Applications of Deep Learning (DL) in SPECT.

Michael King, Ph.D. and Clifford Lindsay, Ph.D.
Department of Radiology, University of Massachusetts Medical School, Worcester, MA

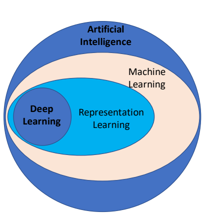
e-mail: Michael.King@umassmed.edu

Disclosure: Dr. King current has 3 NIH grants and in the past had a research grant from Philips Medical Systems
Much Cardiac SPECT portion of talk is from R01 HL122484 Joint IIT and UMass

Outline of Talk

- A Shallow Introduction to Deep Learning (DL)
- DL Dose / Imaging Time Reduction in CT
- DL Dose / Imaging Time Reduction in PET
- Image Reconstruction and Processing Dose / Imaging Time Reduction in SPECT
- DL Dose / Imaging Time Reduction in Cardiac SPECT
- Summary

AI, Machine & Deep Learning in Perspective



Venn Diagram

Artifical Intelligence (AI): Colloquially, the term "artificial intelligence" is applied when a machine mimics "cognitive" functions that humans associate with other human minds, such as "learning" and "problem solving".

Machine Learning (ML): A machine learning algorithm is an algorithm that is able to learn from data. Computers trained without explicit programing.

Representational Learning (RL): Computers learn features by which to classify the data.

Deep Learning (DL): Type of RL where the learned features are hierarchical.

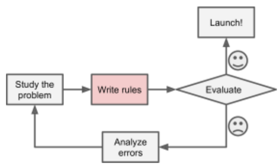
Adapted From:
Ian Goodfellow, Yoshua Bengio, Aaron Courville, Deep Learning, MIT Press, 2016
And
Gabriel Chartrand, et al Deep Learning: A Primer for Radiologists. RadioGraphics, 2017

C. Lindsay, U Mass Med School

Computational Problem Solving

Solution Loop
- Problem Understanding
- Codified Conditions (Rules)
- Evaluation & Error Analysis

Disadvantages
- Hard problems are not trivial
- Solution likely a long list of complex rules
- Hard to maintain



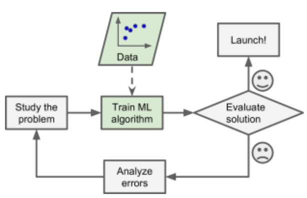
C. Lindsay, U Mass Med School

Computational Learning Approach

Similarities
- Problem Understanding Required
- Evaluation & Error Analysis

Differences
- Adaptive Rules
- Data Mutable Rules

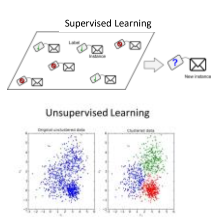
Intuition
- Program Output ➡ Results
- M.L. Output ➡ Program



C. Lindsay, U Mass Med School

Classifying M.L. Methods & Types

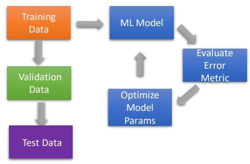
Data/Input Types
- **Supervised (inductive) learning**
  - –Training data includes desired outputs
- **Unsupervised learning**
  - –Training data does not include desired outputs
  - –Find hidden structure in data
- **Semi-supervised learning**
  - –Training data includes a few desired outputs



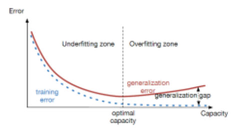
C. Lindsay, U Mass Med School

Expanded ML Diagram

Training
- Divide Data into Train, Validation & Test (e.g., 60/20/20) or do cross-validation
- Train Data - used to fit the model each forward and backward propagation
- Validation Data - provide an evaluation of model fit while tuning model hyperparameters
- Epoch is a complete exhaustion of Train and Validation Data
- Test Data - provide an unbiased evaluation of a final model fit

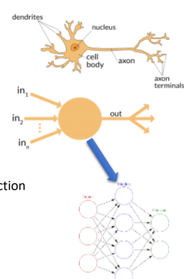


Error
- Lower = in general better, stopping is application dependent
- Ideally Test error = Validation error (then likely good generalization)
- Too much training can result in overfitting
- Too little can result in underfitting



C. Lindsay, U Mass Med School

Artificial Neural Networks (ANN)

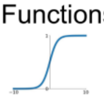


What is it?
- ANN models are loosely based on biological neurons
- Artificial neuron may have multiple Input and output
- Neuron body acts as signal integrator & activation function
- Data is propagated from 1 or more neurons to others
- A Net may have multiple layers

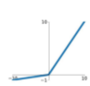
C. Lindsay, U Mass Med School

Activation Functions

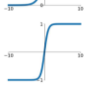
Sigmoid
$\sigma(x) = \frac{1}{1+e^{-x}}$



Leaky ReLU
$\max(0.1x, x)$

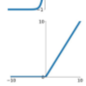


tanh
$\tanh(x)$

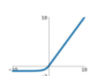


Maxout
$\max(w_1^T x + b_1, w_2^T x + b_2)$

ReLU
$\max(0, x)$



ELU
$\begin{cases} x & x \geq 0 \\ \alpha(e^x - 1) & x < 0 \end{cases}$

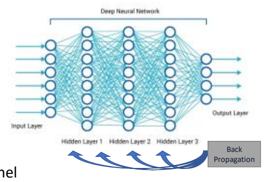


C. Lindsay, U Mass Med School

What is Deep Learning?

- Typically a CNN with multiple layers
- Apply many layers of CNNs
- Only visible layers are 1st & last

- This model shows a feed-forward net
- Each Model Update modifies the Kernel weights



C. Lindsay, U Mass Med School

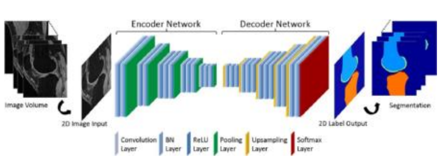
DL Networks are Intensely Data Hungary

- Large datasets with labels are difficult to obtain in medical imaging
- What size is needed depends on nature and complexity of task (segmentation may need more training data than denoising).
- Augmentation of the data available by flipping, rotation, translation, zooming, skewing, etc can sometimes be used. Also different noise realizations and divide slices into patches.
- Transfer learning has also been used where a network trained for one application on a large dataset is retasked to another purpose, and then trained on a small dataset relevant to the new task.

C. Lindsay, U Mass Med School

Deep Learning Algorithms

- Encoder/Decoders
- Denoising Autoencoders



C. Lindsay, U Mass Med School

DL Dose / Imaging Time Reduction in CT

- The success of DL in other areas inspired a number of investigators to investigate its usage in reconstruction and denoising low-dose CT studies.
- Excellent results have been observed for DL post-reconstruction denoising in comparison to iterative reconstruction and other post-processing methods visually and using the RMSE and SSIM to full dose.
- Example: Chen et al, TMI 36 (12) 2524-2535, 2017 – LDCT = ¼ HDCT

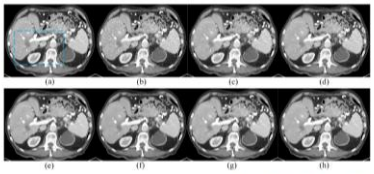


Fig. 10. Results from the abdominal image with a metastasis in the liver for comparison. (a) NDCT, (b) LDCT, (c) TV-POCS; (d) K-SVD, (e) BM3D, (f) CNN10, (g) KAIST-Net, and (h) RED-CNN.

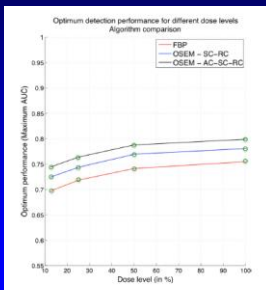
Modeling System Spatial Resolution in Iterative Reconstruction for Reduced Dose / Time

- SPECT Myocardial Perfusion Imaging a number of investigators have found that modeling resolution can be used to reduce dose / time by 2 to 4 fold by various metrics
  - Ali, et. al., JNC 2009
  - Bateman, et. al., JNC 2009
  - DePuey, et.al., JNC 2012
  - Zafrir, et. al., JNC 2013
  - Zoccarato, et. al. JNC 2014
- Similar results were observed in pediatric SPECT imaging
  - Sheehy, et.al., Radiol 2009
  - Stansfield, et. al., Radiol 2010

Investigation of Lowering Activity / Imaging Time in Cardiac SPECT - Perfusion

- Create lower-count studies from full-count list-mode studies by sampling with desired probability of keeping count.
- Select 190 of studies read clinically as normal and appear to have uniform LV distributions when reconstructed with all corrections (attenuation, scatter, resolution, body and respiratory motion).
- Create hybrid studies from these with range of defections of variation in size, contrast, and location based of what observed clinically.[1]
- Perform ROC studies using total perfusion deficit score (TPD) of QPS which depends of defect severity and extent to select reconstruction parameters (smoothing and # of iter) using 130 of studies with matching processing polar map data base for 30 males and second for 30 females.
- 1. Svane B. Polar presentation of coronary angiography and Thallium-201 single photon emission computed tomography. PhD Thesis. Stockholm; 1990

Investigation of Lowering Activity / Imaging Time in Cardiac SPECT - Perfusion



1. AUC OSEM–AC-SC-RC > FBP

2. AUC OSEM–AC-SC-RC at 12.5% = FBP full-dose

3. AUC OSEM–SC-RC is lower but closer to AUC OSEM–AC-SC-RC

Ramon, AJ et al, J Nucl Card, 2018

Investigation of Lowering Activity / Imaging Time in Cardiac SPECT - Perfusion

- For 4 Readers (2 MD and 2 Physicists) evaluating these studies we obtained.

Recon Method	Ave AUC	SD AUC
FBP Full-Dose	0.73	0.03
OSEM Full-Dose	0.89	0.03
OSEM 25% Dose	0.87	0.03

- OSEM Full-Dose and 25% not statistically significantly different

Pretorius PH, et al, J Nucl Card, Epub 2019

Investigation of Lowering Activity / Imaging Time in Cardiac SPECT - Perfusion

Male Pat AC Map

FBP

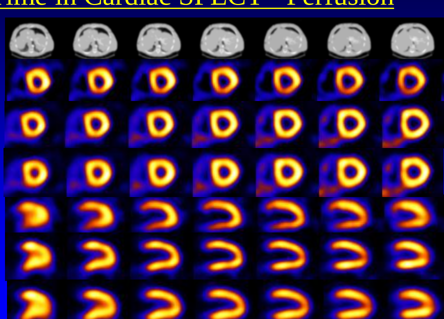
OSEM Full

OSEM 25%

FBP

OSEM Full

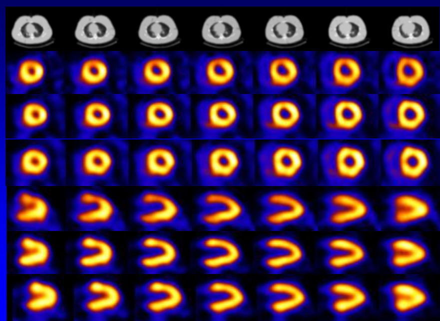
OSEM 25%



Pretorius PH, et al, J Nucl Card, Epub 2019

Investigation of Lowering Activity / Imaging Time in Cardiac SPECT - Perfusion

Female Pat AC Map
FBP
OSEM Full
OSEM 25%
FBP
OSEM Full
OSEM 25%



Pretorius PH, et al, J Nucl Card, Epub 2019

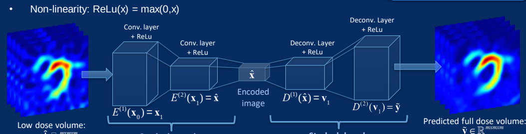
Ramon, AJ et al, Proceed 2018 IEEE NSS + MIC

3D Convolutional auto-encoders (3D-CAE) for denoising of low-dose SPECT-MPI images

- Structure based on chain of layers:[1,2]
  - Convolutional layers (stacked encoders)
    - Local feature extractors
    - Suppress noise and artifacts from images
  - Deconvolutional layers (stacked decoders)[1]
    - Recover image structures lost during previous convolutions
    - Symmetry with encoding layers (recover image of same size)
- Non-linearity: ReLu(x) = max(0,x)

Noise reduction model:

-Low dose volume: $\mathbf{x}_0 \in \mathbb{R}^{mxmxm}$
-Full dose volume: $\mathbf{y} \in \mathbb{R}^{mxmxm}$
$\mathbf{x}_0 = S(\mathbf{y})$, where $S : \mathbb{R}^{mxmxm} \to \mathbb{R}^{mxmxm}$
-CAE models f so that:
$\arg\min_f \|f(\mathbf{x}_0) - \mathbf{y}\|_2^2$



Stacked encoders

$$E^{(l)}(\mathbf{x}_{l-1}) = \max(0, \mathbf{W}_l * \mathbf{x}_{l-1} + \mathbf{b}_l), \quad l = 1,\ldots,L$$

$\mathbf{W}_l$ and $\mathbf{b}_l$: weight and biases for layer l
$\mathbf{x}_0$: input low dose image
$\mathbf{x}_{l-1}$: feature map from previous layer

Stacked decoders

$$D^{(d)}(\mathbf{v}_{d-1}) = \max(0, \mathbf{W}_d \otimes \mathbf{v}_{d-1} + \mathbf{b}_d), \quad d = 1,\ldots,D$$

$\mathbf{W}_d$ and $\mathbf{b}_d$: weight and biases for layer l
$\mathbf{v}_{d-1}$: feature map from previous layer

MIRC MEDICAL IMAGING RESEARCH CENTER

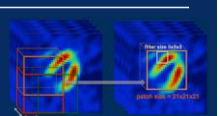
1 – Mao et al., 2016
2 – Chen et al., 2017

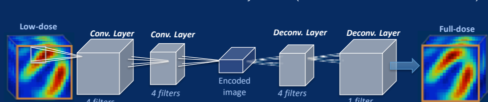
UMASS MEDICAL SCHOOL
ILLINOIS INSTITUTE OF TECHNOLOGY

Ramon, AJ et al, Proceed 2018 IEEE NSS + MIC

Experimental framework

- **CAE structure (for training) and parameter selection**
  - **Patch based training (3D patches):**
    - Extracted from heart ROI of size 42x42x21 voxel
    - Patch size = 21x21x21 voxel. Stride = 7 voxel
  - **Convolutional auto-encoder structure:**
    - Filter shape: 3x3x3 voxel (stride 1, no padding) [1,2]
    - Conv. layers (2) + Deconv. layers (2)
  - **Implementation:**
    - Loss function: mean squared error (MSE)
    - Optimizer: Adam (stochastic gradient descent)
    - Keras with Tensor Flow[3] backend in Python 3.5 (NVIDIA GeForce GTX 1080 Ti 12GB)





MIRC MEDICAL IMAGING RESEARCH CENTER

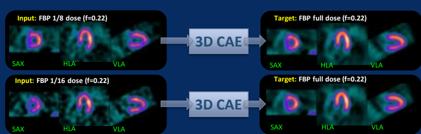
1 – Mao et al., 2016
2 – Chen et al., 2017
3 – Abadi et al., 2016

UMASS MEDICAL SCHOOL
ILLINOIS INSTITUTE OF TECHNOLOGY

Ramon, AJ et al, Proceed 2018 IEEE NSS + MIC

Experimental framework (cont.)

- **Clinical dataset of 930 clinical SPECT-MPI images**
  - **Training:** 740 patients *(mixed normal/abnormal perfusion/motion)*
  - **Test:** 190 patients corresponding to ROC study for perfusion-defect detection[1]
- **Reconstruction algorithms:**
  - Optimized for maximum perfusion defect detection[1]
  - **FBP** (cutoff freq. of order-5 Butterworth filter)
  - **OS-EM w/ AC-SC-RC** (Gaussian width parameter [voxels], # of iterations)
- **Training:**
  - **Target:** 100% dose with optimal reconstruction parameters[1]
  - **Input:** Low dose (i.e. 1/2, 1/4, 1/8 or 1/16) using same recon. parameters as 100% dose



Patient: Female, Age: 75, BMI: 20.5

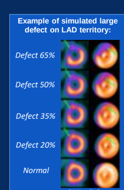
1 – Juan Ramon et al., 2017

MIRC MEDICAL IMAGING RESEARCH CENTER · UMASS MEDICAL SCHOOL · ILLINOIS INSTITUTE OF TECHNOLOGY

Ramon, AJ et al, Proceed 2018 IEEE NSS + MIC

Experimental framework (cont.)

- **Simulated low dose data**
  - Reduce dose by a fixed uniform proportion across all patients
  - Reductions of 1/2, 1/4, 1/8 and 1/16 with respect to full clinical dose
  - Low-dose scans simulated by statistical subsampling of full dose studies
- **Performance evaluation**
  - ROC studies for perfusion-defect detection
  - **Quantitative Perfusion SPECT (QPS)** as a surrogate for human readers[1]
    - Detects abnormalities by comparing to reference databases of normal images
    - "Total perfusion deficit" (TPD) score
  - Test data (190 patients) divided in:
    1. 60 patients (30/30 male/female) for QPS reference
    2. 130 patients for ROC study
       - (58 normal and 72 hybrid/simulated defects)

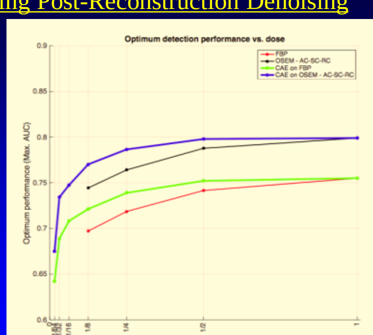


MIRC MEDICAL IMAGING RESEARCH CENTER · UMASS MEDICAL SCHOOL · ILLINOIS INSTITUTE OF TECHNOLOGY

Deep Learning Post-Reconstruction Denoising

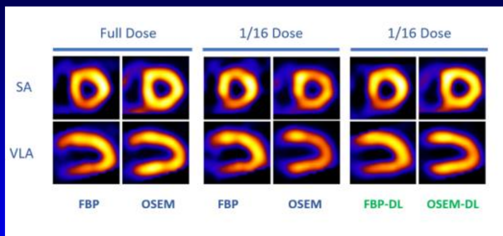
1. AUC for both FBP and OSEM decrease at significantly lower rate than with 3D post Gaussian filtering

2. AUC at dose at 6.25% (~2mCi) with DL ~same AUC as OSEM at 12.5% dose without DL or FBP at Full dose.



Ramon, AJ et al, Proceed 2018 IEEE NSS + MIC

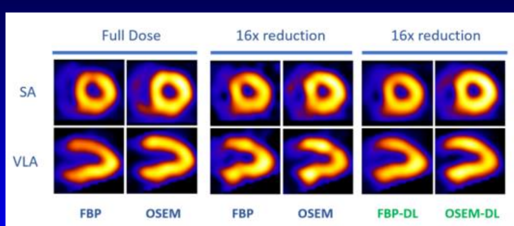
Deep Learning Post-Reconstruction Denoising



FBP and OSEM-AC-SC-RC for full and 16x dose reduction for 3D post-Gaussian vs **deep learning** (DL) with 16x dose reduction for male, age=75, BMI=29.7. The artefactual mild anterior and strong inferior cooling of the LV in FBP with full dose is corrected in OSEM with AC. With dose reduced by 16x, both FBP and OSEM exhibited visible distortion in the wall shape due to reduced counts. In contrast, such distortion is corrected with DL for both methods.

Ramon, AJ et al, 2018 IEEE MIC + NSS

Deep Learning Post-Reconstruction Denoising



FBP and OSEM-AC-SC-RC for full and 16x dose reduction for 3D post-Gaussian vs **deep learning** (DL) with 16x dose reduction for female, age=44, BMI=35.2. The artefactual anterior cooling of the LV in FBP with full dose is corrected in OSEM with AC. With dose reduced by 16x, both FBP and OSEM exhibited visible distortion in the wall shape due to reduced counts. In contrast, such distortion is corrected with DL for both methods.

Ramon, AJ et al, 2018 IEEE NSS + MIC

SUMMARY

- DL has found numerous applications in medical imaging.
- DL denoising has the potential to significantly reduce dose and / or imaging time in emission imaging (factors of 3-10, or more, have been suggested as possible depending on the modality and criterion).
- DL can also be used directly in reconstruction where it has direct access to the projection data.
- DL systems are dependent on network design, and the data and the error metric (MSE, L1, …) used in training.
- DL systems are opaque and generally not easy to clearly understand how the network is performing tasks.
- Beware of spurious behavior – loss of contrast of small objects.