

Devising an explicit algorithm based on simple rules is difficult! L1 reg:  $\ell = err(y, \hat{y}) + \lambda \sum_{i=1}^N |w_i|$  favours few non-0 coefs, L2 favours small coefs  
under-fitting  $\rightarrow$  high bias (high training, high test error)  $\rightarrow$  add features, decrease regularization term  $\lambda$ , increase degree of polynomial)  
over-fitting  $\rightarrow$  high variance (low training, high test error)  $\rightarrow$  get more data, remove features, increase regularization term  $\lambda$ , decrease degree of polynomial)

**Challenges in Semantic Segmentation** (every pixel in an image belongs to a class)

- noise** – high-frequency pixel variability (not relevant/may obscure target)
- partial volume** – quantized version of object (pixels may contain mix of two objects and both contribute to pixel value) and object may be elevated (unclear where to begin/end object)
- intensity inhomogeneities** – varying contrast and intensity differences across the image plan
- anisotropic resolution** – (not isotropic, where voxels are cubes) causes ↓ clarity in coarse dims
- imaging artifacts** – implants may interfere with imaging modality
- limited contrasts** – different tissues may have similar physical properties and leak boundaries
- morphological variability** – variability in physiological conditions or imaging modalities

#### Pitfalls in Segmentation Evaluation

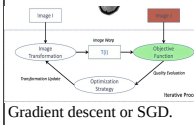
- Structure Size** – equal differences between small and big structures change spatial overlap lots
- Structure Shape** – spatial overlap metrics are unaware of complex shapes
- Spatial alignment** – HD & DSC & IoU don't capture object centre point alignment
- Holes** – Boundary-based metrics ignore overlap between structures
- Noise** – Affects HD as it is spiked by a far away FP
- Empty Label-Maps** – scores of 0 or NaN for each method with combo of empty ref. or predict.
- Resolution** – same prediction shapes at different resolutions give different results
- Over vs Under-segmentation** – for equal HD, DSC may be better for over than undersegment.

#### Segmentation Methods

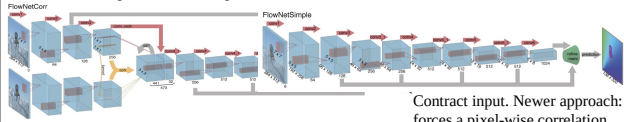
- Intensity Segmentation:** (hist)  $\times$  regions must be homogenous, leakages, threshold loc. Hard
- Region Based:** (start from seed)  $\times$  requires user points, leakages, assumed homogeneity
- Atlas Based:** (averaged templates) **Registration:** mutate multiple atlases into target and fuse labels (majority voting) (this saves pdf indicating contention between sources).  $\checkmark$  robust, accurate, automatic  $\times$  comput. expensive, poor for abnormalities, not for tumour segmentation.
- Random Forests:** different modalities of 1 image, construct a tree to classify a pixel based on rules. **Ensemble** it by averaging answer of many trees.  $\times$  no hierarchal features  $\checkmark$   $\parallel$  & accurate

- (up)pooling and max (un)pooling with stored spatial location
- Transposed Convolution:  
$$(M-1) \times S - 2P + D \times (K-1) + P_{output} + 1$$
- Convolution:  $\left\lfloor \frac{M+2P-D+(K-1)-1}{S} \right\rfloor + 1$
- Atrous spatial pyramid pooling: repeated max-pooling and striding reduces spatial resolution of the resulting feature map
- Padding during upsampling may introduce artifacts

#### Registration iterative process



**FlowNet:** tries to predict dense displacement field between two video frames.



Then upsample for p.w. displacement. Train w/ flying rendered chairs (you know Ground Truth). Next evolution of **FlowNet2.0** passes image through once, applies the translation, and passes it into the next layer for further fine-tuning. In parallel, there is detailed matching, then concat all.

**Optical Flow with Semantic Segmentation and Localized Layers:** segment 'Things', 'Planes' & 'Stuff'. Then perform flow estimation on segmented objects for a sharper answer.

**Non-rigid Image Registration Using Multi-scale 3D CNNs:** randomly deform an image, then train a model to predict your known deformation. To use this network, you need to slide this network across the image and generate for each pixel a displacement vector.

**Spatial Transformer Networks:** takes feature map (original or pre-processed) and predicts transformation and transform the image according to this transform map. There is a localisation net which trains  $\theta$  to then deform the grid.

**Unsupervised Deformable Image Registration:** Two images are fed into an NN to predict deformation. Then feed into spatial transformer, this transforms input and calculates sim. metric.

**Voxel Morph:** u-net architecture which produces a dense displacement field. Then it uses the spatial transformer to warp the image to the fixed image then minimise the loss to the network.

**Generative-based learning:** teaching the network to reconstruct an image from a corrupted version.

- Vision Transformers:** as above, non-overlapping patches learn representation for patches.
- Masked Auto-encoders are scalable vision learners:** divide the image in multiple sub-patches and randomly mask some of the patches. Feed it through the vision transformer. The encoder gets a representation f.e. patch and then fills in the blanks with a mask token you learn during training. The decoder predicts each patch (this is smaller since encoder does most of the work)
- Loss:**  $MSE = \sum (\hat{x}_i - x_i)^2$ , where  $i$  is the pixel index. Masking ratio of >75% is best.

**Joint-Embedding Prediction (i-Jepa):** a mix of both.

Here, we pass available patches onto the encoder. In  $\parallel$ , sample several other regions and pass it through the same encoder. The task here, is to predict the encoded representation (instead of the output image) instead of wasting compute reconstructing ever single pixel in the image, we are going to reconstruct the important information which there should be if the network is trained summarised. **Loss:**  $\frac{1}{N} \sum_{i=1}^N D(s_y(i), s_y(i)) = \frac{1}{N} \sum_{i=1}^M \sum_{j \in B_i} \|s_{y_j} - s_{y_i}\|_2^2$ .

**Inverse Problem:** recover original image e.g. Inpainting, De-blurring/noising, Super-resolution.

$y = Ax + n$ , **Classical Approach:** least squares:  $(D \text{ data-consistency term}) \arg \min_x D(Ax, y)$ ,  $D(Ax, y) = \frac{1}{2} \|Ax - y\|_2^2$  for which the solution is  $\hat{x} = (A^T A)^{-1} A^T y$ . **Ill-posed Problem:** slight differences to the image may yield drastically different results.  $\arg \min_x D(Ax, y) + \lambda R(x)$  with  $R(x) = \frac{1}{2} \|x\|_2^2$  ( $R$  prior knowledge on  $x$  – regularization term, with reg. Param  $\lambda$ ). Therefore  $\hat{x} = (A^T \lambda I)^{-1} A^T y$  which makes it better conditioned and noise suppression.

- Tikhonov Regularizer:  $R(x) = \|x\|_2^2$  (L-2 norm of gradient)
- Total Variation Regularization:  $R(x) = \|x\|_{TV,1} = \sum_{i=0}^N \sqrt{|x_i^{(d)}|}$  (L-1 norm of grad)
- Wavelet Regularization:  $R(x) = \|\Psi x\|_1$  (apply a sparsifying transformation and min that)
- Dictionary Learning: patches then encode each patch by a sparse combination of (e.g.) wavelet denoising and combine these to reconstruct the original image

Instead of choosing  $R$  a-priori based on a simple model of the image, learn  $R$  from training data

**Model Agnostic:** (don't use anything about the forward transformation) **Partly-model agnostic:** upsample with a classical algorithm like linear interpolation which estimates the known transformation then train a model to remove difference between upsample on original.

**Decoupled Approach: Deep-Proximal Gradient:** estimate with Gradient Descent: set  $\hat{x}^{(1)}$  and stepsize  $\eta$ , compute  $\hat{x}^k = \hat{x}^{(k)} + \eta A^T (y - A \hat{x}^{(k)})$ ,  $\hat{x}^{(k+1)} = \arg \min_x \|x^k - x\|_2^2 + \eta \lambda R(x)$  we can replace the second term with a NN with a GAN: which returns 0 for realistic images (on the manifold) with generator and discriminator. Assume you know  $A$

$\min_G \max_D V(G, D) = \mathbb{E}_{x \sim p_{data}(x)} [\log D(x)] + \mathbb{E}_{x \sim p_G(x)} [\log(1 - D(G(x)))]$ . We then redefine

the problem w.r.t  $G$  and  $D$ :  $R(x) = \begin{cases} 0 & x \in \text{range}(G) \\ \infty & \text{otherwise} \end{cases}$ . Here, we restrict the space to the image manifold so  $\hat{x} = \arg \min_{x \in \text{range}(G)} \|y - Ax\|_2^2 = G(z)$  and  $\hat{z} = \arg \min_z \|y - AG(z)\|_2^2$

**Unrolled Optimization:** assuming  $R(x)$  is differentiable: the first term is GD for data consistency, & second is GD for regularization.  $\hat{x}^{(k+1)} = \hat{x}^{(k)} + \eta A^T (y - A \hat{x}^{(k)}) - \eta \nabla R(\hat{x}^{(k)})$ . Then replace GD for reg. with an NN.

**Image Reconstruction:** x-ray scan captures information by measuring the x-ray energy on the opposite side of emitter. The rotated scanner produces a Sinogram (x to go from CT  $\rightarrow$  Sinogram (forward) but inverse is not). (Same goes for K-Space  $\rightarrow$  MRI). The problem becomes "Recover an image  $x \in \mathbb{K}^N$  from a set of observations  $y \in \mathbb{K}^N$  which are corrupted by a noise  $n \in \mathbb{K}^N$ ." **Reconstruction approach: Image domain:** use as much physics knowledge as possible (forier transformation) and use nn to remove artifacts, or **k-space domain** for nn to create new frequency space then inverse forier transform to upsample.

**Linear Transformations**

translation vectors      direction vectors      scaling matrix

$$\begin{pmatrix} X \\ Y \\ 1 \end{pmatrix} = \begin{bmatrix} 1 & 0 & t_x \\ 0 & 1 & t_y \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} \cos \theta & \sin \theta & 0 \\ -\sin \theta & \cos \theta & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} s_x & 0 & 0 \\ 0 & s_y & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{pmatrix} x \\ y \\ 1 \end{pmatrix}$$

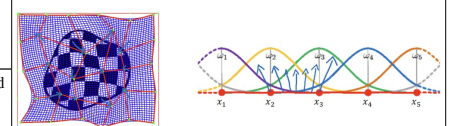
If there is more than one world, then:

$$\begin{pmatrix} x_A \\ y_A \end{pmatrix} = T_{W_I}^{-1} T_{B \rightarrow A} T_{W_B} \begin{pmatrix} x_B \\ y_B \end{pmatrix}$$

In 3D, there are identity (0 dof) rigid (translation and rotation, 3+3 dof), similar (scaling, 3+3+1 dof), affine (shear 12). In affine, if two lines are  $\parallel$ , after affine T, its still true.

$$\text{shearing} = \begin{bmatrix} \cos \omega & \sin \omega & 0 \\ -\sin \omega & \cos \omega & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

#### Non-linear Transformations



Embed image onto grid, prescribe motion at each grid point (red) and underlying blue grid is as a result of linear interpolation.

**Medical Applications:** Cardiac Motion and Respiration Motion tracking, Multi-modal Image Fusion, Pre- and Post-op comparison

**Intra-Subject Registration:** create an atlas and transform.

**Objective:**  $C(T) = D(I \circ T, J)$  (Transformation, Dissimilarity measure, (J) Fixed image,  $(I \circ T)$  Moving Image  
**Optimization:**  $T = \arg \min_T C(T)$

**Mono-modal Registration:** Image intensities are related by a (simple) function. Assumption: the identity relationship between intensity distributions. Not good when brightness changes and subtraction is no longer the best metric.

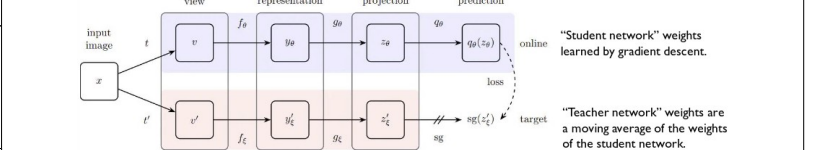
- Sum of squared differences:  $D_{SSD}(I \circ T, J) = \frac{1}{N} \sum_{i=1}^N (I(T(x_i)) - J(x_i))^2$
- Sum of absolute differences:  $D_{SAD}(I \circ T, J) = \frac{1}{N} \sum_{i=1}^N |I(T(x_i)) - J(x_i)|$

$$\text{Correlation Coefficient: } D_{CC}(I \circ T, J) = - \frac{\frac{1}{N} \sum_{i=1}^N (I(T(x_i)) - \mu_I)(J(x_i) - \mu_J)}{\sqrt{\frac{1}{N} \sum_{i=1}^N (I(T(x_i)) - \mu_I)^2} \sqrt{\frac{1}{N} \sum_{i=1}^N (J(x_i) - \mu_J)^2}}$$

**Multi-modal Registration:** Image intensities are related by a complex function or statistical relationship. Measures "When are these two images the most statistically aligned". To avoid local minimas: increase dof, or gaussian smoothing. May require linear interpolation

- Intensity Histograms: plot intensities of both images on x and y, discretize histogram with bins. A Registered image will have more clustered regions (identity will be line  $x = y$ )
  - $p(i, j) = \frac{h(i, j)}{N}$  at a point, in one image i and other image j counts in the histogram.  $p(i) = \sum_j p(i, j)$  sim for  $p(j)$
  - Shannon Entropy:  $H(I) = - \sum_j p(i) \log p(i)$  low value if every pixel has the same value, or high if randomness
  - Joint Entropy:  $H(I, J) = - \sum_{i,j} p(i, j) \log p(i, j)$  measures how clustered a space is, and minimising that entropy is a good criterium
  - Mutual Information:  $MI(I, J) = H(I) + H(J) - H(I, J)$  describes how well one image can be explained by another image.  $MI(I, J) = \sum_{i,j} p(i, j) \log \frac{p(i, j)}{p(i)p(j)}$  with dissimilarity:  $D_{MI}(I \circ T, J) = -MI(I \circ T, J)$
  - Normalized Mutual Information:  $NMI(I, J) = \frac{H(I) + H(J)}{H(I, J)}$  with dissimilarity similar to above

**Contrastive-based learning (SIMCLR):** teaching the network to recognise meaningful pairs of images. Idea: create multiple versions of the same image and teach the network to recognise the correct pair. An encoder outputs hidden state  $h$  and the small MLP gets a smaller representation (in high dimensional space, comparing similarities is harder, and not necessarily robust). **Augmentation Pipeline:** Needs to reflect what information the model should disregard and what it should focus on. Needs to be difficult, otherwise, trivial features may be learnt. **Normalised temperature contrastive loss:**  $\text{sim}(\vec{u}, \vec{v}) = \frac{\vec{u}^T \vec{v}}{\|\vec{u}\| \|\vec{v}\|}$  with **Loss**  $\ell_{i,j} = - \log \frac{\exp(\text{sim}(\vec{x}_i, \vec{x}_j)/\tau)}{\sum_{k=1}^N \mathbb{1}_{k \neq i} \exp(\text{sim}(\vec{x}_i, \vec{x}_k)/\tau)}$   $\tau$  temperature controls how much to penalise hard negatives (lower temp penalises more)  $\mathbb{1}_{k \neq i}$  evaluates to 1 iff  $k \neq i$ . **Triplet Loss:** where  $x$  is the image,  $x^+$  is the positive image, and  $x^-$  is a random negative  $\mathcal{L}_{Triplet}(\vec{x}, \vec{x}^+, \vec{x}^-) = \sum_{x \in \mathcal{X}} \max(0, \|f(x) - f(x^+)\|_2^2 - \|f(x) - f(x^-)\|_2^2 + \epsilon)$ . You evaluate the model with **Fine-tuning** (all params) or **linear probing** (freeze encoder). Batch size should be high (4096). Since large batch size is expensive: **BYOL**: (more robust to small batch-size) removes the need to use negative pairs in the loss function, instead optimize similarity on positive pairs. Needs new architecture (trivial solution where all inputs go to 0)



Prediction head in the student asserts "output of the student after the pred = output of target network without the pred." It matches the output of online and target. **DINO** uses visual transformers as encoders and use the attention to visualise the attention map of the network when they create the self-supervised encoding; creates self-supervised segmentation maps.

**Post-upsampling super-resolution:** directly upsampled LR image into SR; requires learnable upsampling layers.  $\checkmark$  fast and low mem. \* network has to learn entire upsampling pipeline, network typically limited to a specific up-sampling factor.

**Pre-upsampling super-resolution:** use traditional upsampling (linear interp.), refine upsampled using a CNN.  $\checkmark$  upsampling operation is performed using interpolation, the correct smaller details, can be applied to a range of upscaling factors and image sizes \* operates on SR image, thus requires more comp & mem. **Progressive upsampling super-resolution:** use a cascade of CNNs to progressively reconstruct higher-resolution images, at each stage, upsample to higher resolution.  $\checkmark$  decomposes task into simpler ones, reasonable efficiency \* difficult to train deep models. **Iterative up-and-down sampling super-resolution:** alternate between upsampling and downsampling operations, mutually connected up-and-down-sampling stages  $\checkmark$  has shown superior performance as it allows error feedback, easier training of deep networks.

**Pixel-wise loss function** (either L1 (non diff) or L2):  $\mathcal{L} = \frac{1}{N} \sum_{i=1}^N |x_i - \hat{x}_i|$  or **Huber loss function**:  $\mathcal{L} = \frac{1}{N} \sum_{i=1}^N \delta(x_i - \hat{x}_i)$ ,  $\delta(a) = \begin{cases} 0.5a^2 & \text{for } |a| \leq 1 \\ |a| - 0.5 & \text{otherwise} \end{cases}$ . However, compute the **Perceptual loss**: loss on output  $\theta$  of an

intermediate layer l of a pre-trained network since the network has been pre-trained on a task to classify objects e.g. then activations describe the image in more perceptual terms.  $L = \frac{1}{M} \sum_{i=1}^M (g_i^{(l)}(x) - g_i^{(l)}(\hat{x}))^2$

**Total Variation:**  $L = \frac{1}{N} \sum_{i=1}^N \sqrt{\sum_d |x_i^{(d)}|}$  assumes absolute value of gradient of image is low (piecewise constant). For 2D images:  $L = \frac{1}{n_1 n_2} \sum_{i=1}^{n_1-1} \sum_{j=1}^{n_2-1} \sqrt{|x_{i,j} - x_{i,j+1}|^2 + |x_{i,j+1} - x_{i+1,j}|^2}$ . **GAN-based loss functions:**

$\min_G \max_D \mathbb{E}_{I \sim p_{data}(I)} [\log D(I)] + \mathbb{E}_{I \sim p_G(I)} [\log(1 - D(I))]$  with aim to discern real high resolution and artificially upsampled. The discriminator output is loss function:  $\mathcal{L} = - \log D(G(I_{LR}))$ .

**Deep Image Prior:** represent an image not by its pixel values, but by the weights of a vector (like latent encoding): start with random-initialized network, given image x, its parameters w are recovered by solving  $\min_w \|x - \Psi(z; w)\|_2^2$ . It is shown that generating noise is hard, and generating real images is easy. For in-painting, we only reconstruct visible pixels and implicitly infer the pixels masked out:  $\min_w \|m \odot (x - \Psi(z; w))\|_2^2$  We can then reconstruct the image by fitting a noise vector into the image, and reconstruct the image.

**Loss function:** e.g. MSE, and learn:  $\theta^{(k+1)} = \theta^{(k)} - \tau \frac{\partial \mathcal{L}(\theta, x)}{\partial \theta} |_{\theta=\theta^{(k)}}$  for low sample size, denoise through convolutions, then match with forier transform into signal domain to check the data is consistent (repeat blocks 5 times). For **Coarse Voxels** acquire thick slices through the organ (e.g. z-dimension) construct a simulation from a high quality image for forward process and generate pairs of H and L resolution data and train nn to absorb all images to high resolution (original). A residual network works well for this.