Department of Medical Physics and Biomedical Engineering

Centre for Medical Image Computing (CMIC)

Wellcome / EPSRC Centre for Interventional and Surgical Sciences (WEISS)



# Deep Learning

MPHY0041 Machine Learning in Medical Imaging

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# Research



## **Selected Research Topic**

Multiple instance learning

Adversarial learning and generative models

Domain adaptation

Meta-learning

Unsupervised learning\*

Reinforcement learning\*

Graph networks\*



# Research | Multiple Instance Learning

# Research | Multiple Instance Learning



# Weakly-supervised learning and Weak labels

- Inaccurate supervision, e.g. noisy labels
- Incomplete supervision, e.g. partial labels
- Inexact supervision, e.g. multiple instance learning



### Bags, instances and labels in MIL

Serge's key-chain



Serge **cannot** enter the *Secret Room* 

Sanjoy's key-chain



Sanjoy **can** enter the *Secret Room* 

Lawrence's key-chain



Lawrence **can** enter the *Secret Room* 



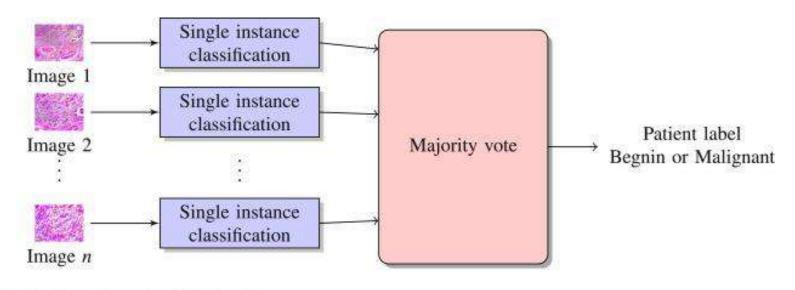
Linkage function between bag-level (known) and instance-level (to infer) relations

$$y_i = \begin{cases} 1 & \text{if } \exists j \text{ s.t. } y_{ij} = 1 \\ 0 & \text{otherwise} \end{cases} \qquad y_i = \max_j \{y_{ij}\}$$

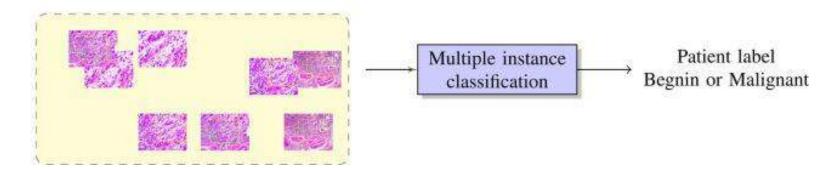
$x_i \in \mathcal{X}$	
$X_i = \{x_{i1}, x_{i2} \dots, x_{im}\}$	$i^{th}$ bag with $m$ instances $x_{ij}$ (MIL)
$y_i \in \mathcal{Y}$	label of $i^{th}$ instance (supervised) or $i^{th}$ bag (MIL)
$y_{ij}$	true label of $j^{th}$ instance in $i^{th}$ bag
y'	(2y-1)
n	instances (supervised) or number of bags (MIL)
m	number of instances per bag
d	dimensionality
h(x)	instance classifier
H(X)	bag classifier



### Segmentation on whole-slide imaging in digital pathology



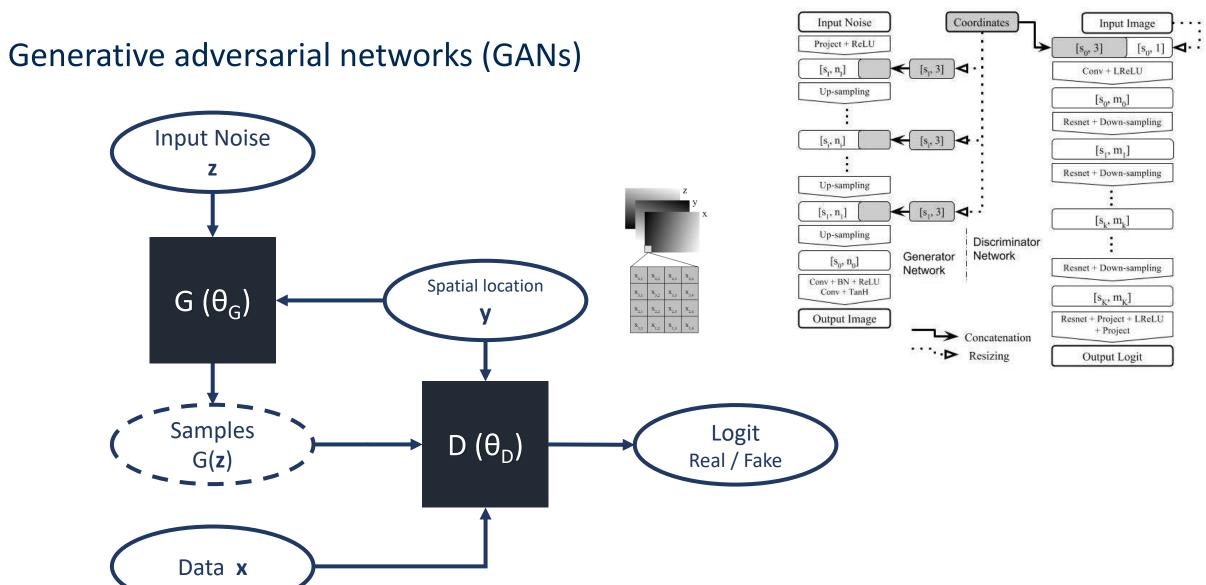
#### Multiple instance learning (MIL) setting





# Research | Adversarial Learning and Generative Models

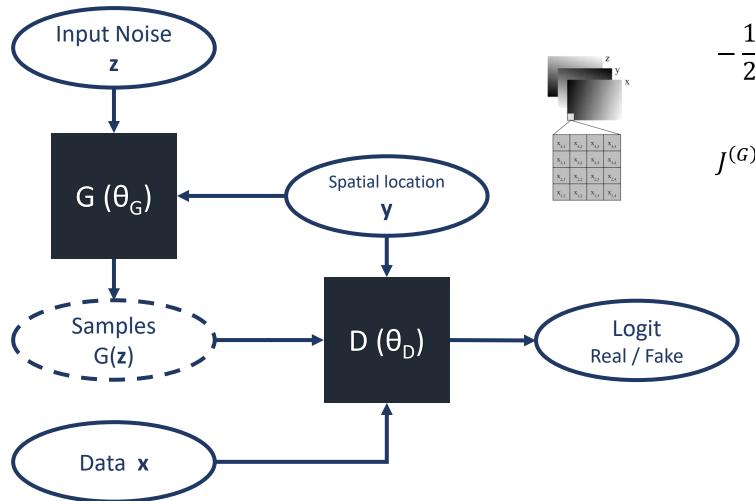




## Research | Adversarial Learning and Generative Models



# Generative adversarial networks (GANs)



$$J^{(D)}$$

$$= -\frac{1}{2} \mathbb{E}_{(\mathbf{x}, \mathbf{y}) \sim P_{data}} \log D(\mathbf{x}, \mathbf{y})$$

$$-\frac{1}{2} \mathbb{E}_{\mathbf{z} \sim N, \mathbf{y} \sim P_{loc}} \log (1 - D(G(\mathbf{z}, \mathbf{y}), \mathbf{y}))$$

$$J^{(G)} = -\frac{1}{2} \mathbb{E}_{\mathbf{z} \sim N, \mathbf{y} \sim P_{loc}} \log D(G(\mathbf{z}, \mathbf{y}), \mathbf{y})$$

# Research | Adversarial Learning and Generative Models

Generative adversarial networks (GANs)

Image synthesis
Regularisation by minimising divergence
Image-to-image translation
Domain adaptation



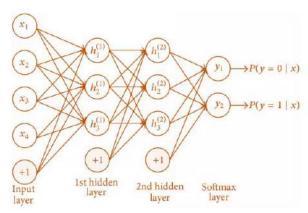












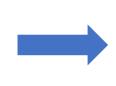


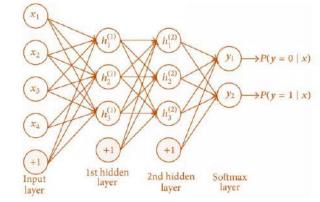




















- Unsupervised domain adaptation
- Semi-supervised domain adaptation

\_\_\_\_ Task-specific Classifier

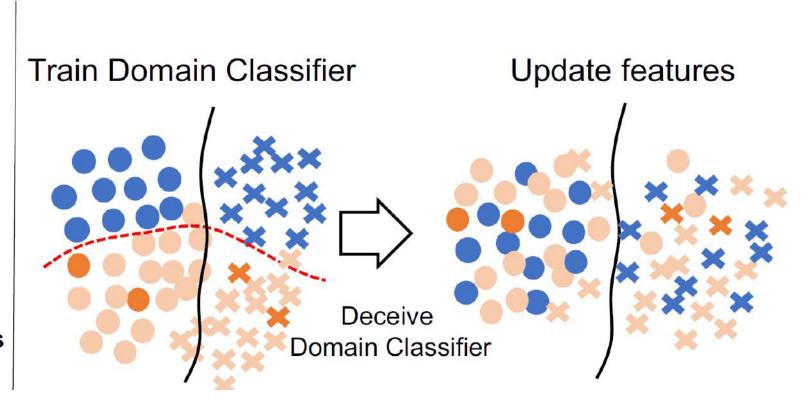
--- Domain Classifier

Labeled Source

Labeled Target

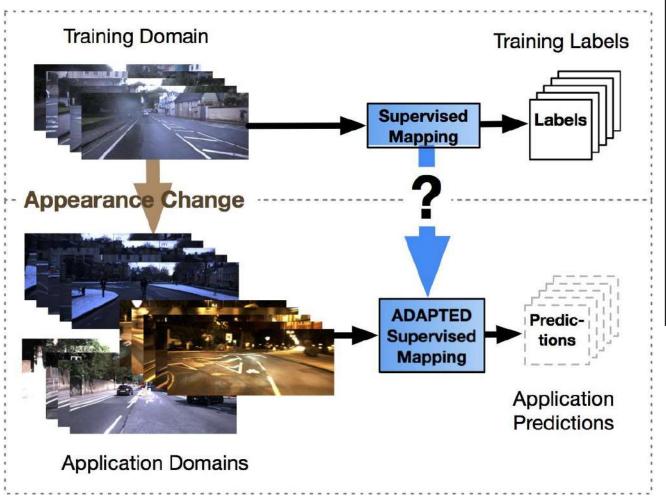
Unlabeled Target

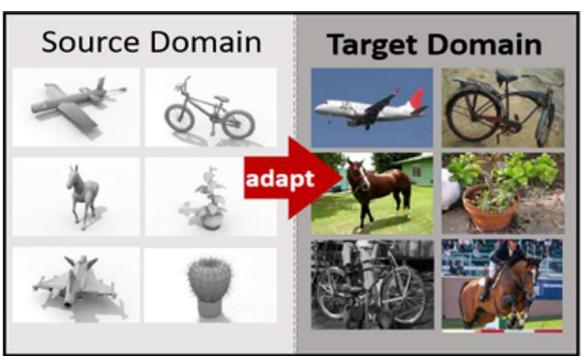
Estimated Prototypes





Availability between domains







- Labelled data are expensive or infeasible
- Distribution "shift" between training and test data sets
- e.g. synthetic or semi-synthetic (image) data different data distribution
- Different types of training data
- e.g. movie vs. books, MR vs. CT
- Y. Gannin et al. 2016: Unsupervised domain adaptation
  - Find a classifier:
    - a) Discriminativeness (the ability to classify)
    - b) Domain-invariance (the ability to use ONLY domain-independent features to classify)
  - By:
    - 1) Label classifier (to predict the correct labels)
    - Domain classifier (to find the features that can discriminate between source and target domain and NOT use them)



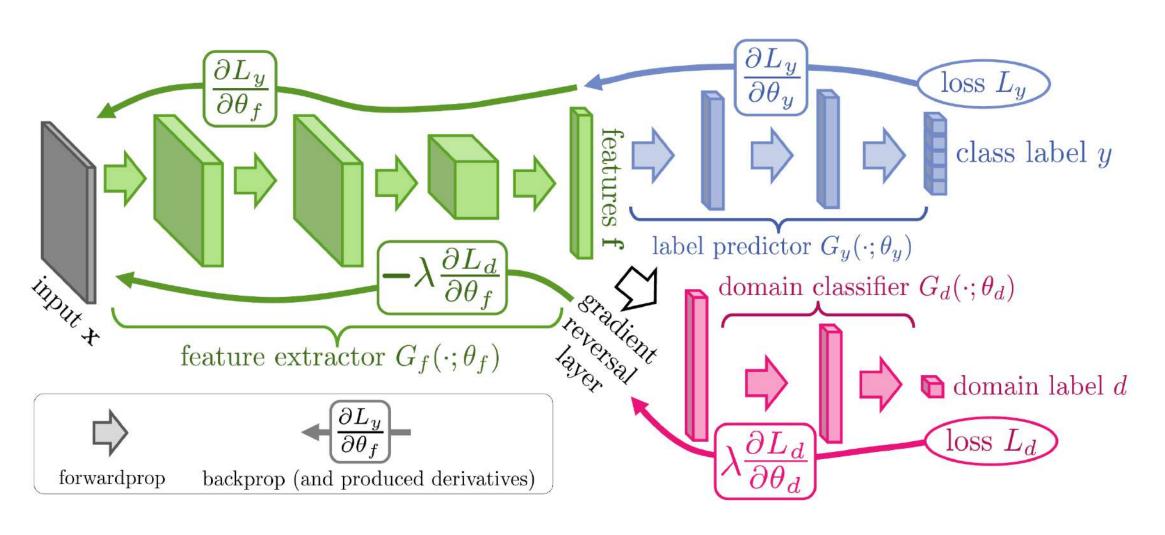
#### Find a classifier:

- a) Discriminativeness (the ability to classify)
- b) Domain-invariance (the ability to use ONLY domain-independent features to classify)
- By:
  - 1) Label classifier (to predict the correct labels)
  - Domain classifier (to find the features that can discriminate between source and target domain and NOT use them)
- That is:
  - 1) Minimise the loss of the label classifier
  - 2) Maximise the loss of the domain classifier
  - 3) Minimise the loss of domain classifier to train the domain classifier

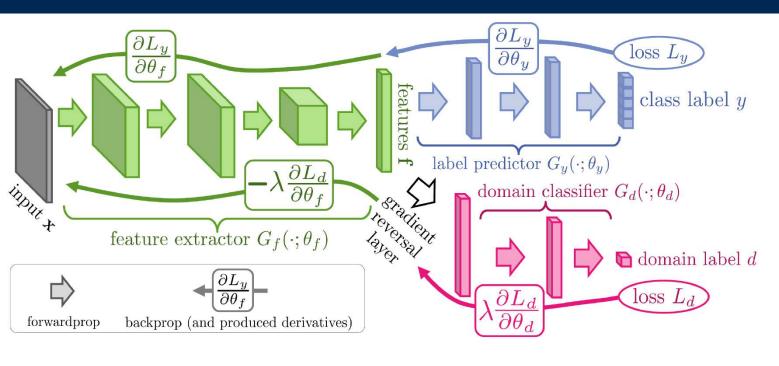


Adversarial learning









$$\mathcal{L}_{y}^{i}(\theta_{f}, \theta_{y}) = \mathcal{L}_{y}(G_{y}(G_{f}(\mathbf{x}_{i}; \theta_{f}); \theta_{y}), y_{i}),$$

$$\mathcal{L}_d^i(\theta_f, \theta_d) = \mathcal{L}_d(G_d(G_f(\mathbf{x}_i; \theta_f); \theta_d), d_i).$$

$$E(\theta_f, \theta_y, \theta_d) = \frac{1}{n} \sum_{i=1}^n \mathcal{L}_y^i(\theta_f, \theta_y) - \lambda \left( \frac{1}{n} \sum_{i=1}^n \mathcal{L}_d^i(\theta_f, \theta_d) + \frac{1}{n'} \sum_{i=n+1}^N \mathcal{L}_d^i(\theta_f, \theta_d) \right),$$

$$(\hat{\theta}_f, \hat{\theta}_y) = \underset{\theta_f, \theta_y}{\operatorname{argmin}} E(\theta_f, \theta_y, \hat{\theta}_d),$$

$$\hat{\theta}_d = \underset{\theta_d}{\operatorname{argmax}} E(\hat{\theta}_f, \hat{\theta}_y, \theta_d).$$

$$\theta_f \leftarrow \theta_f - \mu \left( \frac{\partial \mathcal{L}_y^i}{\partial \theta_f} - \lambda \frac{\partial \mathcal{L}_d^i}{\partial \theta_f} \right),$$

$$\theta_y \leftarrow \theta_y - \mu \frac{\partial \mathcal{L}_y^i}{\partial \theta_y},$$

$$\theta_d \leftarrow \theta_d - \mu \lambda \frac{\partial \mathcal{L}_d^i}{\partial \theta_d},$$

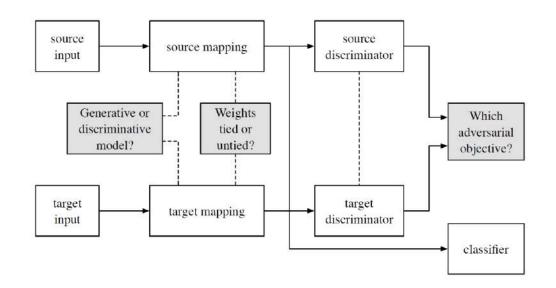


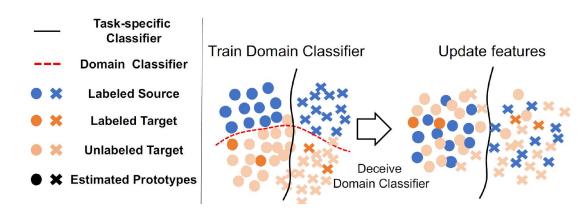


#### Distance between source and target distribution, e.g. H-divergence ©

$$\hat{d}_{\mathcal{H}}(S(G_f), T(G_f)) = 2\left(1 - \min_{\eta \in \mathcal{H}} \left[\frac{1}{n} \sum_{i=1}^{n} I[\eta(G_f(\mathbf{x}_i)) = 0] + \frac{1}{n'} \sum_{i=n+1}^{N} I[\eta(G_f(\mathbf{x}_i)) = 1]\right]\right).$$

$$\mathcal{L}_d^i(\mathbf{W}, \mathbf{b}, \mathbf{u}, z) = \mathcal{L}_d(G_d(G_f(\mathbf{x}_i; \mathbf{W}, \mathbf{b}); \mathbf{u}, z), d_i)$$



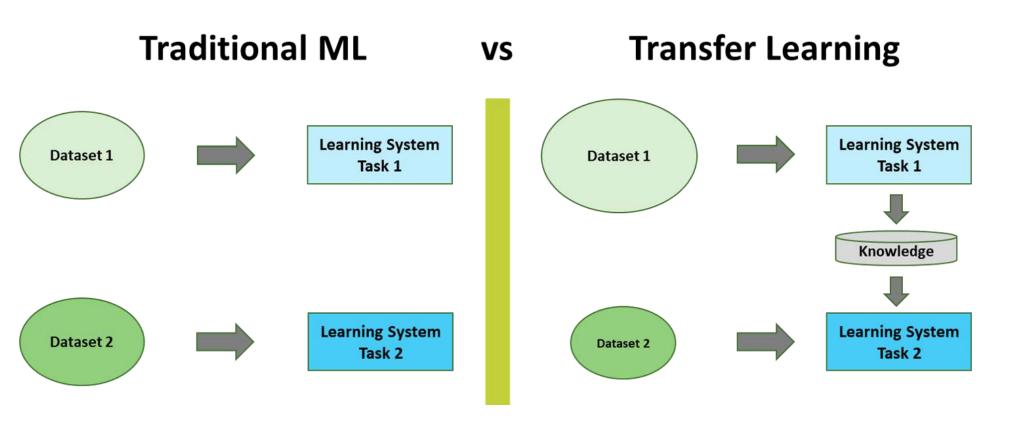




# Research | Meta-Learning

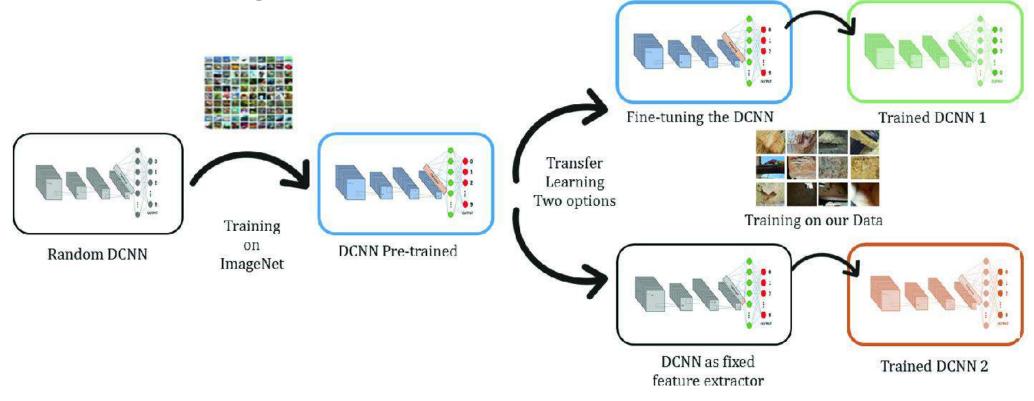


## Transfer learning



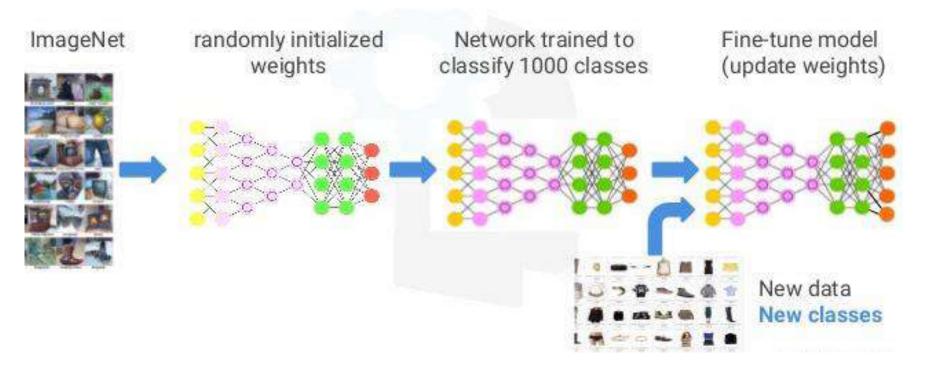


# Transfer learning





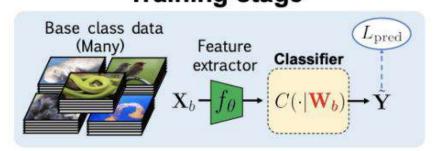
## Transfer learning for few-shot learning



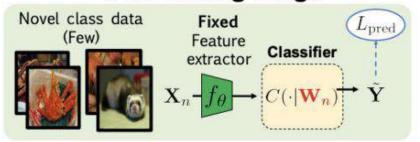


#### Few-shot learning and meta-learning



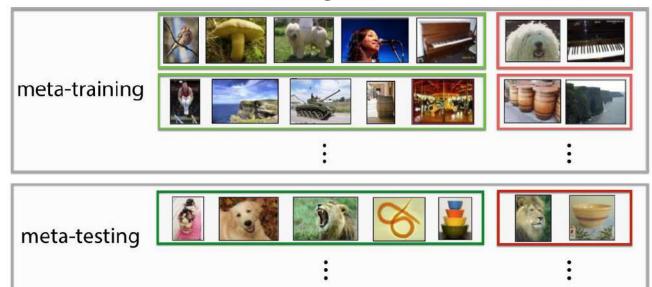


#### Fine-tuning stage



training data

test set





# Terminology and taxonomy

Learning Settings		Source and Target Domains	Source and Target Tasks	
Traditional Machine Learning		the same	the same	
	Inductive Transfer Learning /	the same	different but related	
Transfer Learning	Unsupervised Transfer Learning	different but related	different but related	
	Transductive Transfer Learning	different but related	the same	

Transfer Learning Settings	Related Areas	Source Domain Labels	Target Domain Labels	Tasks
Inductive Transfer Learning	Multi-task Learning	Available	Available	Regression, Classification
	Self-taught Learning	Unavailable	Available	Regression, Classification
Transductive Transfer Learning	Domain Adaptation, Sample Selection Bias, Co-variate Shift	Available	Unavailable	Regression, Classification
Unsupervised Transfer Learning		Unavailable	Unavailable	Clustering, Dimensionality Reduction



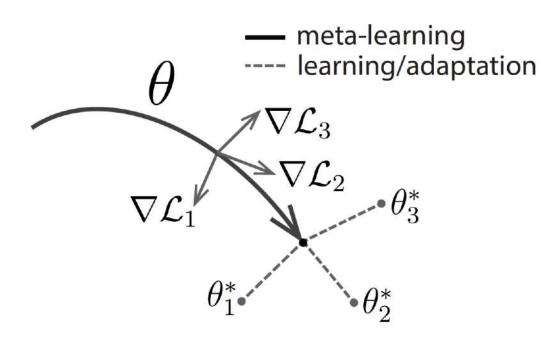








### Model-agnostic meta-learning (MAML)



#### **Algorithm 1** Model-Agnostic Meta-Learning

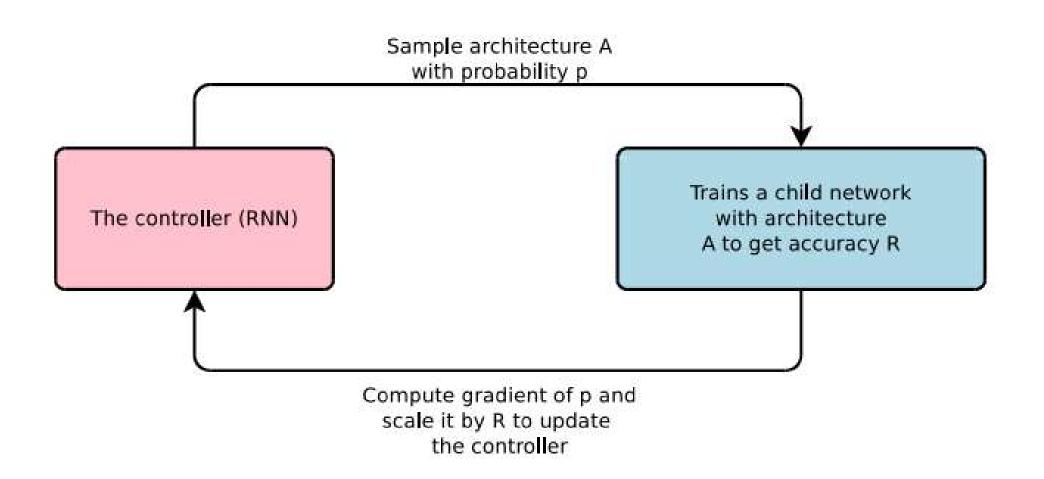
**Require:**  $p(\mathcal{T})$ : distribution over tasks

**Require:**  $\alpha$ ,  $\beta$ : step size hyperparameters

- 1: randomly initialize  $\theta$
- 2: while not done do
- 3: Sample batch of tasks  $\mathcal{T}_i \sim p(\mathcal{T})$
- 4: for all  $\mathcal{T}_i$  do
- 5: Evaluate  $\nabla_{\theta} \mathcal{L}_{\mathcal{T}_i}(f_{\theta})$  with respect to K examples
- 6: Compute adapted parameters with gradient descent:  $\theta'_i = \theta \alpha \nabla_{\theta} \mathcal{L}_{\mathcal{T}_i}(f_{\theta})$
- 7: end for
- 8: Update  $\theta \leftarrow \theta \beta \nabla_{\theta} \sum_{\mathcal{T}_i \sim p(\mathcal{T})} \mathcal{L}_{\mathcal{T}_i}(f_{\theta'_i})$
- 9: end while



Searching for hyper-parameters (architecture, loss, data augmentation...)





#### "Transferability" from computer vision to medical imaging

- Applications:
  - Encoder-decoder U-Net segmentation
  - Optical flow registration
  - GANs synthesis
  - ...
- Data size
- Data availability
- Data variability, equipment, protocols, demography etc.
- Ground-truth, inc. label uncertainty, fidelity etc.
- Test significance, e.g. 1% effect size, 20 subjects, ~10% variance
- Clinical relevance