

Machine Learning in Ophthalmic Diagnostics

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- Nidek
- Topcon
- Quark

Outline

- What is artificial intelligence / machine learning / deep learning?
- Types of machine learning tasks
 - Supervised learning
 - Unsupervised learning
- Deep learning
- Applications in ophthalmic diagnostics

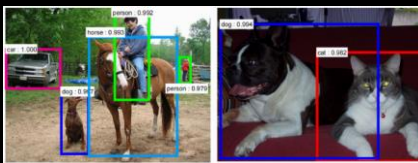
Machine learning is changing our lives



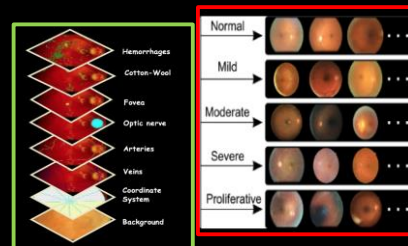
Recommendation Engines



Autonomous Driving



Object Recognition



Ophthalmology

What is artificial intelligence (AI), machine learning and deep learning?

WHY DEEP LEARNING IS SUDDENLY CHANGING YOUR LIFE

Fortune Magazine: September 28, 2016 by Roger Parloff

A GLOSSARY OF ARTIFICIAL-INTELLIGENCE TERMS

- **ARTIFICIAL INTELLIGENCE**

AI is the broadest term, applying to any technique that enables computers to mimic human intelligence, using logic, if-then rules, decision trees, and machine learning (including deep learning).

- **MACHINE LEARNING**

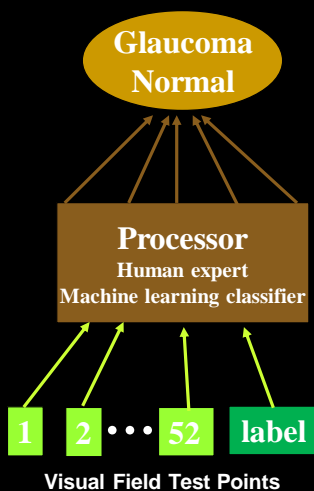
The subset of AI that includes abstruse statistical techniques that enable machines to improve at tasks with experience. The category includes deep learning.

- **DEEP LEARNING**

The subset of machine learning composed of algorithms that permit software to train itself to perform tasks, like speech and image recognition, by exposing multilayered neural networks to vast amounts of data.

Types of Machine Learning Tasks

Supervised learning
(labeled data)

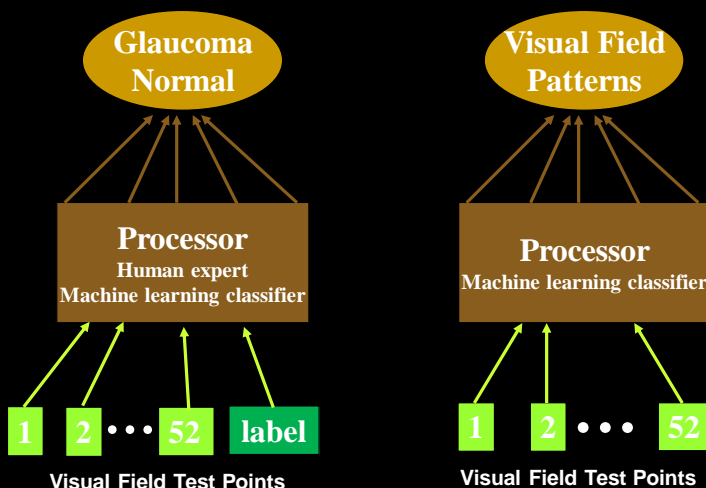


Courtesy of Michael Goldbaum MD

Types of Machine Learning Tasks

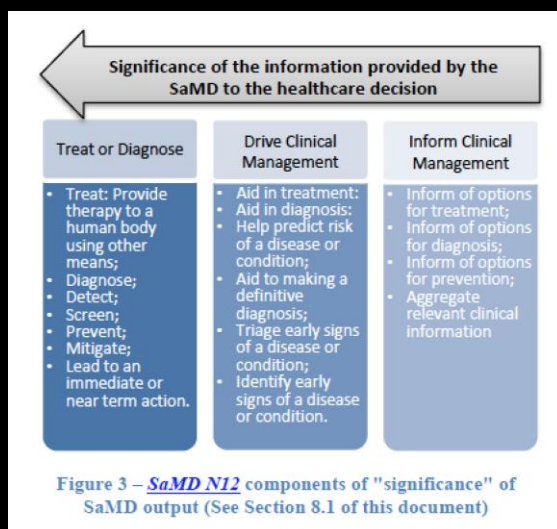
Supervised learning
(labeled data)

Unsupervised learning
(unlabeled data)



Courtesy of Michael Goldbaum MD

Machine Learning Applications: 3 categories of Software as a Medical Device (From: FDA draft guidance Aug 2016)



Machine Learning in Ophthalmic Diagnostics 1990-2017

Early Applications in Ophthalmology early 1990s and 2000s

Supervised

- To detect glaucomatous visual field damage
- To detect retinal disease and retinal lesions

1990s: Detection of glaucomatous visual field damage

Interpretation of Automated Perimetry for Glaucoma by Neural Network

Michael H. Goldbaum,* Pamela A. Sample,* Halbert White,§ Brad Côté,*
Paul Raphaelian,* Robert D. Fechtner,† and Robert N. Weinreb*

IOVS 1994;35:3362-3373

Purpose. Neural networks were trained to interpret the visual fields from an automated perimeter. The authors evaluated the reliability of the trained neural networks to discriminate between normal eyes and eyes with glaucoma.

Methods. Inclusion criteria for glaucomatous and normal eyes were the intraocular pressure and the appearance of the optic nerve; previous visual fields were not used. The authors compared the backpropagation learning method used by automated neural networks to those used by two specialists in glaucoma to classify the central 24° automated perimetric visual fields from 60 normal and 60 glaucomatous eyes.

Results. The glaucoma experts and a trained two-layered network were each correct at approximately 67%. The average sensitivity of this test was 59% for the two glaucoma specialists and 65% for the two-layered network. The corresponding specificities were 74% and 71% for the specialists and the two-layered network, respectively. The experts and the network were in agreement about 74% of the time, which indicated no significant disagreement between the methods of testing. Feature analysis with a one-layered network determined the most important visual field positions.

Conclusions. The authors conclude that a neural network can be taught to be as proficient as a trained reader in interpreting visual fields for glaucoma. Invest Ophthalmol Vis Sci.

Presented at ARVO 1990

1990s: Detection of glaucomatous visual field damage

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Conclusions: "...A neural network can be taught to be as proficient as a trained reader in interpreting visual fields for glaucoma."

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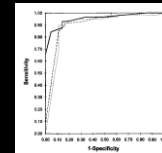
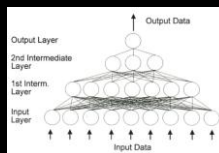
Presented at ARVO 1990

1990s and 2000s (selected examples): Detection of glaucomatous damage and progression

Neural Networks to Identify Glaucoma With Structural and Functional Measurements

L. BRIGATTI, M.D., D. HOFFMAN, B.A.,
AND J. CAPRIOLI, M.D.

AJO 1996; 121:511-521



Automatic Detection of Glaucomatous Visual Field Progression With Neural Networks

Luca Brigatti, MD, Kourou Nouri-Mahdavi, MD, Marc Weitzman, MD, Joseph Caprioli, MD

Arch Ophthalmol 1997; 115:725-728

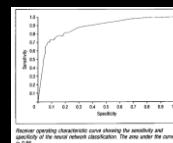
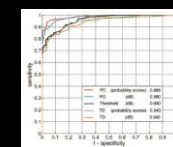


Figure showing characteristic curve showing the sensitivity and specificity of the neural network classification. The area under the curve is 0.88.

Effects of Input Data on the Performance of a Neural Network in Distinguishing Normal and Glaucomatous Visual Fields

Boel Bengtsson, Dimitrios Ixtos, and Anders Heijl

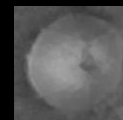
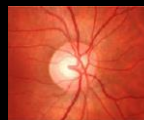
IOVS 2005; 46:3730-3736



Glaucoma risk index: Automated glaucoma detection from color fundus images

Rüdiger Bock^{1,2}, Jörg Meier³, László G. Nyúl¹, Joachim Hornegger^{1,2}, Georg Michelson^{1,2,4}

Medical Image Analysis 2010;14:471-481



1990s and 2000s (selected examples): Detection of retinal lesions and diabetic retinopathy

Detection of Blood Vessels in Retinal Images Using Two-Dimensional Matched Filters

SUBHASIS CHAUDHURI, STUDENT MEMBER, IEEE, SHANKAR CHATTERJEE, MEMBER, IEEE,
NORMAN KATZ, MARK NELSON, AND MICHAEL GOLDBAUM

IEEE Trans Med Imaging 1989;8:263-9

Automatic detection of diabetic retinopathy using an artificial neural network: a screening tool.

G G Gardner, D Keating, T H Williamson and A T Elliott

Br J Ophthalmol 1996; 80 937-938

AUTOMATED DIAGNOSIS AND IMAGE UNDERSTANDING WITH OBJECT EXTRACTION, OBJECT CLASSIFICATION, AND INFERENCE IN RETINAL IMAGES

Michael Goldbaum, Saeed Moazzzi, Adam Taylor, Shankar Chatterjee, Jeff Boyd, Edward Hunter, and Ramesh Jain

Proceedings: IEEE Intl Cong of Image Processing:1996;695-598

Automated detection of microaneurysms in digital re- free photographs: a diabetic retinopathy screening tool

J. H. Hipwell^a, F. Strachant, J. A. Olson^a, K. C. McHardy^a, P. F. Sharp^a and
J. V. Forrester^b

Diab Med 2000;17:588-599

Screening for diabetic retinopathy using computer based image analysis and statistical classification

Bernhard M. Ege^{a,*}, Ole K. Hejlesen^a, Ole V. Larsen^a, Karina Møller^a,
Barry Jennings^b, David Kerr^b, David A. Cavan^b

Comp Methods and Prog in Biomedicine 2000;62:165-175

Automatic Detection of Red Lesions in Digital Color Fundus Photographs

Meindert Niemeijer^a, Bram van Ginneken, Member, IEEE, Joos Staal, Member, IEEE, Maria S. A. Suttorp-Schulten,
and Michael D. Abramoff, Member, IEEE

IEEE Trans Med Imaging 2005;24:584-592

Automated Detection and Differentiation of Drusen, Exudates, and Cotton-Wool Spots in Digital Color Fundus Photographs for Diabetic Retinopathy Diagnosis

Meindert Niemeijer^{1,2,3}, Bram van Ginneken^{1,2,3}, Sjoegheim R. Russell^{2,4},
Akinshi Mizutani, Graduate Student, Clara I. Sánchez, Member, IEEE, Bob Zhang,
Roberto Hornero, Member, IEEE, Mathieu Lamard, Chisako Muramatsu, Xiangjian Wu,
Guy Cazuguel, Member, IEEE, Jane You, Agustín Mayo, Qin Li, Yuji Hatamaka, Beatrice Cochener,
Christian Roux, Senior Member, IEEE, Fakhr Karay, María García, Student Member, IEEE,
Hiroshi Fujita, Member, IEEE, and Michael D. Abramoff, Member, IEEE

IOVS 2007;48: 2260 -2267

Automated grading for diabetic retinopathy: a large-scale audit using arbitration by clinical experts

Alan D Fleming,¹ Keith A Goatman,¹ Sam Philip,² Gordon J Prescott,³ Peter F Sharp,¹
John A Olson²

Br J Ophthalmol 2010;94:1606e1610

Retinopathy Online Challenge: Automatic Detection of Microaneurysms in Digital Color Fundus Photographs

Meindert Niemeijer^a, Bram van Ginneken, Member, IEEE, Michael J. Cree, Senior Member, IEEE,
Akinshi Mizutani, Graduate Student, Clara I. Sánchez, Member, IEEE, Bob Zhang,
Roberto Hornero, Member, IEEE, Mathieu Lamard, Chisako Muramatsu, Xiangjian Wu,
Guy Cazuguel, Member, IEEE, Jane You, Agustín Mayo, Qin Li, Yuji Hatamaka, Beatrice Cochener,
Christian Roux, Senior Member, IEEE, Fakhr Karay, María García, Student Member, IEEE,
Hiroshi Fujita, Member, IEEE, and Michael D. Abramoff, Member, IEEE

IEEE Trans Med Imaging 2010;29:185-194

Computer-aided diagnosis of diabetic retinopathy: A review

Muthu Rama Krishnan Mookiah ^{a,*}, U. Rajendra Acharya ^{a,b}, Chua Kuang Chua ^a,
Choo Min Lim ^a, E.Y.K. Ng ^c, Augustinus Laude ^d

Computers in Biology and Medicine 2013;43:2136–2155

Lesion Detection Literature Review: Segmentation of microaneurysms and hemorrhages.

Authors	Methods (dataset size)	Salient feature	Performance measure
Segmentation of MA			
Spencer et al. [125]	Morphological methods and matched filter (Not Available (NA))	Region growing	Sensitivity-82%, specificity-80%
Cree et al. [126]	Peak of correlation function and region growing (20)	Shape, intensity, and rule based classifier combination	Sensitivity-82%, specificity-84%
Frame et al. [128]	Matched filter, region growing, LDA, NN and Rule based method (88)	Circularity and grayscale intensity used to detect MA	Specificity-84%, specificity-85%
Hansen et al. [124]	Matched filter, region growing and Peak of correlation function (3)	Matched filter and region growing used to detect MA	Sensitivity-95.30% (DWT), sensitivity-93.00% (PFC)
Hipwell et al. [113]	Size and shape (3783)	Rule based classifier	Sensitivity-81%, specificity-91%
Sethuapathi [131]	RBCT and most operator (30)	Most operator sharpen the red lesion edges	Sensitivity-77.50%, specificity-88.20%
Stroeter and Cree [129]	Top-hat, matched filter and region growing (20)	Can detect MA with greater than ten pixels	Sensitivity-56%
Larsen et al. [131]	Size and shape (200)	Retinalyzer System	Red lesion detection specificity-71.4%
Usher et al. [131]	RBCT and most operator (1273)	Most operator sharpen the red lesion edges	Sensitivity-95.10%, specificity-96.30%
Narender [117]	Pixel classification using k-NN (140)	Performs well with pixel similarity, color, first and second order Gaussian filters	Sensitivity-100%, specificity-87%
Fleming et al. [131]	Contrast normalization and watershed retinal region growing method (144)	Contrast normalization discriminates MA and dots	Sensitivity-85.40%, specificity-83.10%
Walter et al. [121]	Gaussian filtering, top-hat (94)	Kernel density estimation with variable bandwidth	Sensitivity-88.3%
Hatazaka et al. [122]	Brightness correction and thresholding (125)	Fake Positive (FP) elimination in the non-contrast images	Sensitivity-80%, specificity-88%
Quebec et al. [123]	Optimal wavelet transform (120)	Automated selection of wavelet basis, subbands, and template-matching parameter	Sensitivity-89.62% (color), 90.24% (green filtered) and 93.74% (angiographs), specificity-85.50% (color), 89.75% (green filtered) and 91.67% (angiographs)
Zhang et al. [128]	Multi-scale correlation filtering and dynamic thresholding (89)	Automated selection of kernel sigma value to detect MA	Sensitivity-71.30%
Astal and Hajdu [134]	Ensemble-based system (1200)	High flexibility for different datasets	AUC-0.90
Lazar and Hajdu [130]	Directional cross-section profile features (60)	Able to distinguish blood vessel bifurcation and crossings from MA	ROC score-0.423
Segmentation of HEM			
Gardner [116]	NN (301)	Statistical threshold tuning	Sensitivity-73.80%
Zhang and Chutalap [132]	PCA and SVM (30)	Use of rotation and illumination invariance	TPR-89.10%
Fleming et al. [134]	Multi-scale, morphological technique and SVM (10846)	Discontinuity assessment method	Sensitivity-98.60%, specificity-95.50%

Computer-aided diagnosis of diabetic retinopathy: A review

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Computers in Biology and Medicine 2013;43:2136–2155

Literature review: Automated diabetic retinopathy detection methods

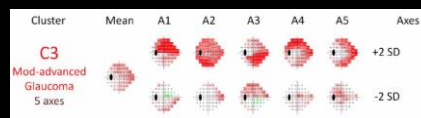
Authors	Features	Methods (Dataset size)	Salient feature	Performance measure
Two class classification				
Garrat et al. [152]	Pupil intensity	NN (301)	Statistical threshold tuning	Sensitivity-88.40%, specificity-83.50%
Osath et al. [154]	HEM, MA, hard exudates and cottonwool spots	FCM (142)	Precisely detect exudates	Accuracy-90.0%
Larsen et al. [156]	Red lesions	DR Visibility threshold (260)	Adjustable visibility thresholding	Sensitivity-96.70%, specificity-71.60%
Sethuapathi et al. [150]	HEM, MA, and hard exudates	NN (767)	Real time screening	Sensitivity-80.21%, specificity-70.66%
Hansen et al. [160]	Red lesions	DR Visibility threshold (83)	With and without pupil dilation	Sensitivity-97%, specificity-73%
Usher et al. [161]	HEM, MA, hard exudates and cottonwool spots	NN (1273)	Detects maculopathy also	Sensitivity-95.10%, specificity-86.30%
Abramoff et al. [27]	Web-based questionnaire, visual acuity measurement	EyeCheck software (876)	Tele diagnosis system	Inter-rater agreement-0.91
Neubauer et al. [153]	Retinal thickness	RFA (81)	RFA used for tele screening of DR	Sensitivity-93 (PDR)
Jittitt et al. [158]	MA	Weaknet automated MA detector (543)	Color non-multiplex images can be analyzed	Sensitivity-85%, specificity-90%
Khalil et al. [153]	MA	statistical learning (143)	Less computational time (10 m)	Sensitivity-100%, specificity-67%
Philip et al. [15]	MA and HEM	Wilson score and kappa statistic (527)	Adaptable to local imaging methods and equipments	Accuracy-95.1%
Apfel et al. [152]	HEM, MA, hard exudates and cottonwool spots	Kappa analysis (158)	Three-field strategy without pupil dilation	Degree of agreement-0.82 (single), 0.90 (three), 0.90 (mydriatic), 0.95 (non-mydriatic)
Sulthamman et al. [29]	Exudates	DR tele screening system (100)	Can handle images from various hospitals	Accuracy-92.5%
Agarwal et al. [157]	AM-IM features	Distance metrics (139)	Rapid retraining	ROC-0.98
Abramoff et al. [162]	MA, HEM, exudates, and CWS	k-NN classifier (16,776)	k can detect poor quality images	AUC-0.819
Dajani et al. [162]	MA, HEM, and exudates	k-NN classifier (761)	k can detect MA	Sensitivity-83.0%, specificity-72.7%
Queiroz et al. [151]	Optimal filter frame work	k-NN (67)	Detects drusen and large plaques also	AUC-0.827
Reza and Dawson [7]	Hard exudates, CWS, and large plaque of hard exudates	Rule based classifier (20)	Accurate grading of NPDR lesions	Accuracy-97%
Kevin Namaha et al. [158]	Wavelet energy features	SVM (240)	DRR	Accuracy-99.7%, sensitivity-99.17%, specificity-99.17%
Three class classification				
Lee et al. [163]	HEM, MA, exudates and CWS	NN (430)	High reproducibility	Normal-82.60%, Non-Proliferative Diabetic Retinopathy-82.60%, Proliferative Diabetic Retinopathy-88.30%
Nayak et al. [30]	Exudates, area of blood vessel, and contrast	NN (140)	Texture and morphological features	Sensitivity-90%, specificity-100% Accuracy-93%
Mookiah et al. [38]	Blood vessels and exudates area, information partition, global texture and entropy	GA optimized PNN classifier (156)	PNN tuning by GA and Particle Swarm Optimization (PSO)	Sensitivity-98.27%, specificity-96.08%, accuracy-96.15%
Four class classification				
Yun et al. [164]	Perimeter of the blood vessels	NN (124)	Morphological features	Sensitivity-90%, specificity-100%, accuracy-84%
Acharya et al. [165]	Co-occurrence matrix and run length matrix	SVM (238)	DRR	Sensitivity-98.9%, specificity-89.3%, accuracy-100%
Five class classification				
Acharya et al. [164]	Higher Order Spectra (HOS)	SVM (300)	Non-linear features	Sensitivity-82.50%, specificity-88.90%, accuracy-82%
Acharya et al. [167]	Blood vessel area, exudates, MA, and MA	SVM (31)	Morphological features	Sensitivity-82%, specificity-80%, accuracy-81.9%

Unsupervised Learning in Ophthalmic Diagnostics

Unsupervised algorithms can detect glaucomatous visual field patterns and progression without labeled data

PATTERNS OF GLAUCOMATOUS VISUAL FIELD LOSS IN SITA FIELDS AUTOMATICALLY IDENTIFIED USING INDEPENDENT COMPONENT ANALYSIS
 BY Michael H. Goldbaum MD,¹ Gil-Jun Jang PhD,² Chris Bowd PhD,³ Juechang Hao PhD,⁴ Linda M. Zangwill PhD,⁵ Jeffrey Liebmann MD,⁶ Christopher Girkin MD,⁷ Tzzy-Ping Jung PhD,⁸ Robert N. Weinreb MD,⁹ AND Pamela A. Sample PhD¹⁰

Trans Am Ophthalmol Soc 2009;107:136-175

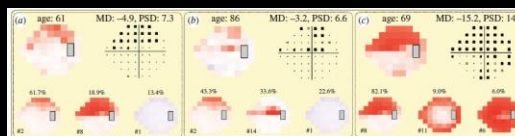


n=1147 normal and 939 glaucoma eyes

Patterns of functional vision loss in glaucoma determined with archetypal analysis

Tobias Elze^{1,2}, Louis R. Pasquale^{3,4}, Lucy Q. Shen⁵, Teresa C. Chen⁶, Janey J. Wiggins⁷ and Peter J. Bay¹

J R Soc Interface 2015;12: 20141118.

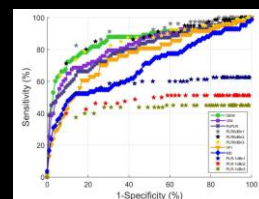


n=7300 subjects

Unsupervised Gaussian Mixture-Model With Expectation Maximization for Detecting Glaucomatous Progression in Standard Automated Perimetry Visual Fields

Siamak Yousefi¹, Madhusudhanan Balasubramanian², Michael H. Goldbaum³, Felipe A. Medeiros⁴, Linda M. Zangwill⁵, Robert N. Weinreb⁶, Jeffrey M. Liebmann⁷, Christopher A. Girkin⁸, and Christopher Bowd⁹

TSVT 2016;5:1-19



n= 1316 subjects (1976 eyes)

Tremendous Progress in Last 3 Years

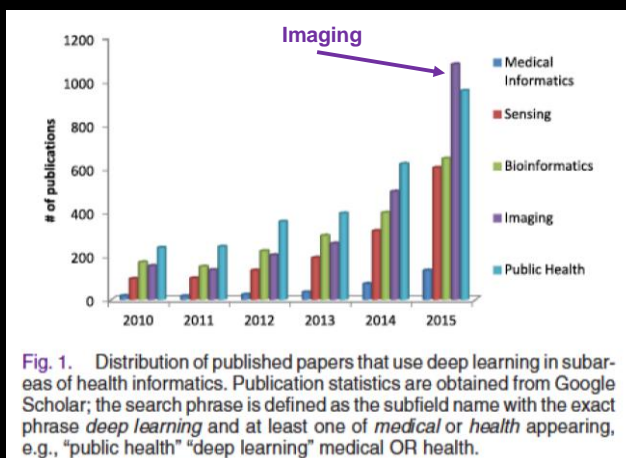
- Deep learning
- Availability of large datasets
- Computational power

IEEE JOURNAL OF BIOMEDICAL AND HEALTH INFORMATICS, VOL. 21, NO. 1, JANUARY 2017

EMBS IEEE ComSoc

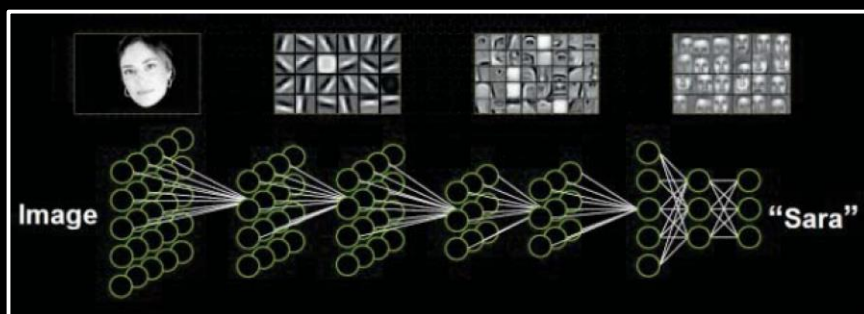
Deep Learning for Health Informatics

Daniele Ravi, Charence Wong, Fani Deligianni, Melissa Berthelot, Javier Andreu-Perez, Benny Lo, and Guang-Zhong Yang, *Fellow, IEEE*



Deep Learning Can be supervised or unsupervised

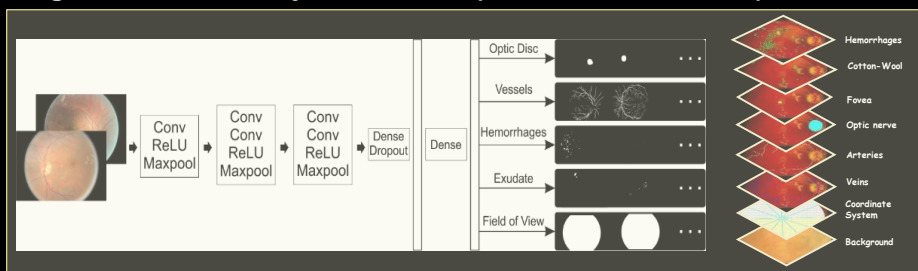
- Deep learning models highly complex relationships within data
- These models can understand complex patterns within images



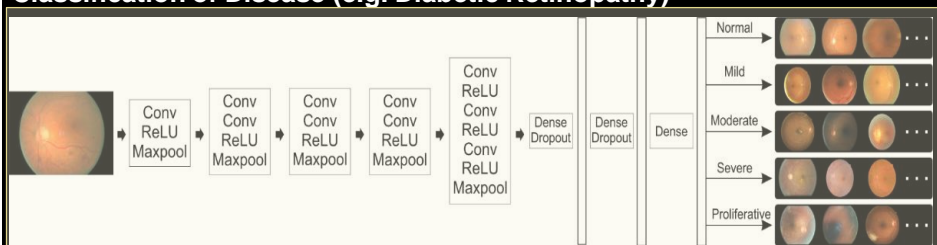
Courtesy of Michael Abramoff, MD, PhD

Deep Learning with Convolutional Neural Networks

Segmentation and Object Detection (Features/Lesions etc.)



Classification of Disease (e.g. Diabetic Retinopathy)



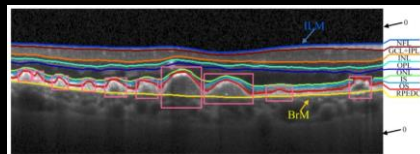
Courtesy of Michael Goldbaum, MD

Deep learning for OCT segmentation/ feature detection

Automatic segmentation of nine retinal layer boundaries in OCT images of non-exudative AMD patients using deep learning and graph search

LEYUAN FANG,^{1,2,*} DAVID CUNEFARE,¹ CHONG WANG,² ROBYN H. GUYMER,³ SHUTAO LI,² AND SINA FARSIU^{1,4}

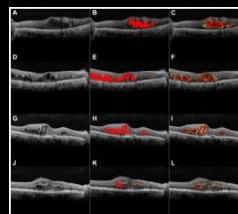
Biomed Optics Express 2017



Deep-learning based, automated segmentation of macular edema in optical coherence tomography

CECILIA S. LEE,¹ ARIEL J. TYRING,¹ NICOLAAS P. DERUYTER,³ YUE WU,¹ ARIEL ROKEM,⁴ AND AARON Y. LEE^{1,2,4,*}

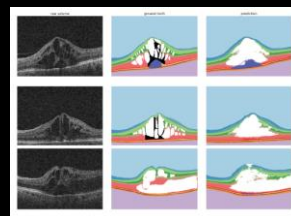
Biomed Optics Express 2017



Joint retinal layer and fluid segmentation in OCT scans of eyes with severe macular edema using unsupervised representation and auto-context

ALESSIO MONTUORO,^{1,2,*} SEBASTIAN M. WALDSTEIN,^{1,2} BIANCA S. GERENDAS,^{1,2} URSULA SCHMIDT-ERFURTH,^{1,2} AND HRVOJE BOGUNOVIĆ²

Biomed Opt Express; 2017;8:187-1888



Competitions Have Spurred Progress

**Kaggle Competition 2015
to classify 5 levels of severity of diabetic retinopathy
from photographs**

- 100,000 images of 50,000 patients generated by community clinic screening sites (EyePACs)
- Well-trained humans are compared to each other, ~80%
- 661 contestants
- Deep learning winner: 0.85 kappa

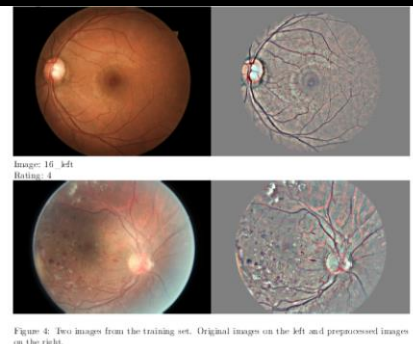


Figure 4: Two images from the training set. Original images on the left and preprocessed images on the right.

Kaggle Diabetic Retinopathy Detection competition report
Ben Graham, PhD
Department of Statistics and Centre for Complexity Science
University of Warwick, UK
August 6, 2015

Deep Learning for Diabetic Retinopathy Detection from fundus photographs (AUC*: 0.94 to 0.99)

Study	Training Datasets	Validation Dataset:
<p>Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning</p> <p>Michael David Abramoff,¹⁻³ Yiyue Lou,⁴ Ali Enginay,⁵ Warren Clarida,³ Ryan Amelton,³ James C. Folk,^{1,3} and Meindert Niemeijer⁶</p> <p><i>IOVS</i> 2016;57:5200-5206</p>	(n=10,000 to 1,250,000) depending on the lesion	MESSIDOR 2 (France) (n= 1748 Images, 874 pts) AUC = 0.98 (referable DR)
<p>Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs</p> <p>Varun Gulshan, PhD, Lijy Peng, MD, PhD, Marc Coram, PhD, Martin C. Stamp, PhD, Derek Wu, BS, Arunachalam Narayanaswamy, PhD, Subhojit Roy, PhD, Md. Kaziem Hossain, MD, Tom Madams, MSc, Jingsi Guo, PhD, Rajarajasekaran, MD, PhD, Ramasamy Ram, MD, PhD, Rishi Ramani, MD, PhD, Philip C. Nelson, BS, MSc, PhD, MEd, MPh, Dale R. Webster, PhD</p> <p><i>JAMA</i> 2016;316:2402-2410</p>	EyePACS U.S. & India (n=128,175) And transfer learning from Imagenet	AUC = 0.99 (referable DR)
<p>Automated Identification of Diabetic Retinopathy Using Deep Learning</p> <p>Rishab Gargya,¹ Theodore Leng, MD, MS²</p> <p><i>Ophthalmology</i> 2017: 124:962-969</p>	EyePACS (US) (n=75,137)	AUC = 0.94 (DR yes vs no)

*AUC = Area under receiver operating characteristic curve

Deep Learning for Diabetic Retinopathy Detection Opening the Black Box?

Study	Training Datasets	Validation Dataset:
<p>Automated Identification of Diabetic Retinopathy Using Deep Learning</p> <p>Rishab Gargya,¹ Theodore Leng, MD, MS²</p> <p><i>Ophthalmology</i> 2017: 124:962-969</p>	EyePACS (US) (n=75 137)	MESSIDOR 2 (France) (n= 1748 Images, 874 pts) AUC = 0.94 (DR yes vs no)

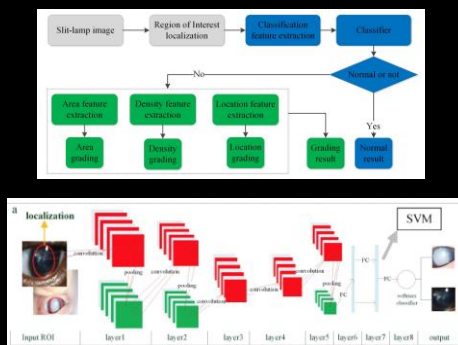
Automated generated heat maps identifying regions for closer examination by a clinician

Deep Learning: Automated diagnosis and grading of pediatric cataracts

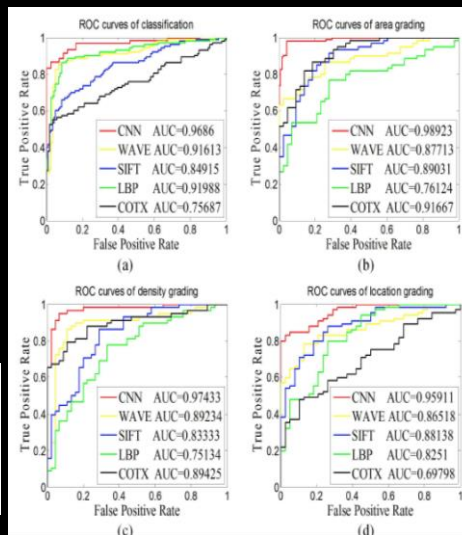
Localization and diagnosis framework for pediatric cataracts based on slit-lamp images using deep features of a convolutional neural network

Xiyang Liu^{1,2*}, Jiawei Jiang^{1*}, Kai Zhang¹, Erping Long³, Jiantao Cui¹, Mingmin Zhu¹, Yingying An¹, Jia Zhang¹, Zhenzhen Liu², Zhuoling Lin², Xiaoyan Li³, Jingjing Chen², Qianzhong Cao², Jing Li², Xiaohang Wu², Dongni Wang², Haotian Lin^{1*}

Plos One 2017;12:



n= 476 normal tissue,
n= 410 pediatric cataracts
4-fold cross-validation



2017 Ophthalmic Diagnostics: UK, India and Europe

OCT

Fundus Photos

News room > News releases > **March 2017**
IDx and IBM Watson Health Forge Alliance for Eye Health
 IBM Watson Health to Distribute IDx-DR Offering in European Economic Area



Fully Automated Diagnostic Device Receives CE Certification;
IDx LLC Planning for Rollout Across Europe

IDx LLC, a company focused on deploying cutting-edge technology to make medical diagnostics more effective, announced earlier today that its first commercial product, IDx-DR, has received CE approval as a Class IIa medical device. CE marking clears IDx-DR for sale in 31 countries that comprise the European Economic Area.

Advantages and Limitations of AI

Advantages

- Objective
- Reproducible
- Increases access to expert assessment
- Sensitivity/Specificity can be modified to match requirements for implementation
- Once model has been “trained,” can be inexpensively deployed

Limitations

- Large datasets needed for training/development for deep learning
 - DR: optimum 60000, 17000 referable DR images (Gulshan)
- High-quality annotations/labels needed
 - Weak labeling possible
- Black box
 - Some visualization already available
- Regulatory and other issues

JAMA 2017

VIEWPOINT

Unintended Consequences of Machine Learning in Medicine

Cabitza F, Rasoini R, Gensini GF. JAMA 2017;318:517-518

- **Reducing the Skills of Physicians** (evidence from radiology)
- **Focus on text (data) and the Demise of Context: Training set matters!**
 - Example: Machine learning based decision support system determined that patients with pneumonia and asthma were at a lower risk of death than patients with pneumonia but without asthma
 - Training set: Patients with asthma who presented with pneumonia were usually admitted directly to intensive care units to prevent complications; this led to patients with pneumonia and asthma having better outcomes
- **Intrinsic Uncertainty in Medicine**
- **The Need to Open the Machine Learning Black Box**

JAMA 2016

JAMA | Original Investigation | INNOVATIONS IN HEALTH CARE DELIVERY

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Naveen Subramanian, PhD; Lily Peng, MD, PhD; Marc Coran, PhD; Martin C. Stormer, PhD; Derek Wu, BS; Anurachalam Narayanasamy, PhD; Subhashini Venugopalan, MS; Kazumi Watanabe, MS; Tom Madams, MEng; Jorge Cuadros, MD, PhD; Ramaasamy Kim, MD, PhD; Raghav Ramani, MS, PhD; Philip C. Nelson, BS; Jessica L. Mages, MD, MPH; Dale R. Webster, PhD

EDITORIAL

Translating Artificial Intelligence Into Clinical Care

Andrew L. Beam, PhD; Isaac S. Kohane, MD, PhD

EDITORIAL

Artificial Intelligence With Deep Learning Technology Looks Into Diabetic Retinopathy Screening

Tian-Yi Wong, MD, PhD; Neil M. Bressler, MD

Unresolved Issues include (from Wong and Bressler):

- Requires a major mind-set shift in how clinicians and patients entrust clinical care to machines; both physicians and patients have to trust a “black box” to determine a disease state.

E.g.: Did machine assign referable diabetic retinopathy to eyes that had poorer pupil dilation and more severe cataract (because people with diabetic retinopathy are more likely to have these features) rather than based on the severity of the clinical diabetic retinopathy?

Future With AI/Deep Learning

- General algorithm for diagnosing retinal and other eye disease
- New scientific and clinical insights
- Reinventing the eye exam
- Seamless integration with electronic medical records and instrument software
- Black box will be opened
- The eye as a window into the body

Computer Science > Computer Vision and Pattern Recognition

Predicting Cardiovascular Risk Factors from Retinal Fundus Photographs using Deep Learning

Ryan Poplin, Avinash V. Varadarajan, Katy Blumer, Yun Liu, Michael V. McConnell, Greg S. Corrado, Lily Peng, Dale R. Webster

(Submitted on 31 Aug 2017 (v1), last revised 21 Sep 2017 (this version, v2))

<https://arxiv.org/pdf/1708.09843>

- Many constraints and unresolved issues

Thank you!

JAMA 2016

JAMA | Original Investigation | INNOVATIONS IN HEALTH CARE DELIVERY

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Vorun Gulshan, PhD, Jiyi Peng, MD, PhD, Marc Cozart, PhD, Martin C. Stampac, PhD, Deniz Wu, BS, Anurachalam Narayanaswamy, PhD, Subhojit Roy, PhD, Karam Mehta, MD, Tom Madams, MEng, Jingsi Guo, PhD, Rameshwar Him, MD, PhD, Raghav Ramani, MS, PhD, Philip C. Nelson, BS, Jessica L. Mages, MD, MPH, Dale R. Webster, PhD

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Challenges include (from Wong and Bressler):

3. How does such software “fit” in a clinical system?
 - a. Should the software be incorporated into retinal cameras and thus used at the point of care?
 - b. Should clinician simply trust the results without viewing the image?
 - c. Should centralized diabetic retinopathy reading centers be established in the United States and, more importantly, in low-resource settings where few ophthalmologists are available to care for all of the patients with diabetes?