Artificial Intelligence in Ophthalmology

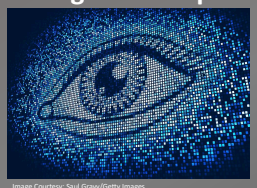

Image Courtesy: Saul Gravy/Getty Images

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Ophthalmology Resident
Casey Eye Institute
Oregon Health and Science University

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Overview

- Brief Introduction to Artificial Intelligence
- FDA Approval for Screening Diabetic Retinopathy
- Intraocular Lens Calculations with Artificial Intelligence
- Future Use with Retinopathy of Prematurity
- Summary

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What is Artificial Intelligence?

Applying learning to non-sentient entities like machines

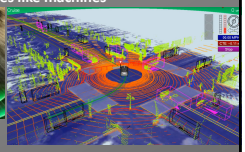

Image Courtesy: Digital Innovation and Transformation, Harvard Business School, 2016.

Image Courtesy: Mashable.Com, 2018

Image Courtesy: Amazon.com, 2018

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Why is Artificial Intelligence (AKA Machine Learning, Deep Learning) Useful?

- Scalability – Eye providers cannot necessarily screen millions at threat for specific diseases. For eyes, pictures are relatively easy to obtain. Interpreting them can be time consuming.
- Quantitative – Humans are subjective. Poor interobserver correlation. Algorithms give us quantitative, objective scores.
- Efficiency – Tracking disease progression much easier with quicker time to treatment.

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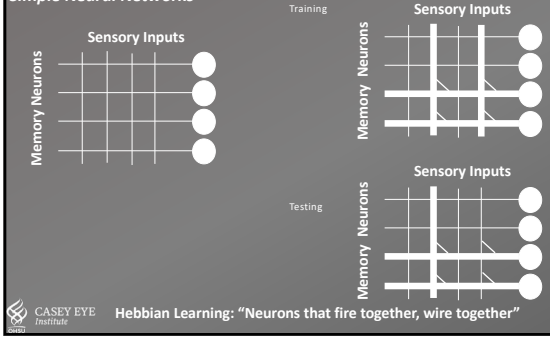
Simple Neural Networks



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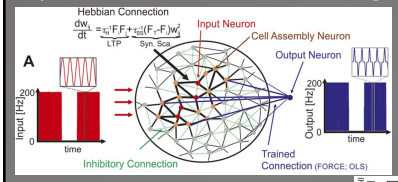
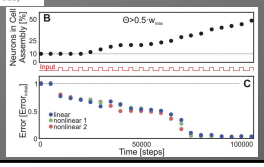
Hebbian Learning: "Neurons that fire together, wire together"

Complex Neural Networks with Hebbian Learning





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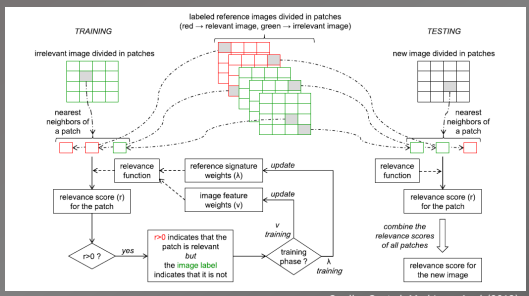
Tetzlaff C, et al. *Scientific Reports* (2015)

Example of Algorithm for Image Feature Extraction



Quellec G, et al. *Med Imag Anal.* (2012)

Pattern Recognition

Ophthalmology is inherently a pattern recognition heuristic to diagnose disease

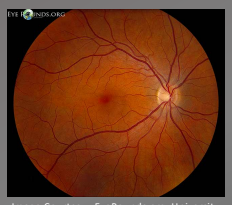


Image Courtesy: EyeRounds.org, University of Iowa Carver Medical School

NORMAL or ABNORMAL?

NORMAL

Pattern Recognition (cont'd)

Image Courtesy: EyeRounds.org, University of Iowa Carver Medical School

NORMAL or ABNORMAL?

ABNORMAL

What features are abnormal?

HUMANS ARE EXCELLENT AT PATTERN RECOGNITION!
BUT WE ARE TERRIBLE AT COMMUNICATING SUBJECTIVE FINDINGS

Applying Algorithm to Fundus Photo of Severe Non-Proliferative Diabetic Retinopathy (nPDR)

The Early Treatment Diabetic Retinopathy Study defined Severe nPDR:

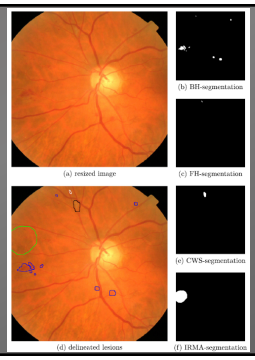
- 4 quadrants of 20 or more Microaneurysms, Dot Blot Hemorrhages, or Intraretinal Hemorrhages

OR

- 2 Quadrants of Venous Beading

OR

- 1 Quadrant of Intraretinal Microascular Abnormality



Quellec G, et al. *Med Imag Anal.* (2012)

IDx-DR – First FDA Approved Deep Learning Algorithm

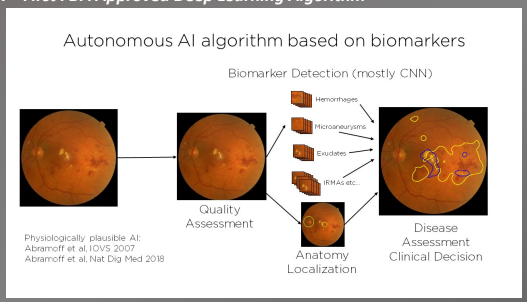


Image Courtesy: IDx-DR, www.eyediagnosis.net

IDx-DR – Intended Screening Guidance

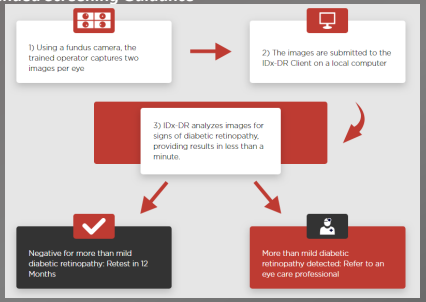


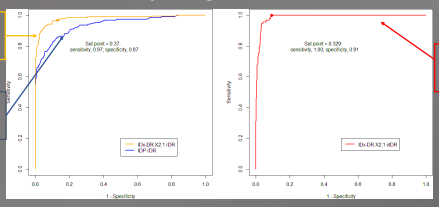
Image Courtesy: IDx-DR, www.eyediagnosis.net

IDx-DR – Validation

Receiver Operating Characteristic Curve

IDx-DR Area Under Curve: 0.980

IDP (3 Readers) Area Under Curve: 0.937



IDx-DR Area Under Curve: 0.989

Referral Diabetic Retinopathy (moderate nPDR or worse)

Vision threatening Diabetic Retinopathy (Severe nPDR or worse)

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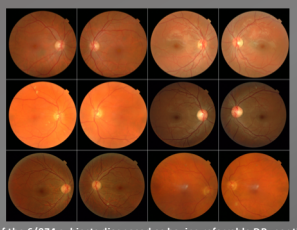
Abramoff MD, et al. *IVOS* (2016)

IDx-DR – Examples of False Negatives



Right and left eye images of the 6/874 subjects diagnosed as having referrable DR, per the adjudicated consensus of the retinal experts, that were false-negatives for the referral DR output (i.e., were missed by the device). All six subjects had consensus grading of moderate DR without ME.

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Abramoff MD, et al. *IVOS* (2016)

Artificial Intelligence in Intraocular Lens Calculations

Image Courtesy: ASCRS/ASOA Symposium 2015

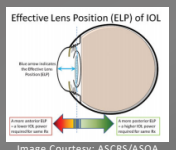

Image Courtesy: ASCRS/ASOA Symposium 2015

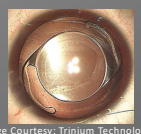

Image Courtesy: Trinium Technology, 2017

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Formula Optimization

STANDARD DOGMA

AL	Formula
<22mm	Hoffer Q
22mm - 26mm	Holladay 1
>26mm	SRK/T

Image Courtesy: ASCRS/ASOA Symposium 2015

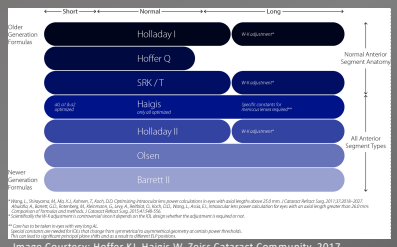

Image Courtesy: Hoffer KJ, Haigis W. Zeiss Cataract Community. 2017.

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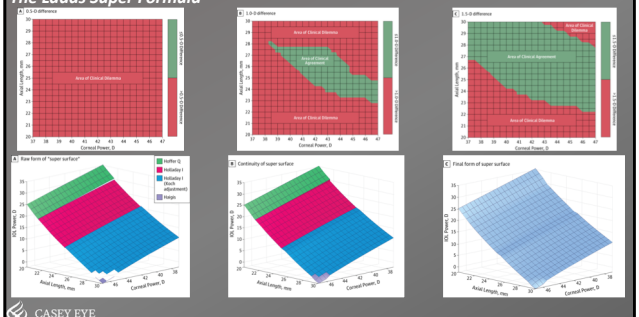
The Ladas Super Formula



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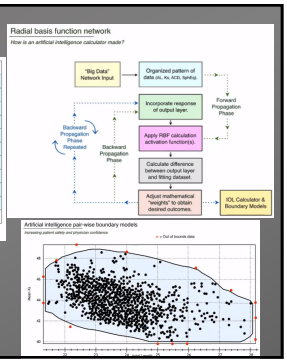
Ladas JG, et al. *JAMA Ophth* (2015)

The Hill-RBF Formula

Version 1.0 was based on 3400 surgeons inputting their data into the database

Number of Factors Selected	4	5	6	7	8	9
	PostOpSE	PostOpSE	PostOpSE	PostOpSE	PostOpSE	PostOpSE
	AL	AL	AL	AL	AL	AL
	Kmean	Kmean	Kmean	Kmean	Kmean	Kmean
		ACD	ACD	ACD	ACD	ACD
			PreOp SE	PreOp SE	PreOp SE	PreOp SE
				Age	Age	Age
					CCT	CCT
						WTW
Fitting Dataset ±0.50 D	92.1	97.8%	93.1	94.6	95.13	94.8
Validation Dataset ±0.50 D	82.6	90.2%	89.3	92.2	91.9	92.7
Number of Out-of Bounds Points	9	15	35	57	73	92
Ranking	6	1	5	2	3	4

The process is repeated and the factors that produce the best performing model are identified over time.



Hill WE, Haag-Streit AG EyeWorld Corporate Education Talk at ASCRS 2017.

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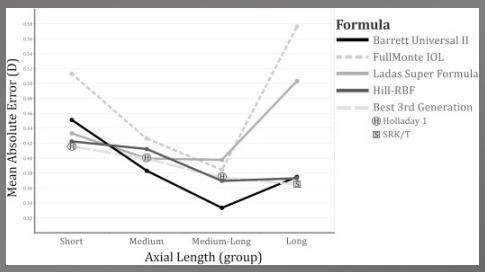
Inter-Formula Validation



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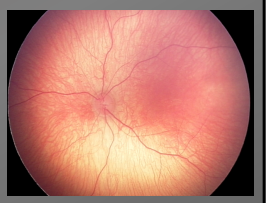
Kane JX, et al. *J. Cataract Refract Surg* (2017)

Retinopathy of Prematurity

Normal Retinal Development:
Nasal Development by 36 weeks Gestational Age
Temporal Development by 40 Weeks Gestational Age

- Premature infants can have maldevelopment of retina known as Retinopathy of Prematurity
- Screening usually performed in infants with…
  - Birth weight < 1500 g
  - gestational age ≤ 32 weeks
- Timing of initial eye exam based on gestational age at birth



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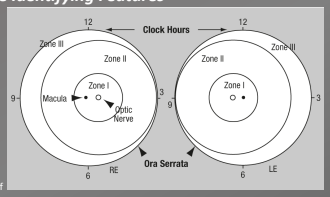
Retinopathy of Prematurity – Disease Identifying Features

- International Classification of Retinopathy of Prematurity (ICROP)
  - Zone
  - Stage
  - Extent
  - Presence of plus disease (vascular dilation and tortuosity)



International Committee for the Classification of Retinopathy of Prematurity. *Arch Ophthalmol* (2005).

WHEN TO TREAT:

ETROP Classification of ROP

Type 1
Zone I, any stage ROP with plus disease
Zone I, stage 3 ROP without plus disease
Zone II, stage 2 or 3 ROP with plus disease

Early Treatment for Retinopathy of Prematurity Cooperative Group. *Arch Ophthalmol* (2003).

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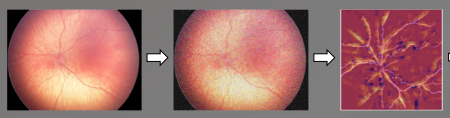
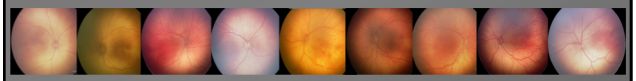
Retinopathy of Prematurity – Deep Learning

- Automated categorization of data representations



i-ROP
Continuous scores between 1 & 9



1 — 9

Continuous values between 1 & 9 designed to a categorize a spectrum of disease

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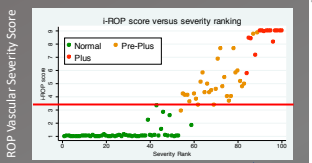
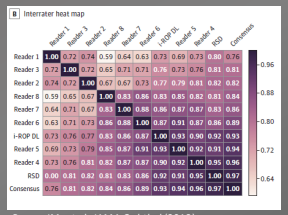
Retinopathy of Prematurity – Validation



Redd T, et al. *ARVO* 2018 Annual Meeting



Brown JM, et al. *JAMA Ophthal* (2018)

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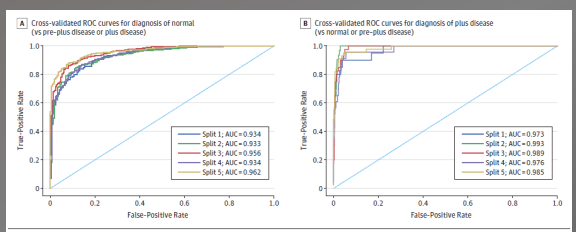
Retinopathy of Prematurity – Validation



Data were analyzed from 5-fold cross-validation of 5511 retinal images. Mean areas under the ROC curves (AUCs) for the 5 sets were 0.94 for identifying normal images (vs pre-plus disease or plus disease; A) and 0.98 for identifying plus disease images (vs normal or pre-plus disease; B).

Brown JM, et al. *JAMA Ophthal* (2018)

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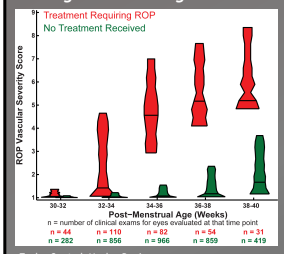
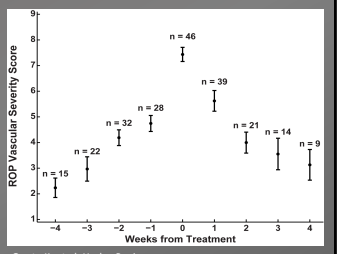
Retinopathy of Prematurity – Tracking Patient Changes with and without Treatment



Taylor S, et al. Under Review.



Gupta K, et al. Under Review.

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Summary

- Artificial intelligence assists in screening conditions with higher throughput than can be accommodated by eye providers.
- Diabetic Retinopathy, IOL Calculations, and Retinopathy of Prematurity all lend themselves to Machine Learning's efficiency and reproducibility with quantitative scoring.
- Machine learning will likely expand to other Ophthalmic and Non-Ophthalmic domains including Corneal Ectactic Disorders, Ocular tumors, etc.
- The purpose of AI is to augment the health care provider…

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Summary

…and not to replace the provider (or humankind) altogether.

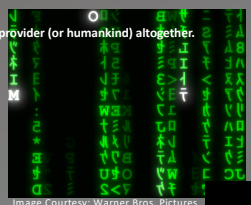

Image Courtesy: Warner Bros. Pictures

OpenAI built a text generator so good, it's considered too dangerous to release

Whittaker Z. TechCrunch. 2018.

Image Courtesy: 20th Century Fox

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References

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8. Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. *Arch Ophthalmol.* 21(12):1684-94. 2003.

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11. Taylor S, Campbell JP, Gupta K, Brown JM, et al. A quantitative severity scale for retinopathy of prematurity using deep learning: monitoring disease progression. Under review at *JAMA Ophthalmol.*
12. Gupta K, Campbell JP, Taylor S, Brown JM, et al. A quantitative severity scale for retinopathy of prematurity using deep learning: monitoring disease regression after treatment. Under review at *JAMA Ophthalmol.*

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