Artificial Intelligence and Data-driven Medicine

2016. 6. 3

Kyu-Hwan Jung, Ph.D Co-founder and CTO

Artificial Intelligence Diagram





Google Trends – Machines are Learning



Smart Money is Moving to AI

Artificial Intelligence, Real Money

Total venture capital money for pure AI startups, by year

\$350 million



Source: CB Insights

Bloomberg III

Tech Giants are Snapping Up

Race To Al: Major Acquisitions In Artificial Intelligence



Date of acquisition

www.cbinsights.com

Huge Market Opportunity

\$500B OPPORTUNITY OVER 10 YRS



SOURCE: "Deep Learning for Enterprise Applications," 4Q 2015, Tractica

Deep Learning as the Core of 'AI' Engine



Deep Learning Make Machines to have 'Perception'



ILSVRC-2012 Task 1 (Classification) Result

Phoneme Recognition Accuracy (TIMIT Data)

77

74.2

Augmented CRF

MLPHMM

3

4

VUNO

83.9%

(World Record)

2014

Now, Machines Learn Deep

• Now, Machines Beat Human in Tasks Once Considered Impossible





5:0 vs Fan Hui (Oct. 2015)



4:1 vs Sedol Lee (Mar. 2016)

Traditional Machine Learning vs Deep Learning

Traditional Machine Learning

Deep Learning



V U U O

Feature Engineering vs Feature Learning



From Yann LeCun

Hierarchical Representation



From Yann LeCun and Zeiler(2013)



Why Now?



Big Data



Computational Power



Deep Learning for Medical Data

"when machine can see, doctors and nurses will have extra pairs of tireless eyes to help them to diagnose and take care of patients."

Fei-Fei Li, March 2015

AI and Medicine in Keynotes

Facebook F8, April 2016



Nvidia GTC, March 2016

DEEP LEARNING FOR MEDICINE

NVIDIA Founding Technology Partner of MGH Center of Clinical Data Science 10B Medical images on DGX-1 to advance radiology, pathology, genomics



"So imagine that, soon every doctor around the world just gonna have the ability to snap a photo and as well as the best doctors in the world be able to diagnose your cancer. That's gonna save lives !"

- Mark Zuckerberg at F8 2016

"If there is one application where a lot of very complicated, messy and unstructured data is available, it is in the field of medicine. And what better application for deep learning than to improve our health, improve life?" - Jen-Hsun Huang, GTC 2016

Google I/O, May 2016



"It's very very difficult to have highly trained doctors available in many parts of the world. Deep learning did really good at detecting DR. We can see the promise again, of using machine learning. - Sundar Pichai, Google IO 2016

Academic Results

Digital Pathology for Breast Cancer

- Deep max-pooling CNN to detect mitosis in breast histology images
 - The number of mitotic figures is an important indicator for cancer screening and assessment
 - 2012 ICPR Mitosis Detection Contest



D. C. Ciresan et. al., Mitosis Detection in Breast Cancer Histology Images with Deep Neur al Networks, MICCAI, 2013

	Layer	Туре	Maps and neurons	Filter size	Weights	Connections
	0	Ι	3M x 101x101N	_	_	_
	1	С	16M x 100x100N	2x2	208	2080000
	2	MP	16M x 50x50N	2x2	_	_
	3	С	16M x 48x48N	3x3	2320	5345280
	4	MP	16M x 24x24N	2x2	_	_
Network Structure	5	С	16M x 22x22N	3x3	2320	1122880
	6	MP	16M x 11x11N	2x2	_	_
	7	С	16M x 10x10N	2x2	1040	104000
	8	MP	16M x 5x5N	2x2	_	_
	9	С	16M x 4x4N	2x2	1040	16640
	10	MP	16M x 2x2N	2x2	_	_
	11	FC	100N	1x1	6500	6500
	12	FC	2N	1x1	202	202

Rank	Team	TP	FP	FN	F-measure	Recall	Precision
1	IDSIA	70	9	30	0.7821	0.70	0.89
2	IPAL	74	32	26	0.7184	0.74	0.70
3	SUTECH	72	31	28	0.7094	0.72	0.70
4	NEC	59	20	41	0.6592	0.59	0.75
5	Utrecht	68	65	32	0.5837	0.68	0.51
6	Warwick	57	65	43	0.5135	0.57	0.47
7	NUS	40	23	60	0.4908	0.40	0.63
8	lsik	68	174	32	0.3977	0.68	0.28
9	ETH-heidelberg	80	247	20	0.3747	0.80	0.24
10	Okan-IRISA-LIAMA	22	6	78	0.3438	0.22	0.79
11	IITG	46	214	54	0.2556	0.46	0.18
12	Drexel	21	122	79	0.1728	0.21	0.15
13	BII	32	278	68	0.1561	0.32	0.10
14	Qatar	94	35567	6	0.0053	0.94	0.00

Predicting Genomic Disorder

Genomic Data Analysis using Deep Leanring





Data-driven Drug Discovery

Drug Discovery



Completed • \$40,000 • 236 teams

Merck Molecular Activity Challenge



 \mathbf{V} U U

Brain Image Segmentation

Using CNN with Multi-modal MR Images for Brain Image Segmentation

- To segment brain into CSF, WM and GM, multi-modal inputs(T1, T2, FA) are used
- CNN is trained with multi-modal brain MR patches for patch classification
- From MR images of 8 infants 10,000 patches are generated for training



W. Zhang et. al. Deep Convolutional Neural Networks for Multi-modality Isointense Infant Brain Image Segmentation, NeuroImage, 2015

Diagnostic Classification

For AD/MCI classification, using deep learning-based feature representation

Stacked auto-encoder







ervised fine-tuning	ŝ
	ervised fine-tuning

			Features			
			LLF	SAEF	LLF+SAEF	
		MRI	$0.817 {\pm} 0.018$	$0.802 {\pm} 0.033$	$0.823 {\pm} 0.025$	
	CIZ CVM	PET	$0.821 {\pm} 0.017$	$0.834{\pm}0.016$	0.838 ± 0.021	
AD vs. HC	SR-SVM	CSF	$0.720 {\pm} 0.017$	$0.763 {\pm} 0.055$	0.799 ± 0.015	
		CONCAT	$0.893 {\pm} 0.019$	$0.832 {\pm} 0.027$	0.853 ± 0.032	
	MK-SVM		$0.945 {\pm} 0.008$	$0.939 {\pm} 0.018$	$0.959{\pm}0.011$	
		MRI	$0.732 {\pm} 0.018$	$0.673 {\pm} 0.015$	0.740 ± 0.021	
	SK-SVM	PET	$0.702 {\pm} 0.032$	$0.673 {\pm} 0.031$	0.682 ± 0.033	
MCI vs. HC		CSF	$0.640 {\pm} 0.021$	$0.660 {\pm} 0.020$	0.680 ± 0.012	
		CONCAT	$0.737 {\pm} 0.017$	$0.701 {\pm} 0.028$	0.769 ± 0.023	
	MK-SVM		$0.840 {\pm} 0.011$	$0.792 {\pm} 0.024$	$0.850{\pm}0.012$	
		MRI	$0.568 {\pm} 0.026$	$0.542 {\pm} 0.034$	0.550 ± 0.027	
	CIZ CVM	PET	$0.626 {\pm} 0.036$	$0.606 {\pm} 0.034$	0.592 ± 0.034	
MCI-C vs. MCI-NC	SR-SVM	CSF	$0.527 {\pm} 0.026$	$0.581 {\pm} 0.029$	0.574 ± 0.015	
		CONCAT	$0.616 {\pm} 0.043$	$0.584{\pm}0.041$	0.603 ± 0.023	
	MK	SVM	$0.718 {\pm} 0.026$	$0.735 {\pm} 0.024$	$0.758 {\pm} 0.020$	

Holistic Lung Classification(MICCAI 15)

- Holistic Classification of CT Attenuation Patterns for Interstitial Lung Diseases via Deep Convolutional Neural Networks
 - CNN for 6 classes : Normal(NM), Emphysema(EM), Ground Glass(GG), Fibrosis(FB), Micronodules(MN), Consolidation (CD).
 - Patches are too small and annotating ROI is labor intensive.
 - "Weakly supervised learning"
- Training
 - Image windowing for 1)low-attenuation value,
 2)high-attenuation value 3)normal lung value to make
 3-channel input
 - Scale jittering and randomly crop 10 224 x 224 images
 - CNN almost identical to AlexNet.(5 conv. + 3 fc layers)



[Low attenuation] HU low= -1400, HU high= -950 [Normal] HU low= -1400, HU high= -200 [High attenuation] HU low= -160, HU high= 240.



Chest Pathology Identification(SPIE 15)

- Deep learning with non-medical training used for chest pathology identification
 - Categories examples: healthy, enlarged heart, right effusion, multiple pathologies: enlarged heart and right effusion.
 - Feature from AlexNet + PiCoDes(Picture Codes : Mix of LBP, GIST)
 - Train SVM for Classification





Table 2. Healthy vs. Pathology.

	Low	Level	High Level	Deep		Deep Fusion		Fusion		
	LBP	GIST	PiCoDes	Decaf L5	Decaf L6	Decaf L7	PiCoDes+Decaf L5			
Sensitivity	0.65	0.68	0.59	0.73	0.89	0.76	0.81			
Specificity	0.61	0.66	0.79	0.80	0.64	0.64	0.79	\mathbf{N}		
AUC	0.63	0.72	0.72	0.78	0.79	0.72	0.79	V		

Computational Mammography (MICCAI 15)

- Computational Mammography using Deep Neural Networks
 - Segment mammography to classes : Pectoral muscle, Fibroglandular tissue, Nipple and General breast tissue. Background is zero-thresholded
 - 40 digital mammography of MLO view manually segmented by expert.



Fig. 1. Manual segmentation. (a, d) Original mammography images. (b, e) Manual labeling into the pectoral muscle (yellow), fibroglandular tissue (cyan), nipple (bordo), breast tissue (light blue), and background (dark blue). (c, f) Manual labeling superimposed over the mammography image.

Fig. 3. Segmentation results. (a) Original image. (b, c) Manual labels. (d, e) Labels obtained using the proposed method. Color coding is as in Figure 1.

IEEE Special Issue on Medical Imaging

Andrew Ng



Special Edition: Deep Learning in Medical Imaging, May 2016

Special Editors: H. Greenspan, B. van Ginneken, R. Summers

IEEE Trans Med Imaging, vol. 34, issue 5, May 2016

MICCAI DLMIA Workshop

LICCA15 DLMIA UNICH St Workshop on Deep Learning in Medical Image Analysis

2nd Workshop on Deep Learning in Medical Image Analysis

Industrial Applications

Watson Is Expanding Its Perceptual Capabilities

Watson to Gain Ability to "See" with Planned \$1B Acquisition of Merge Healthcare

Deal Brings Watson Technology Together with Leader in Medical Images

AI Startups in Healthcare

Startups – Medical Domain

Intracranial Hemorrhage

HealthMind

tically identify

on head CT imaging

Diabetic Retinopathy

Our algorithm accurately identifies the

We focus on decreasing the radiologist's readtime of lung cancer scans. Artificial intelligence approaches can identify nodules with higher

Malignent 92% similarity 28.7mm diameter Medium spiculatio

Healthmind

- Deep Learning startups
- Intracranial Hemorrhage dataset more than 30M (Virtual Radiologic)

Intracranial Hemorrhage

Our algorithms automatically identify intracranial hemorrhage on head CT imaging with very high accuracy--optimizing workflow and saving time when every minute counts.

Our algorithm accurately identifies the presence of diabetic retinopathy, a leading cause of blindness in the US, which can result in immediate, accurate detection of this disease.

Lung Nodule

We focus on decreasing the radiologist's read*time* of lung cancer scans. Artificial intelligence approaches can identify nodules with higher accuracy and lower false-positive rates.

Enlitic

- Medical + Deep learning startup found by Jeremy Howard
- Analysis several datasets such as medical images, doctors' notes and EMR
- A variety of visualization

Clarifai

 With collaboration with endoscopic technology startup i-Nside, and based on more than 100, 000 ear images, Clarifai has built diagnostic API for identifying ear problems.

Butterfly Network

- Device + Deep Learning + Cloud
- 3D ultrasound device => cloud => diagnosis by deep learning

MedyMatch

- Using AI Technology to Prevent Stroke
 - Instant intra-cranial hemorrhage detection

Arterys

4D Flow

• Visualize and Quantify Heart Flow in Realtime using MRI

VUNO

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Company Business Overview

VUNO is solving problems in medical domain using deep learning/machine learning

VUNO-Med

- Autonomous categorization/quantification of disease based on extensive medical data
- Provision of supportive Information to physicians for efficient clinical decision making (Pre-/Post- Screening)
- Visualization of extracted information and knowledge for better understanding of patients

Deep Learning-based Medical Data Analytics Platform

VunoNet is our proprietary deep learning engine.

* Tech giants like Google/Facebook lead general-purpose open source deep learning engines

- Open source deep learning engines are late for adopting latest techniques in deep learning. Open source engines are also hard to optimize to individual deep learning tasks.
- VunoNet was developed in order to optimize deep learning engines to our specific needs and implement most recent breakthroughs

VunoNet, is performance-oriented flexible deep learning engine.

✤ By using VunoNet, accurate models can be trained faster.

- In our benchmark test against open-source deep learning frameworks, more accurate models could be trained order of

• TIMIT is a one of the most popular benchmark dataset for speech recognition task (Text Instrument – MIT)

• WR1(World Record) - "Speech Recognition with Deep Recurrent Neural Networks", Alex Graves, ICCASP(2013)

WR2(World Record) – "Kaggle Competition: <u>https://www.kaggle.com/c/cifar-10</u>"

VunoNet support state-of-the art deep learning techniques effciently

Sased on Cuda, Cudnn and other GPU-optimized techniques, VunoNet is continuously expanding its capability and efficiency.

Layers	Tasks	Optimization and Miscs
Convolution	Classification	Multi-GPU Support
Pooling	Regression	ResNet Building Blocks
LSTM	Localization	Dropout for RNNs
MD-LSTM	Semantic Segmentation	Initialization for ReLUs
Spatial Pyramid Pooling	Connectionist Temporal Classification	Batch Normalization
Fully Connected		Dropout
Concatenation		Data Augmentation

VUNO's Deep learning Technology matches those of global giants

Won 5th place in ILSVRC, the Olympics of Deep learning (2015.12)

ILSVRC 2015 (ImageNet Large Scale Visual Recognition Challenge)

Selected as 5 deep learning startups to follow in 2016

5 deep learning startups to follow in 2016 Jordan Novet December 25, 2015 6:30 AM TAGE: ARTIFICIAL INTELLIGENCE, DEEP INSTINCT, DEEP LEARNING, LUNIT, NNAISENSE, TERADEEP, VBREWIND, VUNO

Above: Part of the Vuno tear Image Credit: Vuno

So much has happened this year in the world of deep learning, that trendy type of artificial intelligence that entails training artificial neural networks on large data sets and then getting them to make inferences about new data.

It's gone. Undo What was wrong with this ad?

Irrelevant

Repetitive

There have been technical breakthroughs, acquisitions, funding deals, open source releases in the field, and even the establishment of a nonprofit research lab backed by the likes of Elon Musk and Peter Thiel.

All of the startups I included in my roundup "5 deep learning startups to follow in 2015" (as well as others, like Clarifa) have made progress of some kind this year. Now, as we wrap up 2015 and get ready for 2016, a different set of deep learning startups are top of mind for me.

Google

http://venturebeat.com/2015/12/25/5-deep-learning-startups-to-follow-in-2016/

Deep learning supports diagnosis by autonomously extracting features from data

- * Classification/prediction algorithm development based on big data and deep learning algorithm
 - Field of medicine has amassed enormous amount of data for decades, but they have not been utilized due to lack of means

We're accumulating our intellectual properties and references on the domain.

✤ 6 patents pending and 5 academic papers published or under review

Country	Application Number	Title	Data
KOR	-	Apparatus and Method for Bone Age Detection based on Deep Neural Network	201508
РСТ	-	Apparatus and Method for Generating and Analysis Image	201509
РСТ	-	Apparatus and Method for Medical image reading efficiency by increasing the user's attention information on the reading process	201509
РСТ	-	Apparatus and Method for Medical Information Service Provision based on Disease Model	201509
U.S	-	Image Generating Method and Apparatus, and Image Analyzing Method	201510
РСТ	-	Apparatus and Method for Bone Age Detection based on Deep Neural Network	201512

Country	Application Number	Title	Data
U.S.	RSNA	An efficient automatic classification platform for differentiation of sub-regional diseased patterns of diffuse infiltrative diseases on high resolution CT(HRCT) using a lung segmentation, non-linear binning, cascading SVM(support vector machine) and CNN(convolutional neural net) classification	201603
U.S.	Medical Physics	Deep learning-based classification of regional patterns of diffuse lung disease in HRCT to overcome interscanner variation	201512
U.S	RSNA	Accuracy enhancement with deep convolutional neural networks for classifying regional texture patterns of diffuse lung disease in HRCT	201512
KOR	Korea Information Processing Society	Scene Text Recognition based on Deep Learning	201502
KOR	Korean Society of Imaging Informatics in Medicine	Deep Learning based Feature Extraction Method for Medical Image Analysis	201401

Research & Development

Research history(est. ~ 2016.04)

Vuno has made accomplishments in medicine using Deep Learning

Research & Development

Lung CT quantification for DILD diagnosis

- Used Convolutional Neural Network optimized for medical image analysis to quantify lung CT
- ✤ Capable of quantifying CT image into 6 classes through deep learning model.
- Model showed exceptionally good results even though CT images were from different vendor machines (GE, Siemens), and different

locations (Korea, U.S)

(a) Normal lung parenchyma, (b) ground-glass opacity, (c) consolidation,(d) reticular opacity, (e) emphysema, and (f) honeycombing.

[Convolutional Neural Network architecture]

Lung CT segmentation/quantification for DILD diagnosis

- ✤ 6~8% performance improvement compared to existing best research. Notable stability dealing with multi scanner, multi center images
- Accuracy analysis (Normal vs Emphysema, Honeycombing vs Reticular Opacity) showed superiority of deep learning model
- RSNA 2015 presentation, Medical Physics journal submission (under review)

Ctudy Cat		Improvement				
Sludy Sel	SVM	SVM p-Value		p-Value	improvement	
Intra-Scanner Set	89.53 ± 2.15	< 0.001	96.09 ± 1.41	< 0.001	6.56%	
Integrated Scanner Set	88.07 ± 1.63	< 0.001	95.12 ± 1.91	< 0.001	7.05%	
Inter-Scanner Set	77.14 ± 3.25	< 0.001	85.59 ± 2.17	< 0.001	8.45%	

Ctuchy Cat	# of Conv.	Classification	Error Rate (%)					
Study Set	Layer	Accuracy (%)	N > E ^{*1}	$E > N^{*2}$	$H > R^{\star 3}$	$R > H^{*4}$		
Integrated Scanner Set	1	81.27 ± 1.57	14.92	22.81	14.71	17.11		
	2	90.67 ± 1.02	5.44	7.69	8.46	7.29		
	3	93.73 ± 0.71	2.50	1.46	7.14	6.13		
	4	95.12 ± 0.52	0.48	1.21	2.12	4.91		

Lung CT segmentation/quantification for DILD diagnosis

- Image Representation of analysis result is provided for lesion classification (Results from Image representation are very close match to medical expert opinion.
- Possible to monitor individual patient progress

Lung CT segmentation/quantification for DILD diagnosis

- Autonomous full lung analysis for detailed/high speed quantification and image representation
- Plan to incorporate search for similar cases and their lapse using quantified features to recommend best treatment plan

Segmentation of lung in CT for autonomous lung disease analysis

- To improve efficiency of lung disease analysis, lung is segmented from entire CT using convolutional neural networks
- Patch based learning using labeled masks of lung and location information.
- High speed segmentation of new lung CT by extracting Superpixel from CT

[Training Set of CT Scans] [Segmentation Mask]

[Convolutional Neural Network Architecture for Lung Segmentation]

Research & Development Segmentation of lung in CT for lung disease diagnosis(2/2)

Segmentation of lung in CT for autonomous lung disease diagnosis

- Performance tested on randomly selected fresh CT scans. Match accuracy: Tanimoto Score 94.3%, Superpixel Label 99.2%.
- MICCAI 2016 Workshop on Deep Learning in Medical Image Analysis(DLMIA) submission preparation in progress

Case	Accuracy	Superpixel Label		
4	0.9429	0.9461		
6	0.9315	0.9463		
11	0.9250	0.9372		
23	0.9456	0.9525		
27	0.9374	0.9418		
33	0.9434	0.9462		
42	0.9313	0.9359		
52	0.9298	0.9363		
97	0.9549	0.9677		
114	0.9429	0.9631		
127	0.9574	0.9623		
132	0.9464	0.9521		
135	0.9609	0.9648		
142	0.9500	0.9542		
145	0.9508	0.9544		

Wrist, hand X-ray based autonomous bone age prediction model development

- Convolutional Neural Network based model can return probability of wrist X-ray to be of certain bone age class
- High level match with expert reading based on Greulich & Pyle standard
- For a fresh wrist, hand X-ray, model will return 3 bone age classes with highest probability.3 class Accuracy is 96.22% (Female, 20classes)
- In addition to autonomous bone age prediction, model can be used to supplement doctor reading, screening possible false readings

Research & Development

Autonomous bone age assessment model example

- *
- Ready to be used in clinical setting *

VUNO	Label	Prob	Age	VUNO	Label	Prob	Age
Top 1	11	0.7134	7y 10m	Top 1	14	0.5282	7년10m
Top 2	12	0.1467	8y10m	Top 2	15	0.3565	8년10m
Тор 3	10	0.1309	6y10m	Тор 3	13	0.0664	6년10m
Reading	-	-	7y10m	reading	-	-	7년10m
Age	-	-	8y5m	Age	-	-	8년5m

[Autonomous Bone age assessment]

- Model prediction and expert reading show high correlation * Expert reading likely to be wrong if high distance from model prediction
 - Based on study of regular readings, there is high error rate in readings **

[R	egular	rea	ading	js]

	Age	reading	
	8y11m	8y10m	
Case	9y7m	9y	
L .	10y1m	14y	
Case 2-2	9y11m	9-10y	
	10y6m	7y10m	
	11y11m	11y	

VUNO	Label	Prob	Age	VUNO	Label	Prob	Age
Top 1	14	0.6452	11y	Top 1	15	0.6002	12y
Top 2	13	0.1709	10y	Top 2	14	0.2767	11y
Тор 3	15	0.1632	12y	Тор 3	16	0.1134	13y
reading	-	-	14y	reading	-	-	7y10m
Age	-	-	10y1m	Age	-	-	10y6m

[false reading monitoring]

Chronological age increasing. But expert reading varies greatly. -> high need monitoring for needed

Early prediction of Arrhythmia through EKG analysis using RNN

- EKG data from Ventricular defibrillator from Medtronic was used to produce early prediction model for arrhythmia
- Recurrent Neural Network, which excels in signal/voice analysis was used
- New deep learning based model bypasses preprocessing and feature extracting requirements of past model achieving better results and better stability.
- Target early prediction warning time is 10 minutes

[Research covered on national TV]

[Typical EKG graph]

Research & Development

Early prediction of Arrhythmia through EKG analysis using RNN

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- Recurrent Neural Network, which excels in signal/voice analysis was used
- New deep learning based model bypasses preprocessing and feature extracting requirements of past model achieving better

Early prediction of Arrhythmia through EKG(1/3)

Early prediction of Arrhythmia through EKG analysis using RNN

- Vuno performance 89.6% vs 76.6% best existing method
- Research for performance improvement is underway
- Additional research for faster prediction(10m prior to 1h prior),

and lower false positive rate is underway

	RNN	RNN with EB Removal
1	0.7763	0.8964
2	0.8043	0.8882
3	0.7319	0.8898
4	0.8092	0.8487
5	0.7730	0.8799
Mean	0.7789	0.8806
Std.	0.0309	0.0188

[prediction accuracy]

Train Error Test Error 0.2 100 150 300

[prediction model learning curve]

Demo : VUNO-Med for DILD

Medical data analysis platform: VUNO-Med

- GUI Based lung analysis software based on DILD analysis research
- CBIR (Case Based Image Retrieval) technology based similar case search system development in progress
- Using GPU, real time lung image segmentation and similar case search will become an integral part of future PACS

Demo : VUNO-Med for DILD

Demo : VUNO-Med for Hand Bone Age Assessement

Putting The World's Medical Data to Work

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