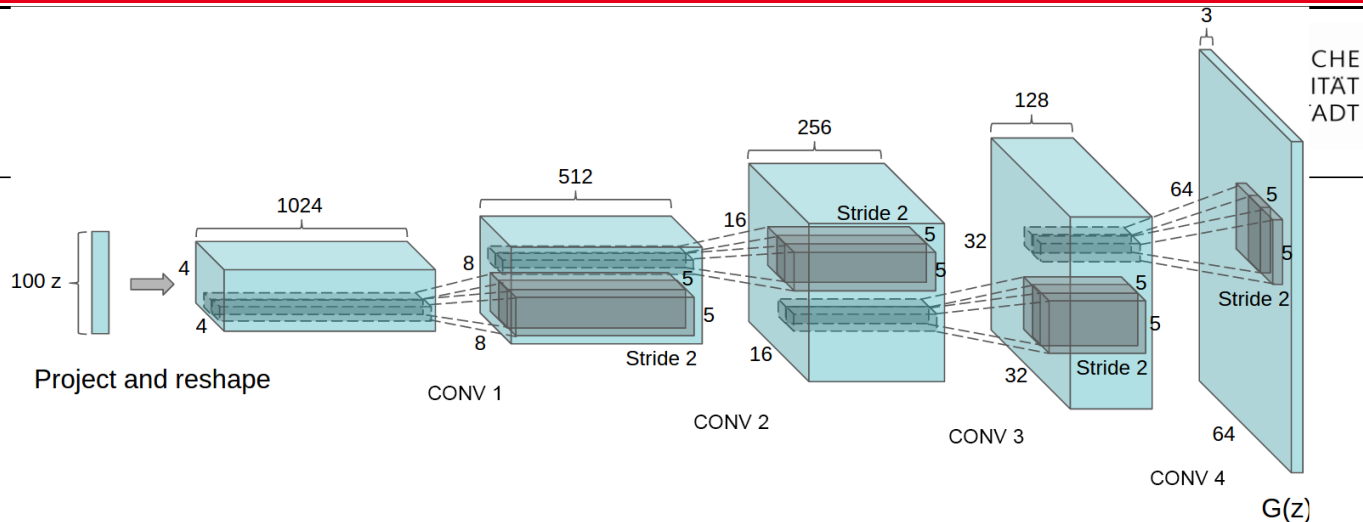
## Unconditnl. (DC-GAN)

- Data Simulation
  - Class Imbalance
  - Data Augmentation
- Prostate Lesions
- Retina Patches
- Skin Lesions

## Conditnl. (C-/ Cycle-GAN)

- CT from MR
- PET from CT/ MRI
- Stain Normalization

# DC-GAN



## Recipe

- Replace pooling layers with strided convolutions (discriminator) and fractional-strided convolutions (generator).
- Use batchnorm
- Use LeakyReLU in discriminator
- Use ReLU in generator for all layers except output, which uses Tanh.