COMP 448/548: Medical Image Analysis

Generative adversarial networks

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Generative adversarial networks (GANs)

- GANs are **generative models**
  - Informally speaking

    They create new data instances that resemble the training data
  - More formally

    They capture the joint probability P(X, Y) or just P(X)

    where X is a set of instances and Y is a set of class labels
  - **Discriminative models** are to differentiate instances of different class labels by capturing the conditional probability P(Y | X)

Generative models tackle a harder problem than discriminative models. They need to model all details in order to produce *fake* data that look like *real* data drawn from the given distribution. For discriminative models, it may be sufficient to learn salient features (not all details) that help make successful differentiation between classes.

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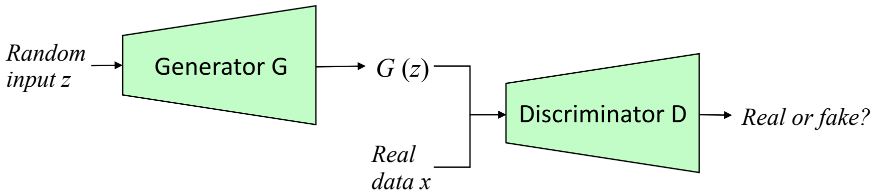
Generative adversarial networks (GANs)

- GANs offer an effective way to train such generative models
- They consist of two sub-networks
  1. **Generator G** tries to produce fake data that is as similar to the real data as possible
  2. **Discriminator D** tries to distinguish the generator's fake data from the real data



Goodfellow et al, 2014. Generative adversarial networks. https://arxiv.org/pdf/1406.2661.pdf
https://developers.google.com/machine-learning/gan

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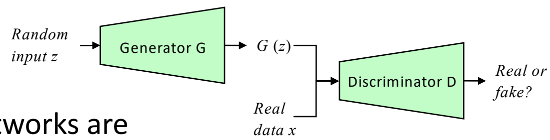
GAN training



- Weights of the generator and discriminator networks are learned together in a minimax game where
  - Generator and discriminator are the two players, each of which takes a turn (for one or more epochs) to update its own network weights

$$min_G \, max_D \, V(D,G) = \mathbb{E}_x[\log D(x)] + \mathbb{E}_z[\log(1 - D(G(z)))]$$

  - Discriminator maximizes $\log D(x) + \log(1 - D(G(z)))$
  - Generator minimizes $\log(1 - D(G(z)))$, which forces the generator to generate instances that have a low probability of being fake
  - Thus, the generator tries to fool the discriminator and the discriminator tries to keep from being fooled

This the minimax loss used in the Goodfellow's paper that introduced GANs. There are alternate loss functions as well.
Goodfellow et al, 2014. Generative adversarial networks.

$D(x)$ is the probability of a real instance being estimated as real

$D(G(z))$ is the probability of a fake instance being estimated as real

$\mathbb{E}_x$ is the expected value over all real instances

$\mathbb{E}_z$ is the expected value over all random inputs to the generator

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Conditional GANs (cGANs)

- In its basic form, a GAN takes random noise as its input and its generator transforms this noise into a meaning output
- In cGANs, the generator and discriminator are conditioned on some additional information y such as class labels, images, and edge maps

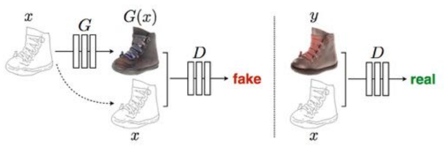
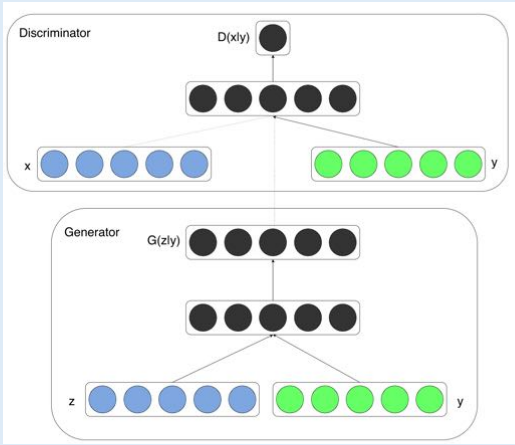


Figure 2: Training a conditional GAN to map edges→photo. The discriminator, D, learns to classify between fake (synthesized by the generator) and real {edge, photo} tuples. The generator, G, learns to fool the discriminator. Unlike an unconditional GAN, both the generator and discriminator observe the input edge map.

Isola et al., 2018. Image-to-image translation with conditional adversarial networks. https://arxiv.org/pdf/1611.07004.pdf



$$min_G \, max_D \, V(D, G) = \mathbb{E}_x[\log D(\boldsymbol{x} \mid \boldsymbol{y})] + \mathbb{E}_z[\log(1 - D(G(\boldsymbol{z} \mid \boldsymbol{y})))]$$

Mirza and Osindero, 2014. Conditional generative adversarial nets. https://arxiv.org/pdf/1411.1784.pdf

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Variants of GAN

- They may use different loss functions, may have different architectures, and/or may take different conditional inputs

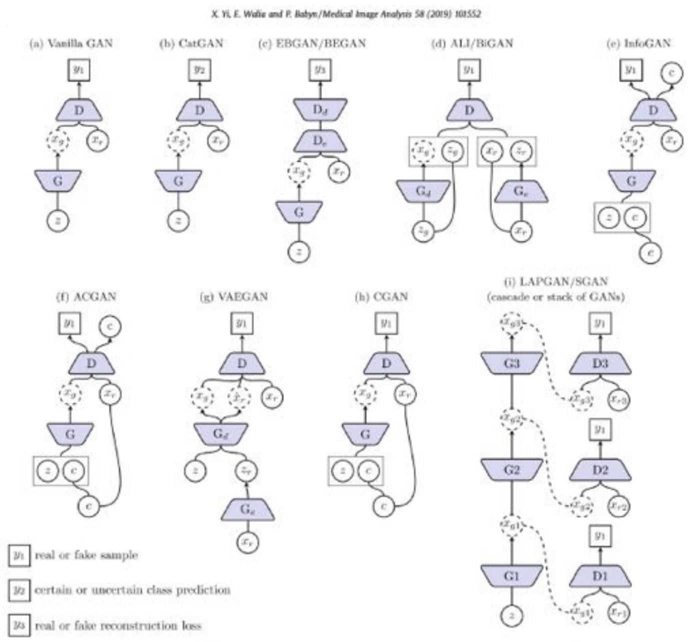

Fig. 3. A schematic view of variants of GAN. c represents the conditional vector. In CGAN and ACGAN, c is the discrete categorical code (e.g. one hot vector) that encodes class labels and in InfoGAN it can also be continuous code that encodes attributes. x_g generally refers to the generated image but can also be internal representations as in SGAN.

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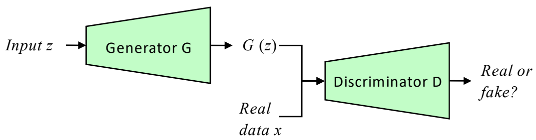
GANs for medical image analysis

Please check the following survey papers for more about the use of GANs for medical image analysis

Yi et al., Generative adversarial network in medical imaging: A review, Medical Image Analysis, 2019.
https://www.sciencedirect.com/science/article/pii/S1361841518308430

Kazeminia et al., GANs for medical image analysis, Artificial Intelligence in Medicine, 2020.
https://www.sciencedirect.com/science/article/pii/S0933365719311510

Motivation



- Unconditional image synthesis for data augmentation when limited data are available and/or there exists the class-imbalance problem
- Conditional image synthesis among cross modalities or different sequences to reduce side effects
  - To reduce exposure to radiation in CT, to avoid injection of a radioactive tracer in PET, to reduce acquisition time in MR, to reduce cost in microscopy, …

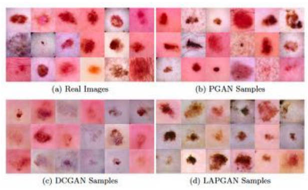


Fig. 1: Samples generated with the different models.

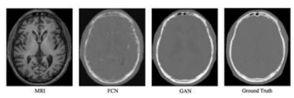
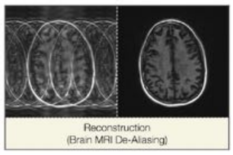
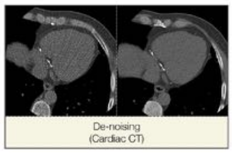


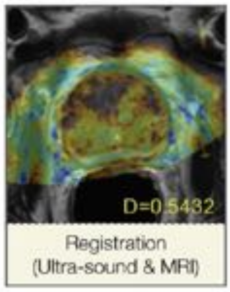
Fig. 4. Visual comparison for impact of adversarial training. FCN means without adversarial training, and GAN means with adversarial training.

Motivation

- Image-to-image translation to reduce noise and artifacts
- Super resolution imaging to recover high-resolution details from a single low-resolution image
- Registration to align images of different sequences and modalities
- Training with adversarial loss for the regularization effect in segmentation and detection
  - Spatial consistency in segmentation, a shape regulator







Example: Unconditional image synthesis

- To generate dermoscopic skin lesion images at sufficiently high resolution

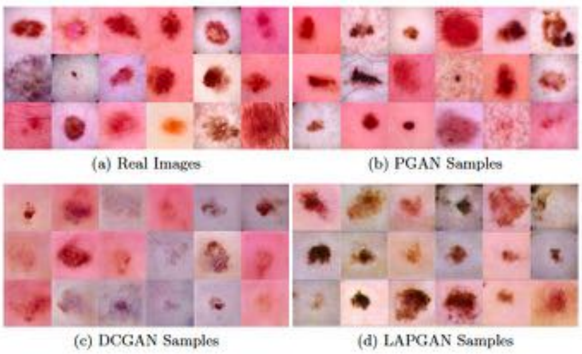


Fig. 1: Samples generated with the different models.

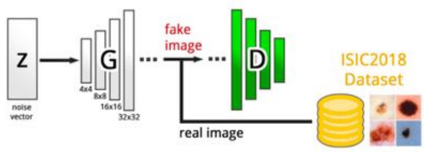


Fig. 2: An overview of the PGAN employed for skin lesion synthesis.

Visual evaluation is typically based on the realism of synthetic images. For that, numerous studies have employed either crowdsourcing or expert user studies.

Baur et al., 2018. Generating highly realistic images of skin lesions with GANs.
https://arxiv.org/pdf/1809.01410.pdf

Example: Synthetic data augmentation

- Unconditional image synthesis by a GAN to augment training data for liver lesion classification in CT images
- The generator network inputs a vector of 100 random numbers drawn from a uniform distribution and outputs a liver lesion image of size 64x64

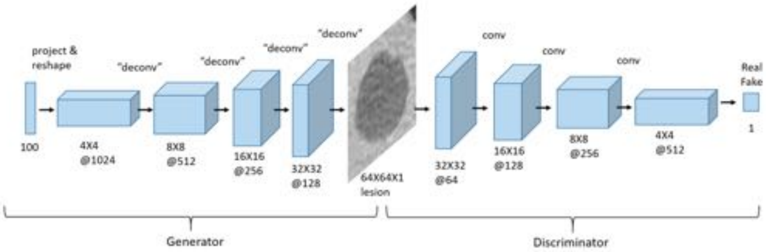


Fig. 2: Deep Convolutional GAN Architecture (generator+descriminator).

Frid-Adar et al., 2018. Synthetic data augmentation using GAN for improved liver lesion classification.
https://arxiv.org/abs/1801.02385

Example: CT synthesis from MR

- Computed tomography requires a patient to expose radiation whereas MRI does not
- Learns to synthesize CT images by training a conditional GAN on pairwise aligned MR and CT images

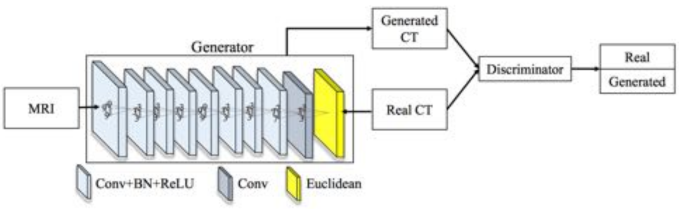


Fig. 2. Architecture used in the Generative Adversarial setting used for estimation of synthetic images.

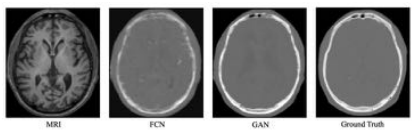


Fig. 4. Visual comparison for impact of adversarial training. FCN means without adversarial training, and GAN means with adversarial training.

Nie et al., 2017. Medical image synthesis with context-aware generative adversarial networks.
https://arxiv.org/pdf/1612.05362.pdf

Example: CT synthesis from MR

- It does not require a training set containing pairs of spatially aligned MR and CT images of the same patients
- Uses a CycleGAN to synthesize CT images from MR images

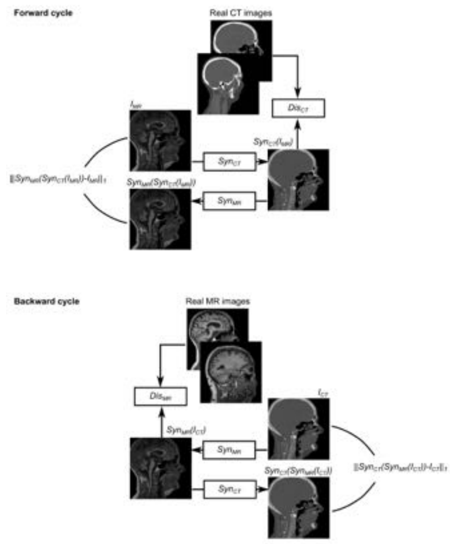


Fig. 3: The CycleGAN model consists of a forward cycle and a backward cycle. In the forward cycle, a synthesis network Syn_{CT} is trained to translate an input MR image I_{MR} into a CT image, network Syn_{MR} is trained to translate the resulting CT image back into an MR image that approximates the original MR image, and Dis_{CT} discriminates between real and synthesized CT images. In the backward cycle, Syn_{MR} synthesizes MR images from input CT images, Syn_{CT} reconstructs the input CT image from the synthesized image, and Dis_{MR} discriminates between real and synthesized MR images.

Wolterink et al., 2017. Deep MR to CT synthesis using unpaired data.
https://arxiv.org/pdf/1708.01155.pdf

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Example: Microscopy

- Transfers images of phase contrast (PC) and differential interference contrast (DIC) microscopies, which are commonly used to monitor live cells
- Uses a conditional GAN with one generator and two discriminators
  - Generator inputs an image from the source modality, an additional cell mask, and random noise
  - Discriminators differentiate between real and fake pairs of images

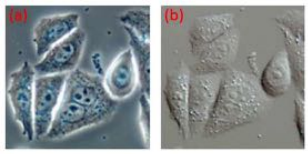
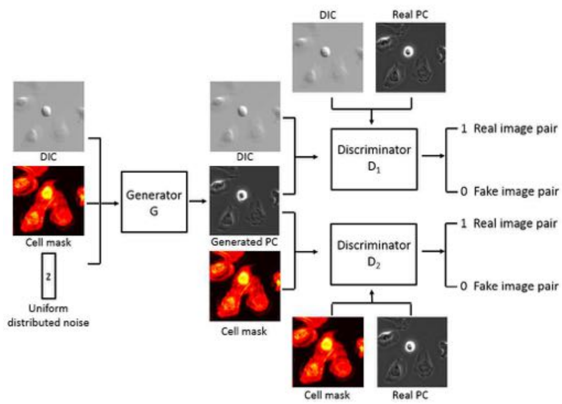


Figure 1. Different microscopy image modalities. (a): Phase Contrast microscopy image. (b): Differential interference contrast microscopy image.



Han and Yin, 2017. Transferring microscopy image modalities with conditional generative adversarial networks.
https://openaccess.thecvf.com/content_cvpr_2017_workshops/w8/papers/Han_Transferring_Microscopy_Image_CVPR_2017_paper.pdf

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Example: Low-dose CT denoising

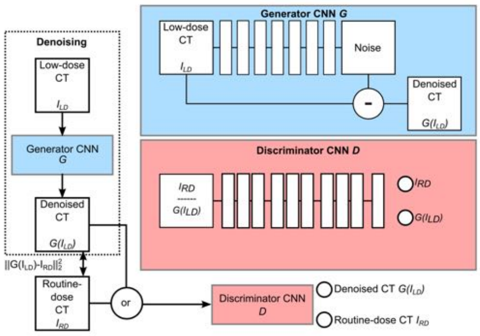
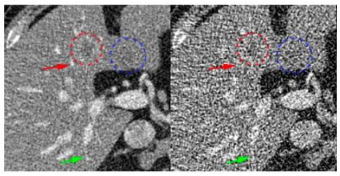


Fig. 1. Overview of the proposed pipeline for noise reduction in low-dose CT. The generative adversarial network consists of two components: a generator CNN and a discriminator CNN. The generator uses regression to determine the routine-dose HU value at every voxel in a low-dose CT. It does this through a skip connection which subtracts an estimated noise image from the input low-dose image. The discriminator tries to distinguish reduced noise CT images from real routine-dose images.

- To learn the appearance of routine-dose CT images from low-dose CT images
- It does not require spatially aligned pairs of low-dose and routine-dose images



(a) Full Dose FBP (b) Quarter Dose FBP

Yang et al., 2018. Low-dose CT image denoising using a generative adversarial network with Wasserstein distance and perceptual loss. https://arxiv.org/pdf/1708.00961.pdf

Wolterink et al., 2017. Generative adversarial networks for noise reduction in low-dose CT. https://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=7934380&tag=1

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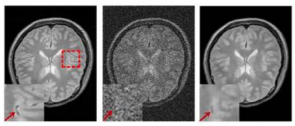
Example: Denoising 3D MR images



Noise-free Noisy Result

- U-Net based generator with residual connections
  - Minimizes MSE loss function, perceptual loss (distances in the feature space extracted by a pretrained VGG network), and adversarial loss

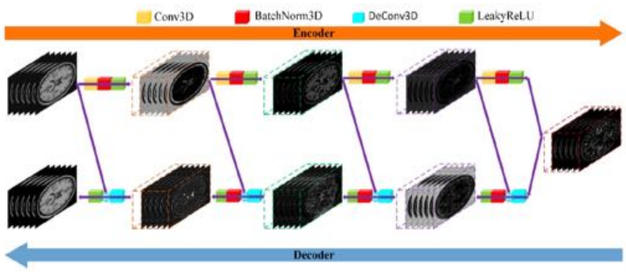


Fig. 2. The architecture of the generator network G.

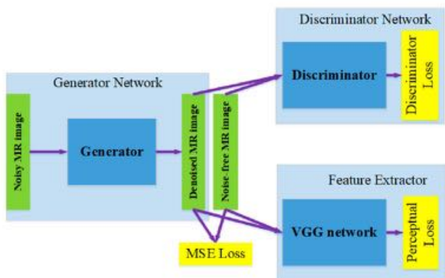


Fig. 1. Overall architecture of our proposed RED-WGAN network.

Ran et al., 2017. Denoising of 3D magnetic resonance images using a residual encoder-decoder Wasserstein generative adversarial network. https://www.sciencedirect.com/science/article/pii/S1361841518306534

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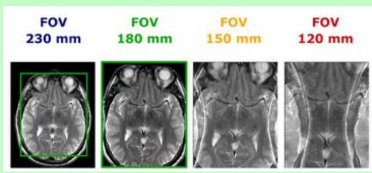
Example: MRI de-aliasing

- U-Net based generator with a refinement connection to reduce aliasing artifacts
  - Minimizes pixel-wise image domain MSE loss, frequency domain MSE loss, perceptual loss, and adversarial loss



Aliasing is an effect that makes different signals indistinguishable when sampled. Aliasing on MRI (wrap-around artifact) occurs when the field of view (FOV) is smaller than the body part being imaged.

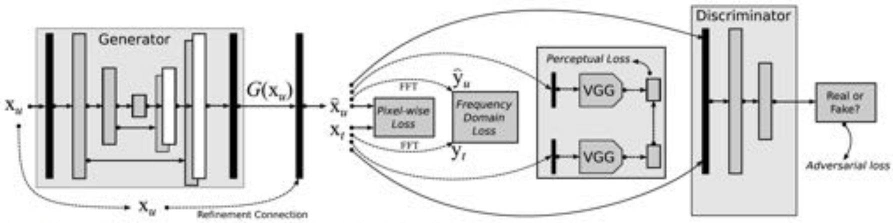
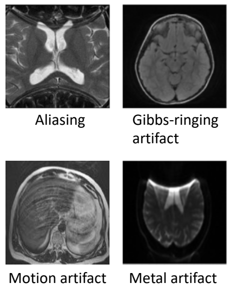


Fig. 1. Schema for our proposed conditional GAN-based de-aliasing for fast CS-MRI (DAGAN).



Yang et al., 2018. DAGAN: Deep de-aliasing generative adversarial networks for fast compressed sensing MRI reconstruction. https://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=8233175

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Example: Stain normalization

- To address the problem of stain differences in digital histopathology slides of different institutions
- Stain-style transfer using a conditional GAN that inputs the gray-scale representation
- Train the generator to minimize feature-preserving and reconstruction losses in addition to the adversarial loss

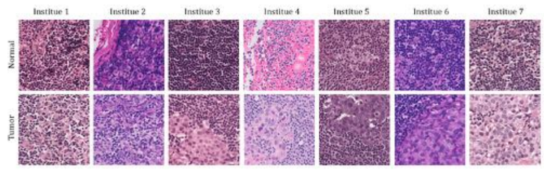

Figure 1: Samples of tissue tiles from different institutes in CAMELYON16cam (2016), 17cam (2017) dataset. The first row shows normal samples, and the second row shows tumor samples. Samples of institute 1, 2 are included cam (2016), the others are included cam (2017) dataset.

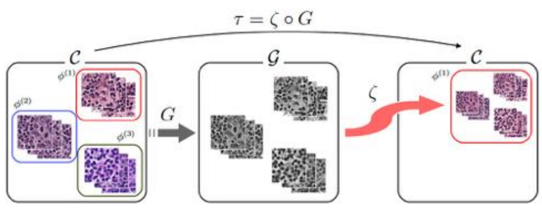

Figure 2: Overview of the stain-style transfer network. The network τ is composed of two transformations: Gray-normalization G and style-generator ζ. G standardizes each stain-style of color images from different institutes and ζ colorizes gray images following the stain-style of certain institute.

Cho et al., 2017. Neural stain-style transfer learning using GAN for histopathological images. https://arxiv.org/pdf/1710.08543.pdf

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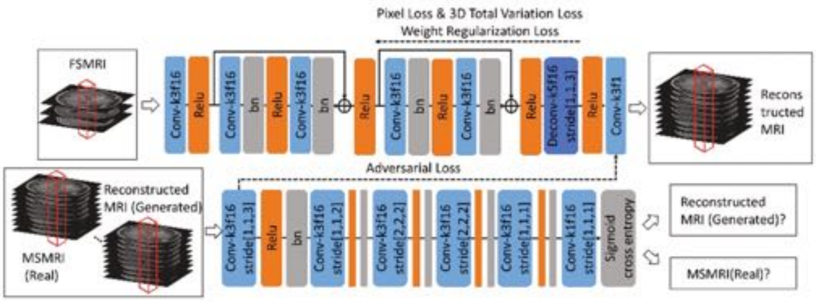
Example: Super-resolution imaging

- To reconstruct MR images with thinner slice thickness from regular thick slice images
  - Thinner slices have higher spatial resolution and provide more diagnostic information, but also have higher imaging cost both in time and expense
- Generator with residual connections
  - Minimizes MSE loss function, L2 regularization loss, 3D total variation loss (the sum of MSE between every neighbor slices of the reconstructed images), and adversarial loss



Li et al., 2017. Reconstruction of thin-slice medical images using generative adversarial network. https://link.springer.com/content/pdf/10.1007%2F978-3-319-67389-9_38.pdf

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Example: Registration

- To align MR and transrectal ultrasound (TRUS) images
- Generator network directly estimates transformation parameters between the input MR and TRUS image pairs
- Image resampler uses either the estimated or the ground truth transformation to interpolate a moving image
  - Parameters: rotation in [-25,25] degrees and translation in [-5,5] mm
- Discriminator network tells whether an input pair is aligned using the estimated or the ground truth transformation

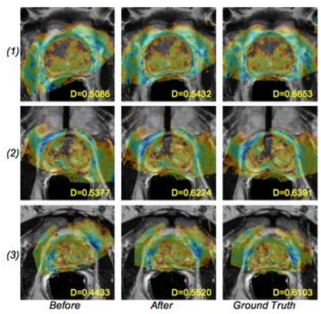
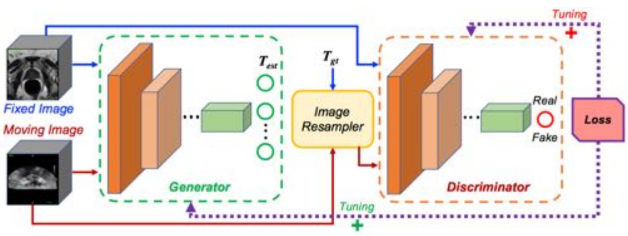


Fig. 2: Example registration results from 3 different cases. MR images are shown in gray level and corresponding TRUS images are superimposed in pseudo color.



Yan et al., 2018. Adversarial image registration with application for MR and TRUS image fusion. https://arxiv.org/pdf/1804.11024.pdf

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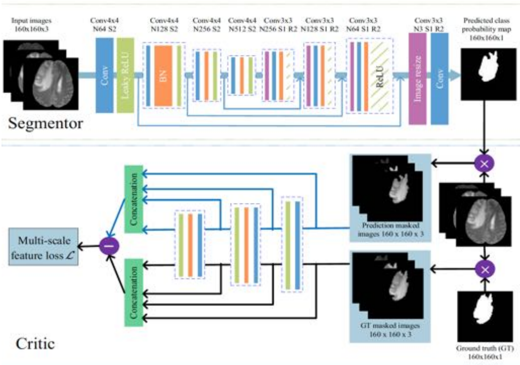
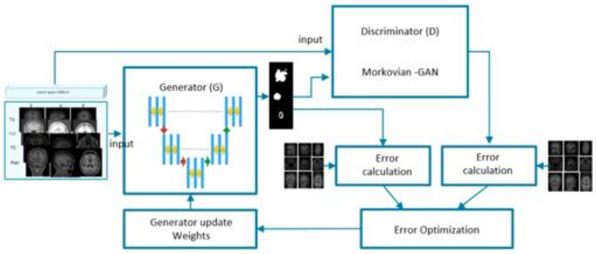
Segmentation networks with adversarial loss



Xue et al., 2018. SegAN: Adversarial network with multi-scale L1 loss for medical image segmentation.
https://link.springer.com/content/pdf/10.1007/s12021-018-9377-x.pdf



Rezaei et al., 2017. SegAN: A conditional adversarial network for semantic segmentation of brain tumor.
https://arxiv.org/pdf/1708.05227.pdf

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Thank you!

Next time:

Multi-instance learning

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