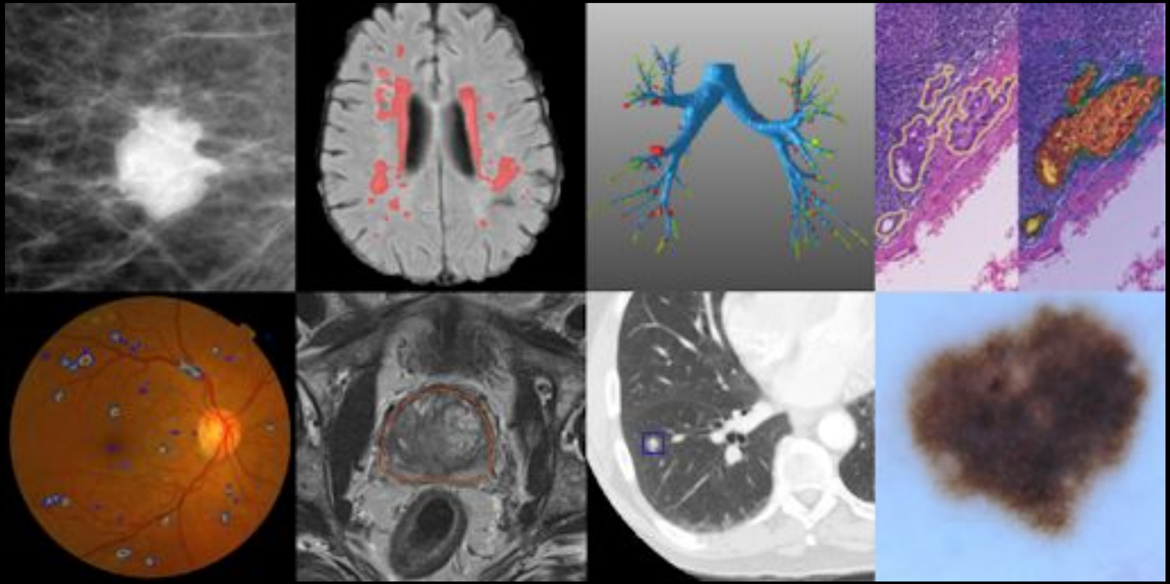
Multimodal Machine Learning Model to Support Medical Diagnosis on Eye Diseases

Santiago Toledo Cortés

Advisor:

Fabio A. González O.

Artificial Intelligence in Medicine



Deep learning represents the state of the art of the automatic image analysis for detection of ocular diseases.

Deep Learning Problems

Deep learning needs huge amounts of data: ~ 10^7	Biggest Eye Fundus Image dataset: ~ 10^4
Medical Images have different particular features	 ImageNet $\neq$  Tomography
Deep learning lacks interpretability	How to trust?

Artificial intelligence / Machine learning

Google's medical AI was super accurate in a lab. Real life was a different story.

If AI is really going to make a difference to patients we need to know how it works when real humans get their hands on it, in real situations.

by **Will Douglas Heaven**

April 27, 2020

Images acquisition is not standard!

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Images acquisition is not standard!

Some solutions

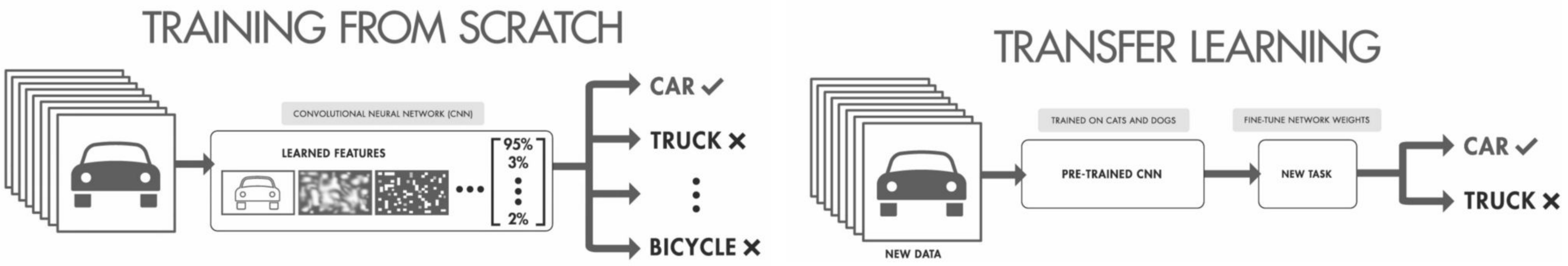
Transfer Learning

Classical Methods

Probabilistic Methods

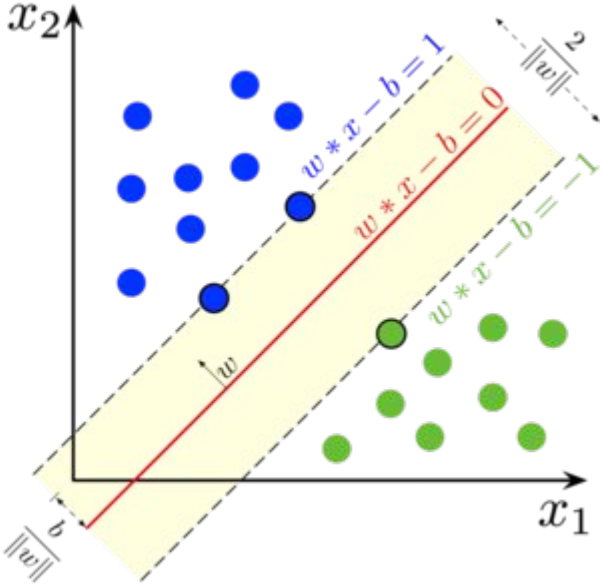
Some solutions

Transfer Learning Classical Methods Probabilistic Methods



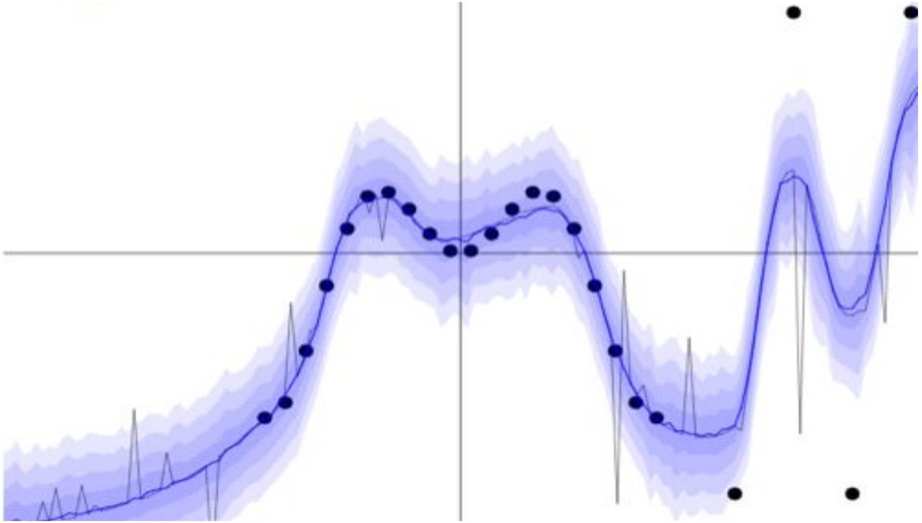
Some solutions

Transfer Learning | **Classical Methods** | Probabilistic Methods



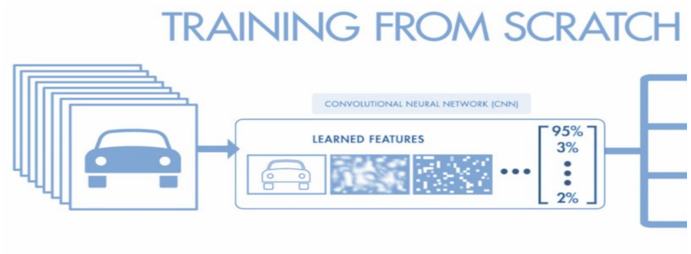
Some solutions

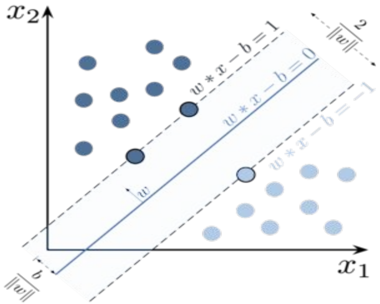
Transfer Learning Classical Methods **Probabilistic Methods**

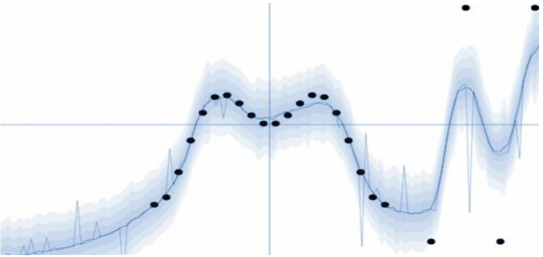


Some solutions

Transfer Learning | Classical Methods | Probabilistic Methods

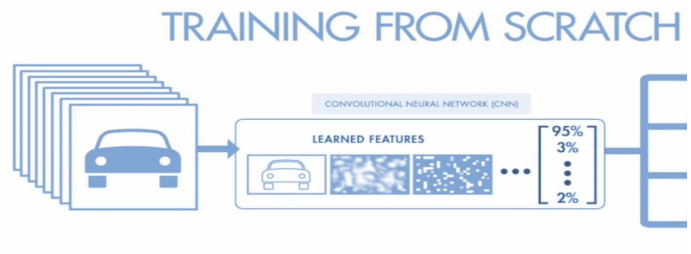


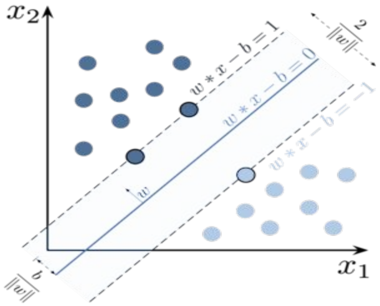


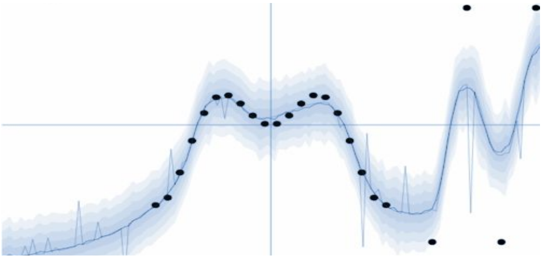


Some solutions

Transfer Learning | Classical Methods | Probabilistic Methods



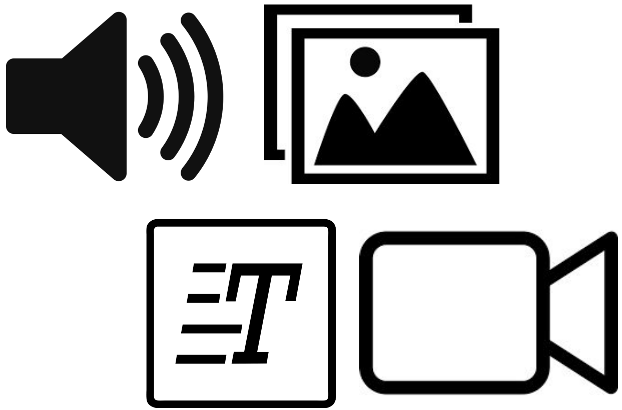




Learn from more sources of information

⬇

Multimodal Learning

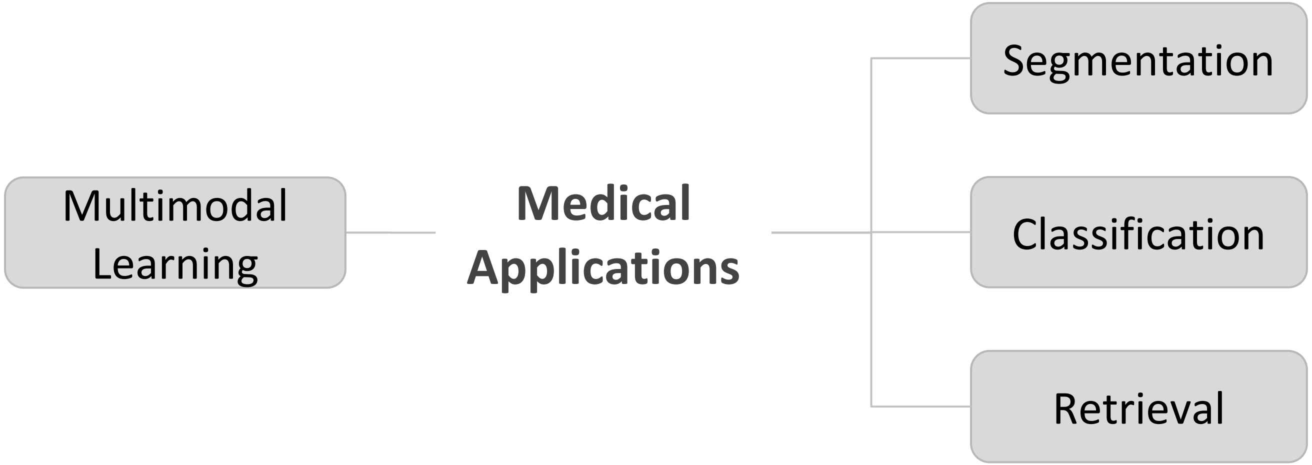


Representation

Fusion

Application

Multimodal approaches, leads to better results in terms of ***precision*** *and even* ***interpretability****, than methods trained with a single modality.*
[Andrearczyk 2018]


Multimodal Learning
Medical Applications
Segmentation
Classification
Retrieval

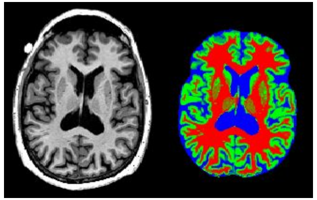
Segmentation

Classification

Retrieval

Brain Tissue

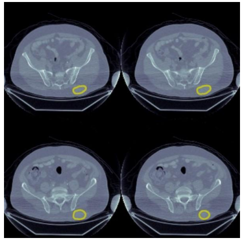
[137] [78]



T1 & T2

Soft Tissue Sarcoma

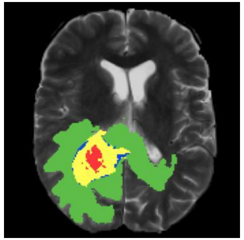
[39] [40]



MRI's
&
Tomographies

Brain Tumors

[22] [25] [30] [44] [54][76][111] [118]



T1 & T2

Segmentation

Classification

Retrieval

Alzheimer's

[91] [95] [135]

MRI's &
Electroencephalogram &
Positron-emission tomography

Glioblastoma

Skin Lesions

Thyroid

Cytopathology

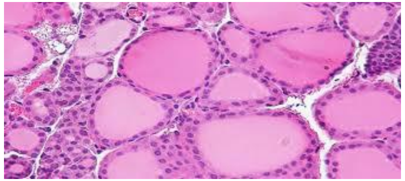
[52] [55] [130]

Images
&
Text
&
Categorical
&
Patient
Metadata

Segmentation

Classification

Retrieval



Histopathology

[13] [48] [49]

Text:
MRI's & Radiological Reports

OR

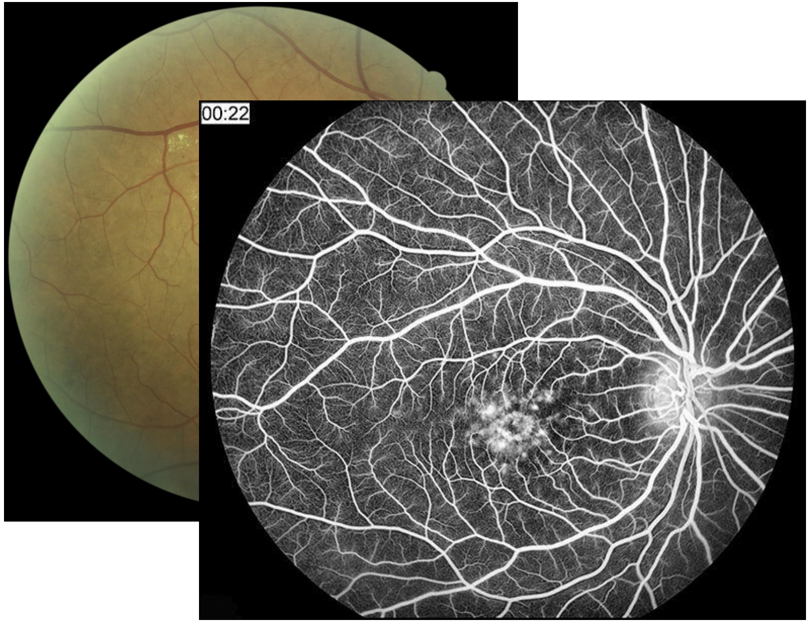
Whole Side Images & Text

Remarks

- **Performance improves** when compared with a **single modalit**y.
- Generation of models with **greater predictive capacity and robustness**.
- Different modalities can act like **soft labels**.
- Can be used to **find clinical correlations**.
- A **good balance** between modalities is needed.

Eye Fundus Image (EFI)

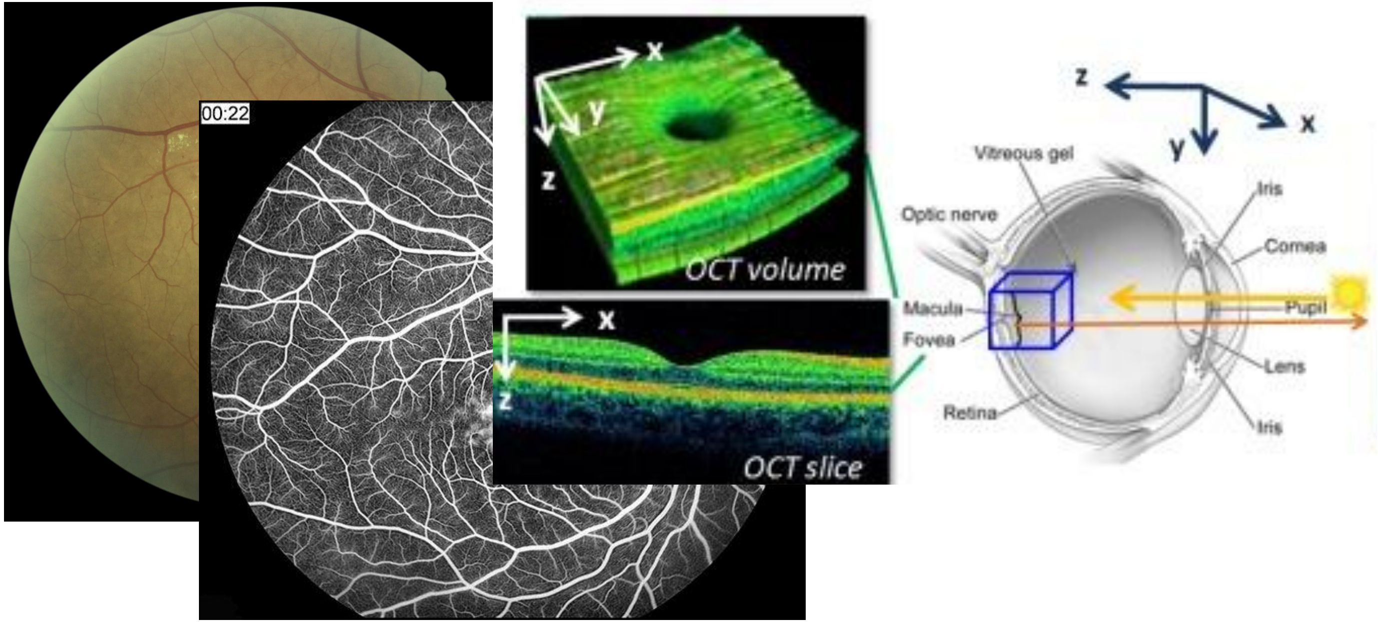
Eye Fundus Image (EFI)



Angiogram

Eye Fundus Image (EFI)

Optic Coherence Tomography (OCT)



Angiogram

Eye Fundus Image (EFI)

Optic Coherence Tomography (OCT)

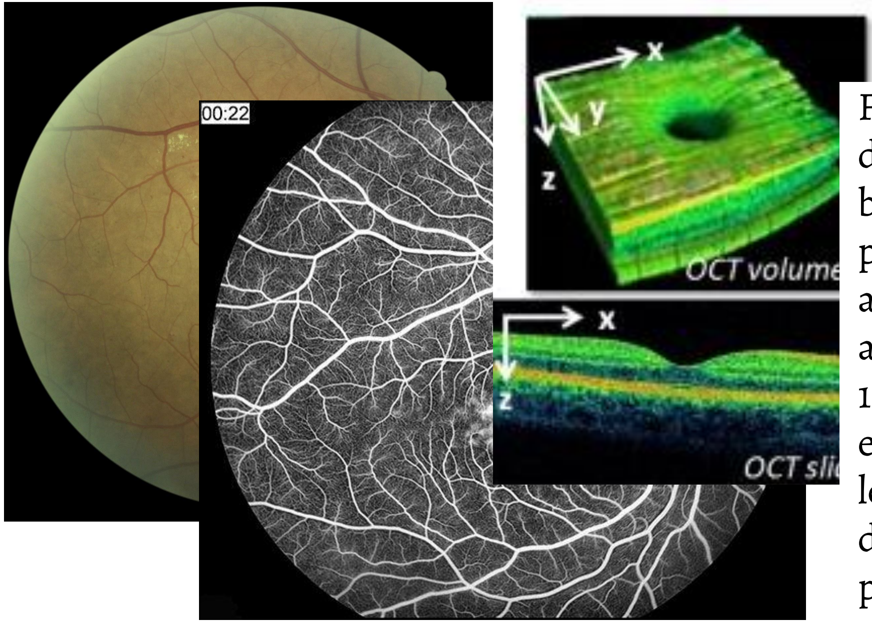


Foto a color de polo posterior de ojo derecho, medios transparentes, disco de bordes bien definidos con mínimas palidez, RCD de 0.4, se observa un adelgazamiento generalizado del árbol arterial, con relación arteriovenosa de 1.0:2.0, se observa en la región macular escasas lesiones amarillentas y múltiples lesiones en punto rojizas. Impresión diagnóstica Retinopatía diabética no proliferativa la leve, drusas maculares.

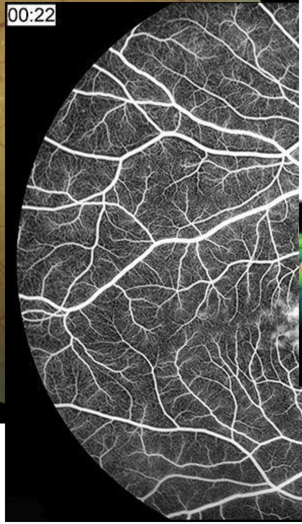
Angiogram

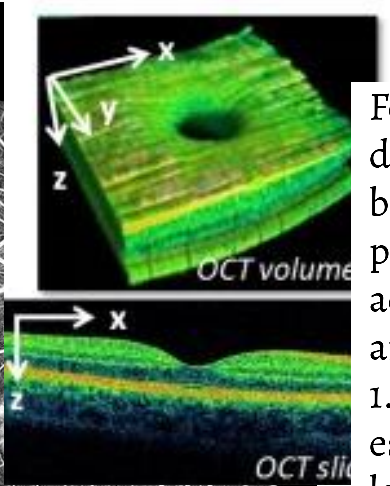
Medical Records

Eye Fundus Image (EFI)

Optic Coherence Tomography (OCT)

Clinical Records





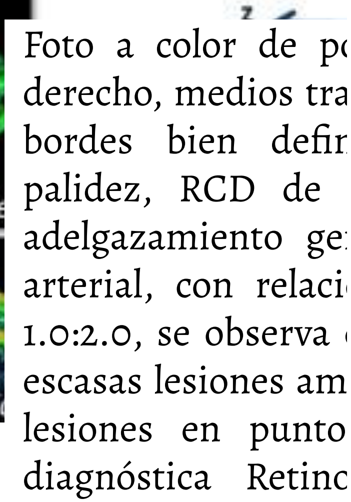
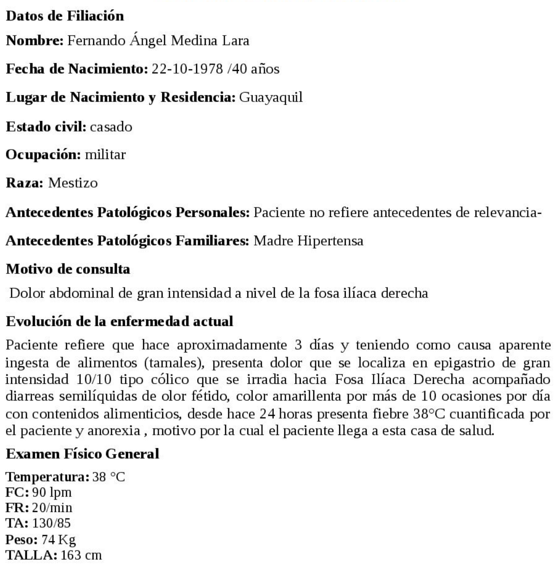


Foto a color de pc
derecho, medios tra
bordes bien defir
palidez, RCD de
adelgazamiento ge
arterial, con relaci
1.0:2.0, se observa
escasas lesiones am
lesiones en punto
diagnóstica Retinc
proliferativa la leve, drusas maculares.


Datos de Filiación

Nombre: Fernando Ángel Medina Lara

Fecha de Nacimiento: 22-10-1978 /40 años

Lugar de Nacimiento y Residencia: Guayaquil

Estado civil: casado

Ocupación: militar

Raza: Mestizo

Antecedentes Patológicos Personales: Paciente no refiere antecedentes de relevancia-

Antecedentes Patológicos Familiares: Madre Hipertensa

Motivo de consulta

Dolor abdominal de gran intensidad a nivel de la fosa ilíaca derecha

Evolución de la enfermedad actual

Paciente refiere que hace aproximadamente 3 días y teniendo como causa aparente ingesta de alimentos (tamales), presenta dolor que se localiza en epigastrio de gran intensidad 10/10 tipo cólico que se irradia hacia Fosa Ilíaca Derecha acompañado diarreas semilíquidas de olor fétido, color amarillenta por más de 10 ocasiones por día con contenidos alimenticios, desde hace 24 horas presenta fiebre 38°C cuantificada por el paciente y anorexia , motivo por la cual el paciente llega a esta casa de salud.

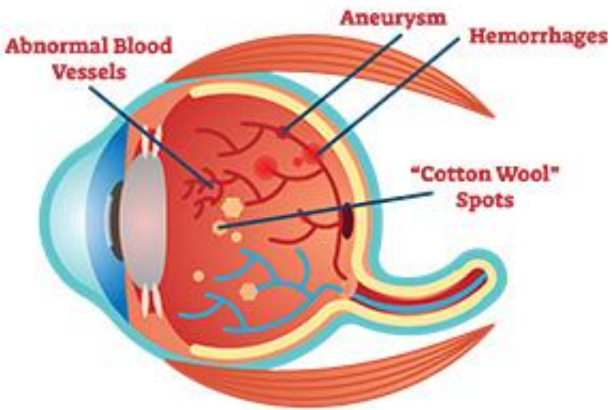
Examen Físico General

Temperatura: 38 °C
FC: 90 lpm
FR: 20/min
TA: 130/85
Peso: 74 Kg
TALLA: 163 cm

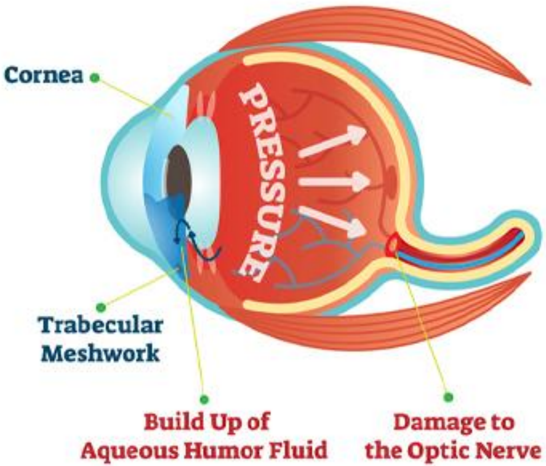
Angiogram

Medical Records

Diabetic Retinopathy (DR)

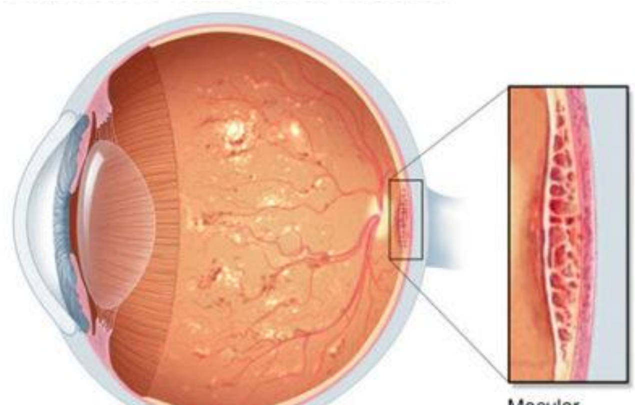


Glaucoma

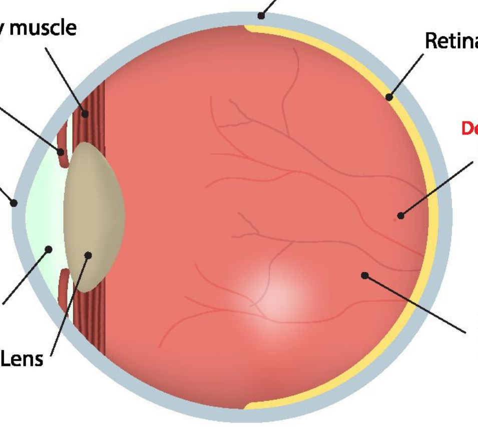


Source: American Optometric Association (AOA)

Diabetic Macular Edema (DME)



Macular Degeneration (AMD)



Source: American Optometric Association (AOA)

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Facultad de Ingeniería
Sede Bogotá

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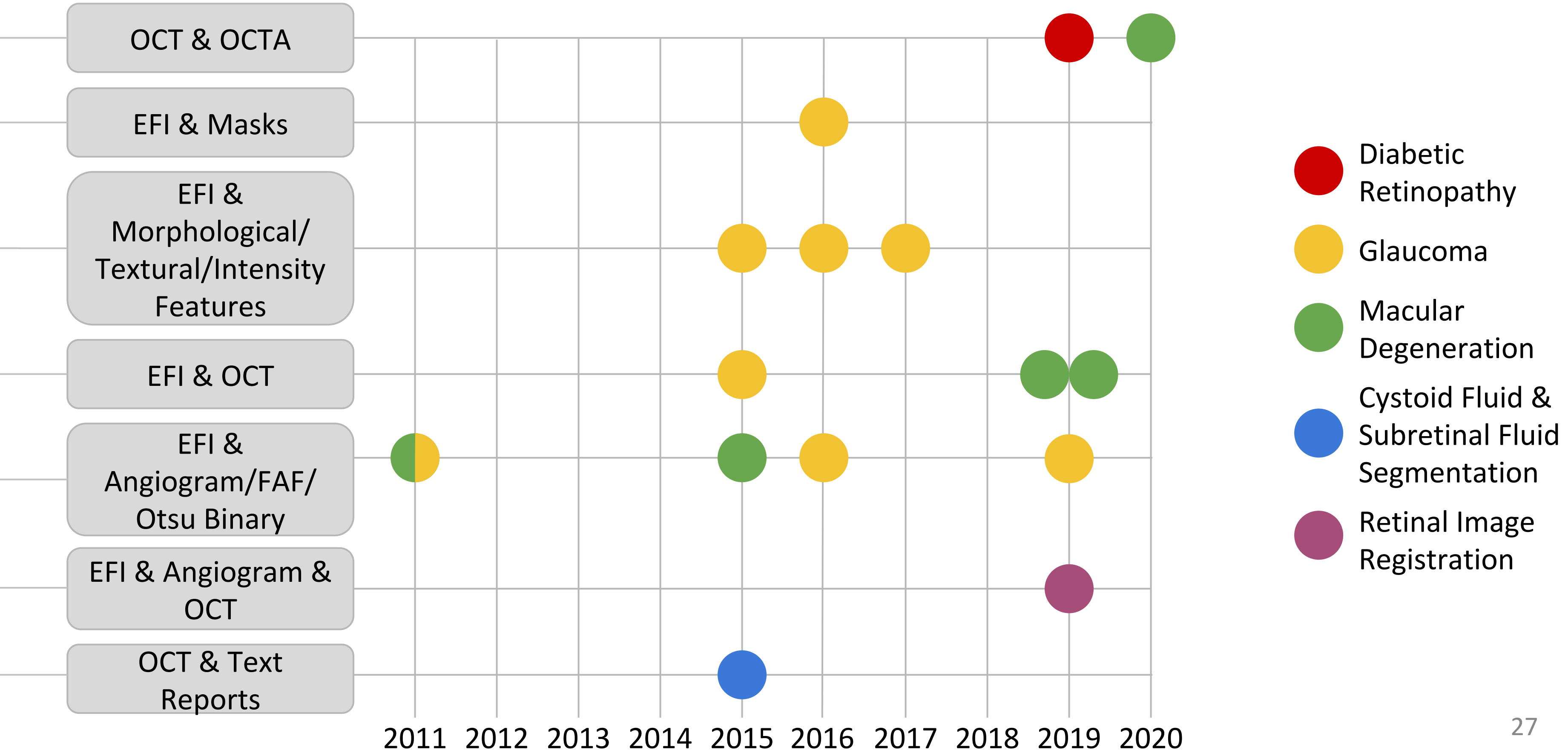
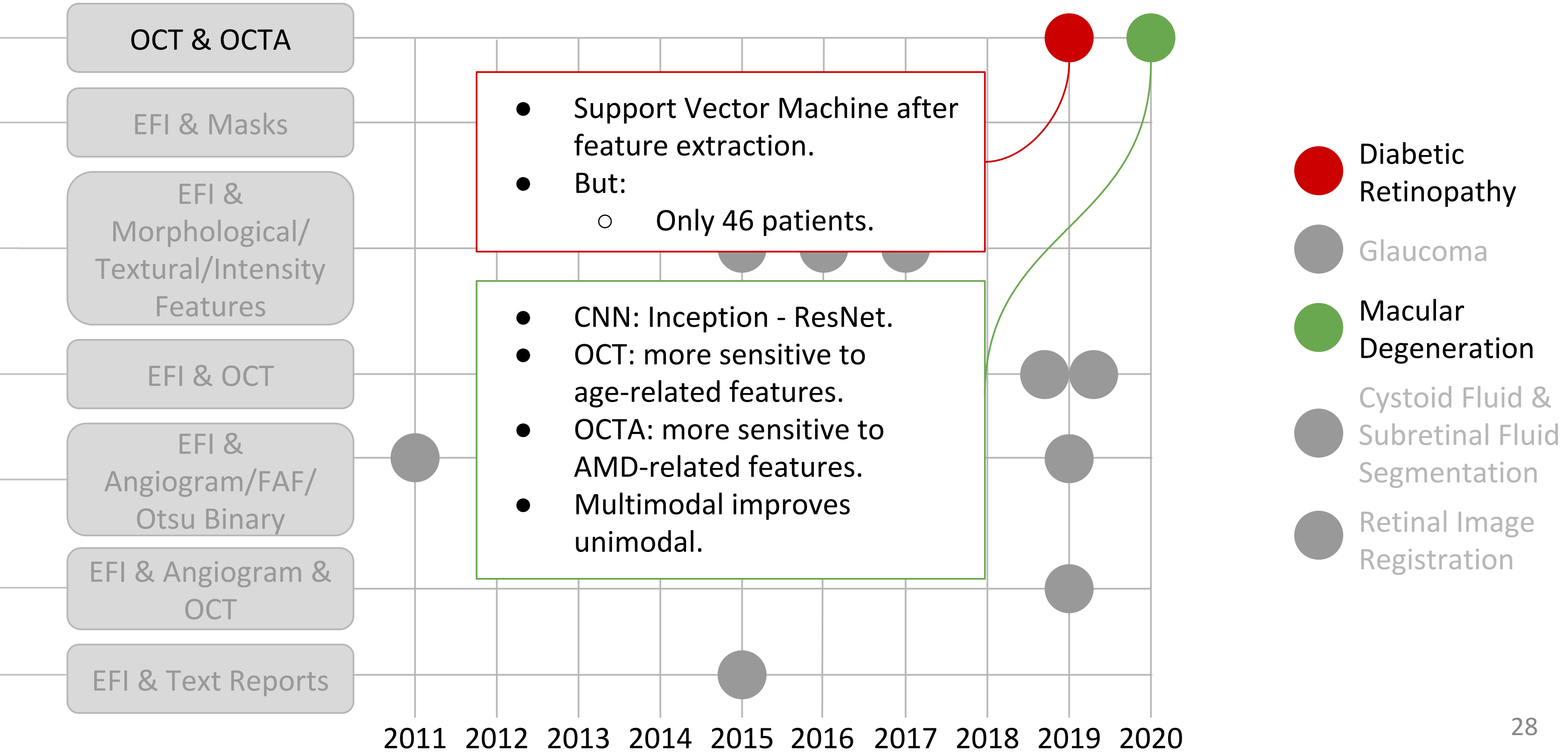
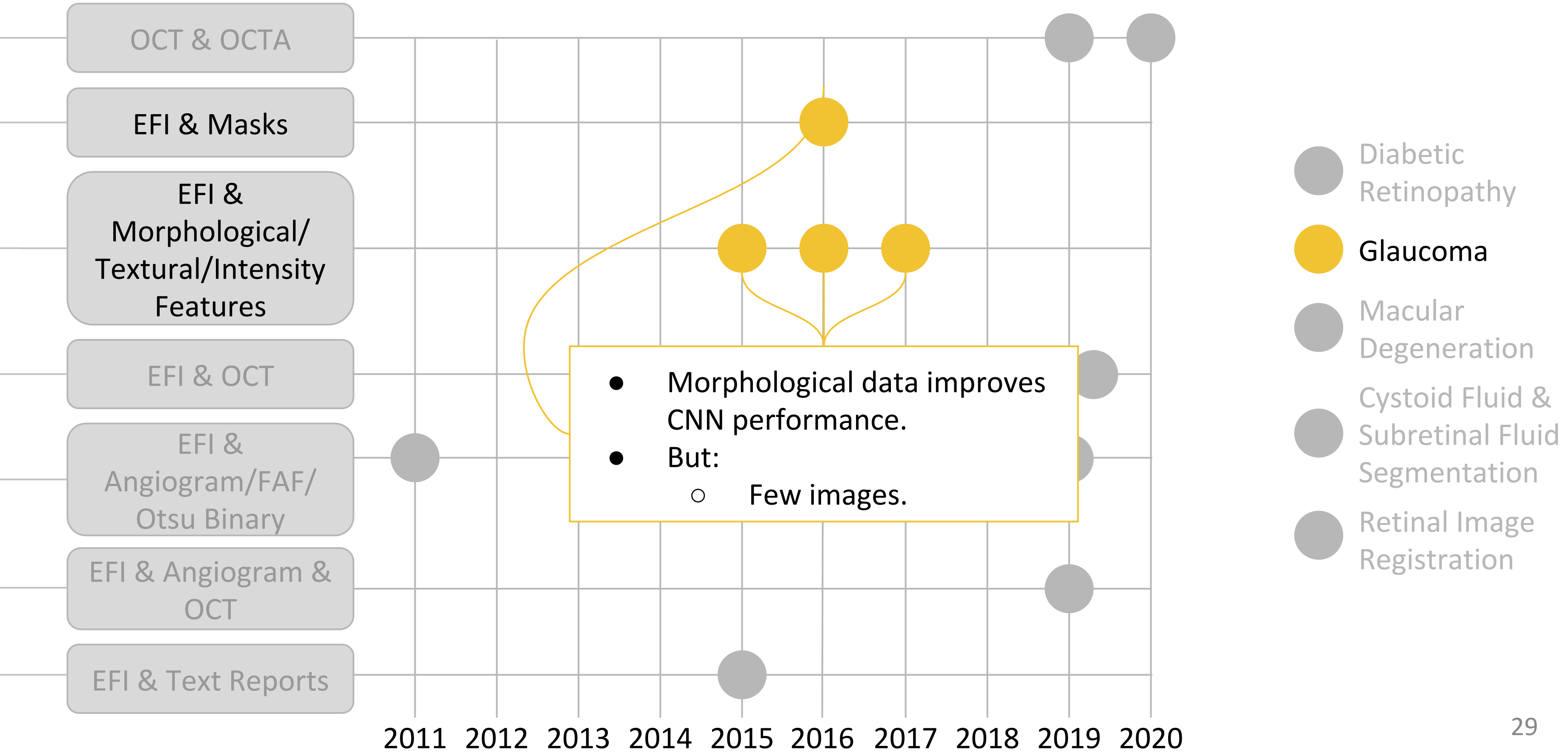
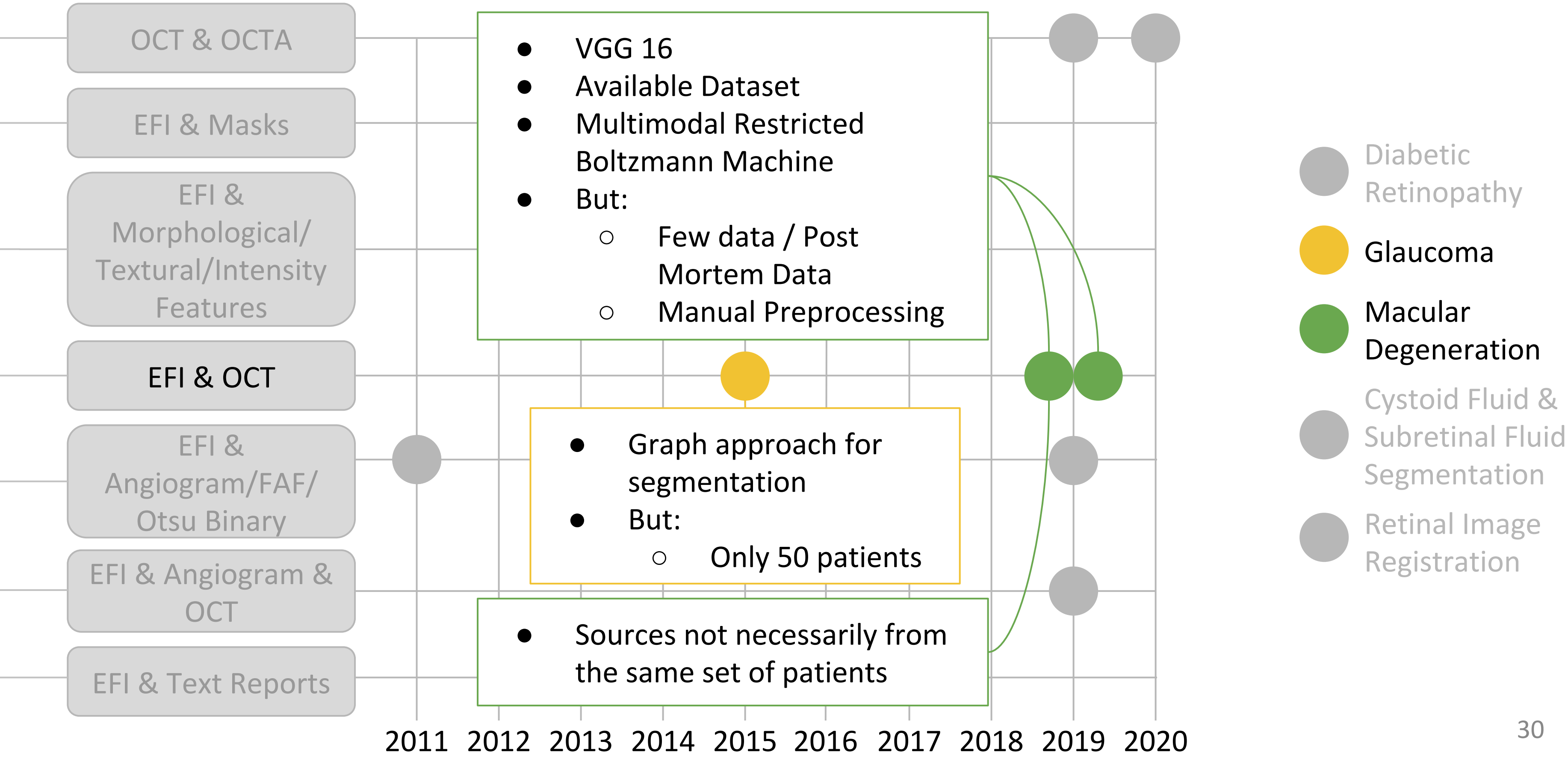




- Support Vector Machine after feature extraction.
- But:
  - Only 46 patients.

- CNN: Inception - ResNet.
- OCT: more sensitive to age-related features.
- OCTA: more sensitive to AMD-related features.
- Multimodal improves unimodal.


OCT & OCTA
EFI & Masks
EFI & Morphological/ Textural/Intensity Features
EFI & OCT
EFI & Angiogram/FAF/ Otsu Binary
EFI & Angiogram & OCT
EFI & Text Reports
Morphological data improves CNN performance.
But:
Few images.
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
Diabetic Retinopathy
Glaucoma
Macular Degeneration
Cystoid Fluid & Subretinal Fluid Segmentation
Retinal Image Registration


OCT & OCTA
EFI & Masks
EFI & Morphological/ Textural/Intensity Features
EFI & OCT
EFI & Angiogram/FAF/ Otsu Binary
EFI & Angiogram & OCT
EFI & Text Reports
VGG 16
Available Dataset
Multimodal Restricted Boltzmann Machine
But:
Few data / Post Mortem Data
Manual Preprocessing
Graph approach for segmentation
But:
Only 50 patients
Sources not necessarily from the same set of patients
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
Diabetic Retinopathy
Glaucoma
Macular Degeneration
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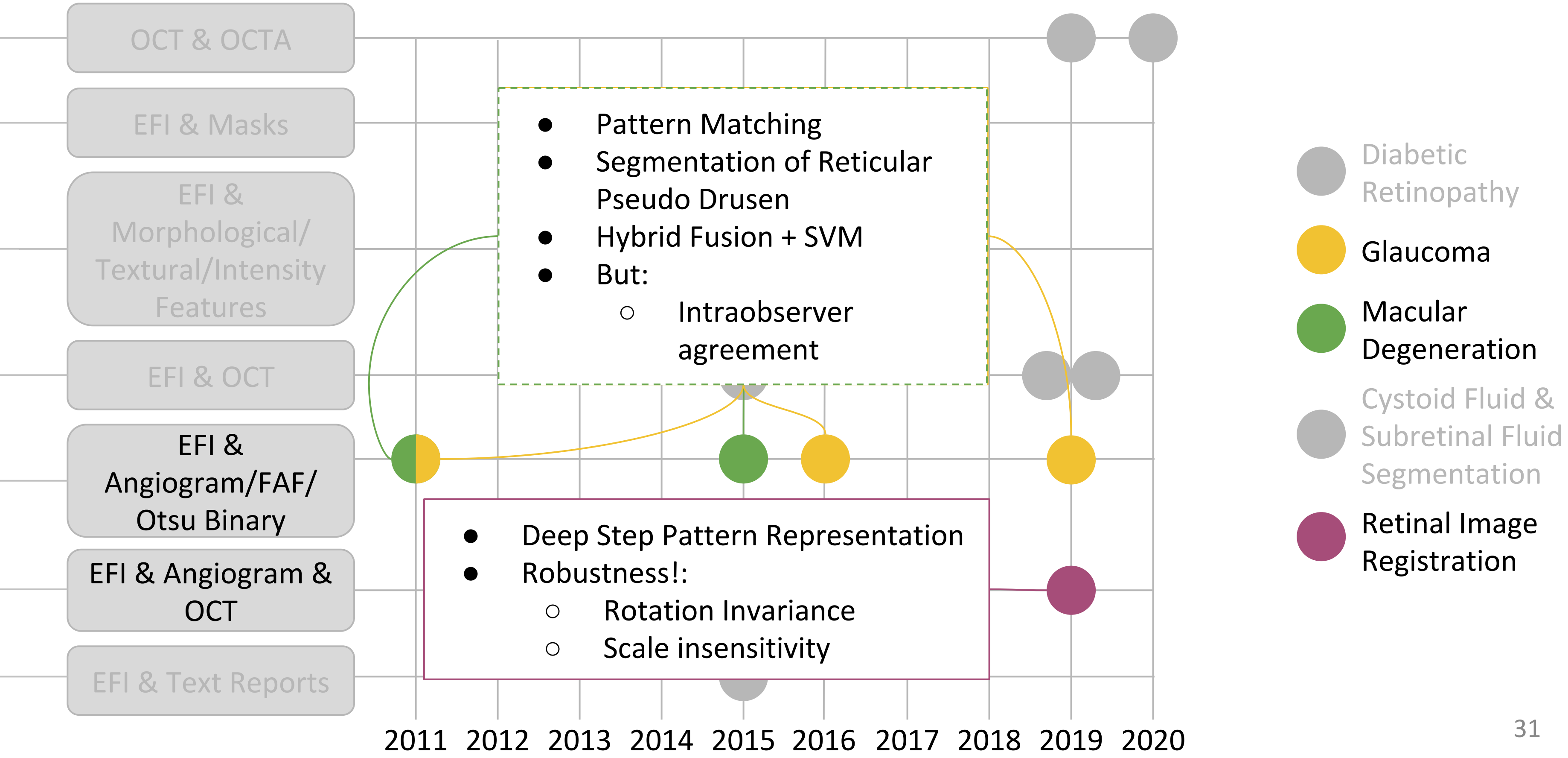
Retinal Image Registration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EFI & Angiogram & OCT
EFI & Text Reports
Pattern Matching
Segmentation of Reticular Pseudo Drusen
Hybrid Fusion + SVM
But:
Intraobserver agreement
Deep Step Pattern Representation
Robustness!:
Rotation Invariance
Scale insensitivity
2011
2012
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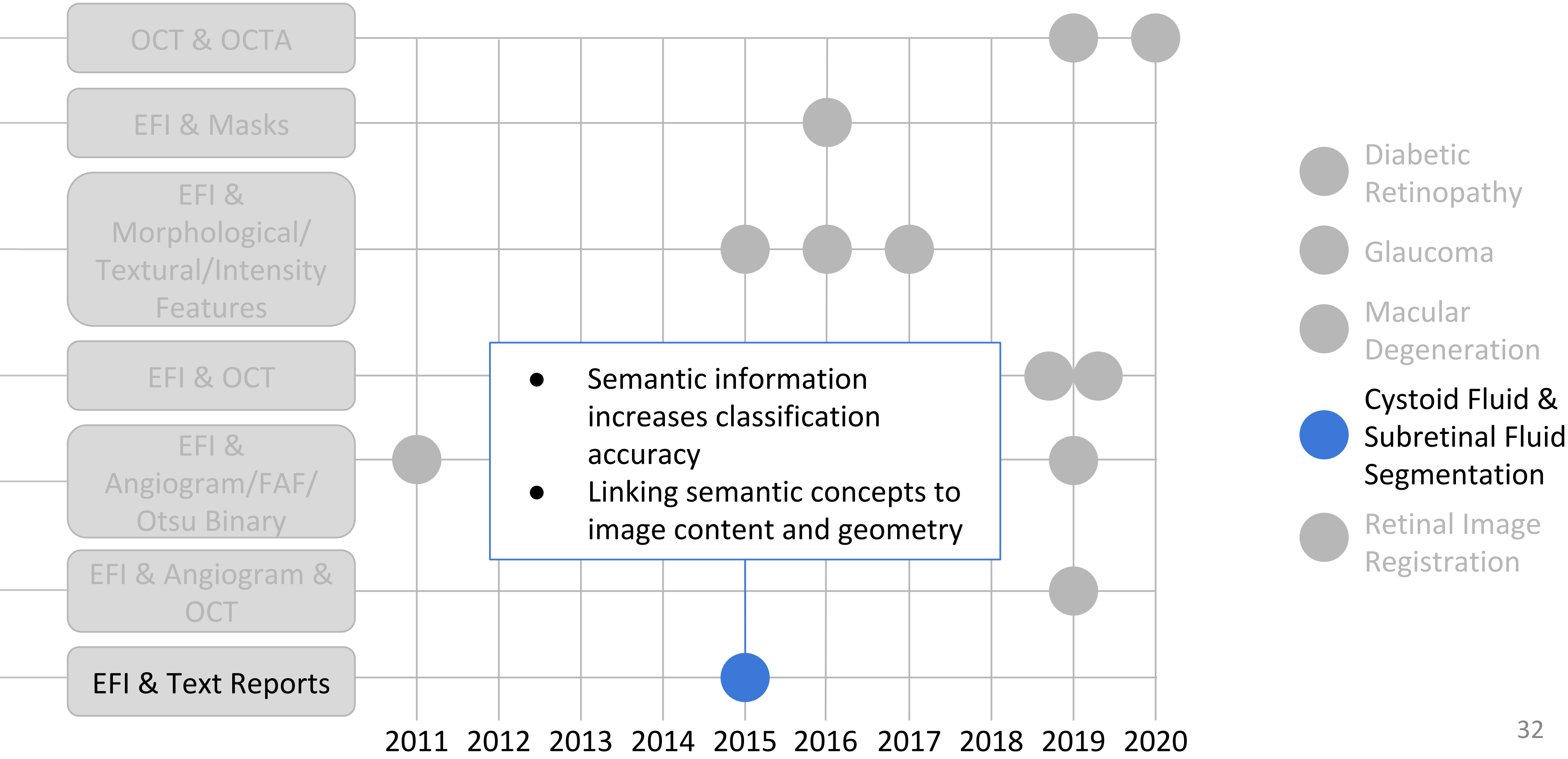


- Semantic information increases classification accuracy
- Linking semantic concepts to image content and geometry

Recurrent Problems of Multimodal Applications in Ocular Diseases

- Lack of multimodal datasets
- Multimodal design

Recurrent Problems of Multimodal Applications in Ocular Diseases

- Lack of multimodal datasets
- Multimodal design

Representation	→	Fusion	→	Evaluation
↓		↓		↓
Preprocessing		Fusion levels		Metrics
What is a good representation?		How to fuse? When to fuse? What to fuse ?		Inter-observer variability

Problem Statement

Due to the **lack of multimodal databases** (Müller 2019) most of the learning models developed to support the diagnosis of eye diseases have **focused on analyzing information from a single modality**, mainly visual (Andrearczyk 2018).

Most of these methods are based on **deep learning** (Perdomo 2019). Several problems arises: the available medical databases are **small** and the methods are **not interpretable**.

Problem Statement

Many multimodal methods combining visual and textual information have been made for various medical applications, but not for the **diagnosis** of eye diseases.

Besides, designing multimodal methods involves learning representations and learning to combine these representations appropriately.

Research Questions

- How to **learn representations** for different data modalities related with the diagnosis of eye diseases?
- How to **design multimodal representations** for different data modalities related with the diagnosis of eye diseases?
- How a **multimodal approach improves the performance** of automatic models for the diagnosis of eye diseases?

Main Goal

To design, implement and evaluate multimodal ***methods*** to support the detection and diagnosis of eye diseases using multiple information sources.

Specific objectives

- To design a strategy for ***learning the representations***.
- To design a strategy for ***fusing different data modalities***.
- To design methods for the ***automatic analysis*** of different data modalities.
- To ***systematically evaluate*** the performance.

Scope

- The main goal of this proposal is the methodological design of new methods of Machine Learning.

- The products will be prototypes, and there will be no products ready for production.

Methodology - 4 Work Packages (WP)

WP1 → **WP2** → **WP3** → **WP4**

WP1	WP2	WP3	WP4
Representation Learning	Fusion	Multimodal Method Design	Evaluation

WP1 → WP2 → WP3 → WP4

Representation Learning → Fusion → Multimodal Method Design → Evaluation

- Joint
- Coordinate

- Neural Networks
- Autoencoders
- Generative Models
- Manifold Learning
- NLP

WP1 → **WP2** → **WP3** → **WP4**

Representation Learning

Fusion

Multimodal Method Design

Evaluation

- Joint
- Coordinate

- Neural Networks
- Autoencoders
- Generative Models
- Manifold Learning
- NLP

A1.1 Creation of Multimodal Datasets

A1.2 Preprocessing

A1.3 Representation Models

A1.4 Evaluation

WP1	→	**WP2**	→	WP3	→	WP4
Representation Learning		**Fusion**		Multimodal Method Design		Evaluation

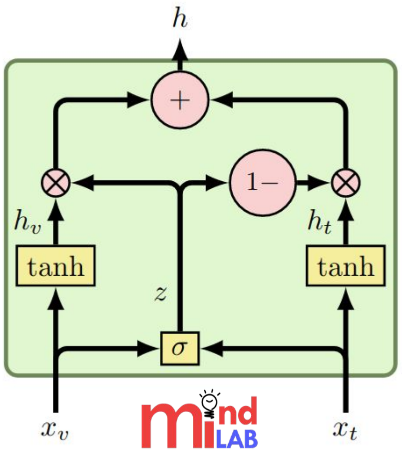
WP1 → **WP2** → **WP3** → **WP4**

Representation Learning | Fusion | Multimodal Method Design | Evaluation

Fusion: Early, Late, Hybrid

- Neural Networks
- Kernel-based
  - Alzheimer's
  - Mammograms
- Graphic Models

- Gated Multimodal Units (GMU's)



WP1 → **WP2** → **WP3** → **WP4**

Representation Learning

Fusion

Multimodal Method Design

Evaluation

Early | Late | Hybrid

- Neural Networks
- Kernel-based
  - Alzheimer's
  - Mammograms
- Graphic Models

A2.1 Relevance of the available modalities.

A2.2 Implement and validate on standard datasets.

A2.3 Design multimodal learning strategy on eye data.

A2.4 Evaluation

WP1 →	WP2 →	**WP3** →	WP4
Representation Learning	Fusion	Multimodal Method Design	Evaluation

WP1 → **WP2** → **WP3** → **WP4**

Representation Learning

Fusion

Multimodal Method Design

Evaluation

A3.1 Multimodal Datasets

A3.2 Design automatic analysis models - Diagnosis

A3.3 Design automatic analysis models - Grading

A3.4 Validation

WP1 → **WP2** → **WP3** → **WP4**

Representation Learning | Fusion | Multimodal Method Design | Evaluation

Validate model capacities on:

- Co-learning
- Alignment
- Translation

Baltrusaitis et al. [6]

A3.1 Multimodal Datasets

A3.2 Design automatic analysis models - Diagnosis

A3.3 Design automatic analysis models - Grading

A3.4 Validation

WP1	→	WP2	→	WP3	→	WP4
Representation Learning		Fusion		Multimodal Method Design		Evaluation

WP1 → **WP2** → **WP3** → **WP4**

Representation Learning

Fusion

Multimodal Method Design

Evaluation

A3.1 Diagnosis

A3.2 Retrieval and Annotation

A3.3 Experts

WP1 → **WP2** → **WP3** → **WP4**

Representation Learning | Fusion | Multimodal Method Design | Evaluation

- Sensitivity
- Specificity
- F1-score
- Gold Standard

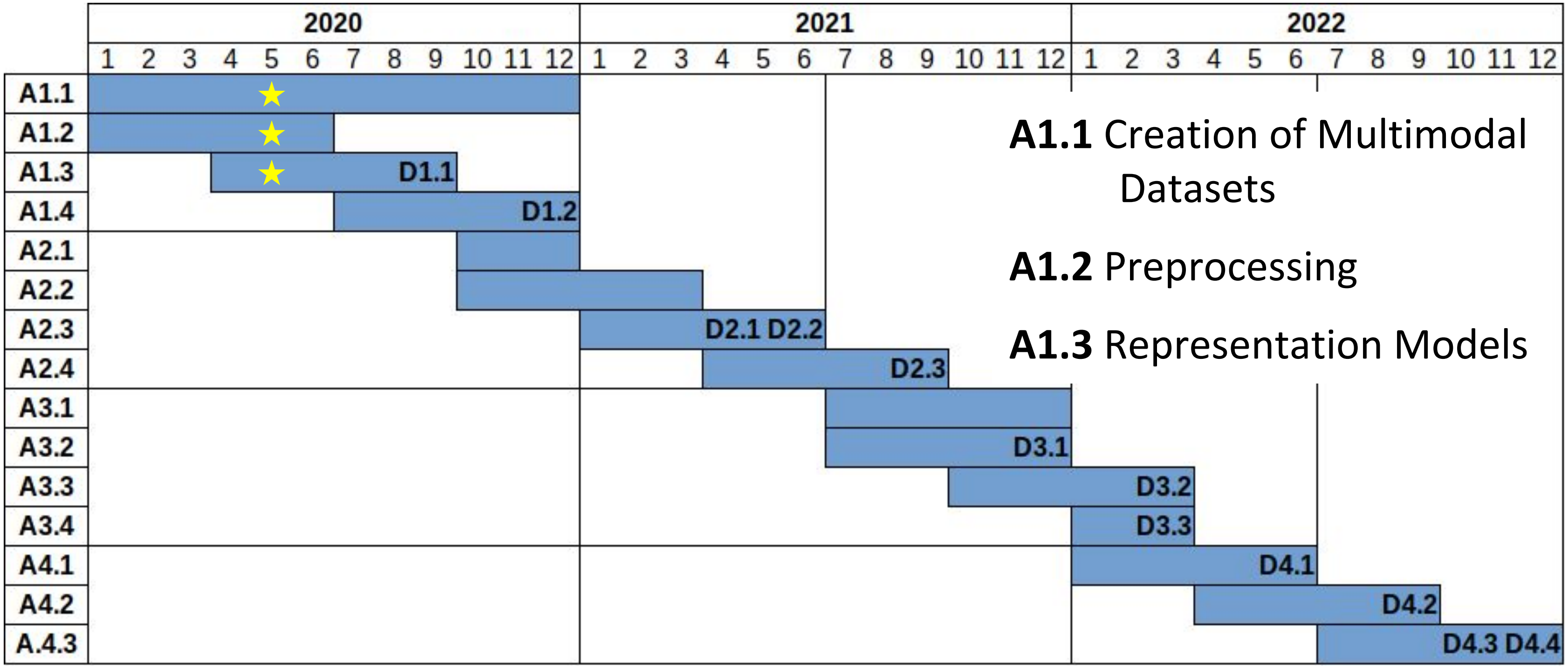
- Inter Observer Variability
  - Cohen's Kappa

A3.1 Diagnosis

A3.2 Retrieval and Annotation

A3.3 Experts

Schedule

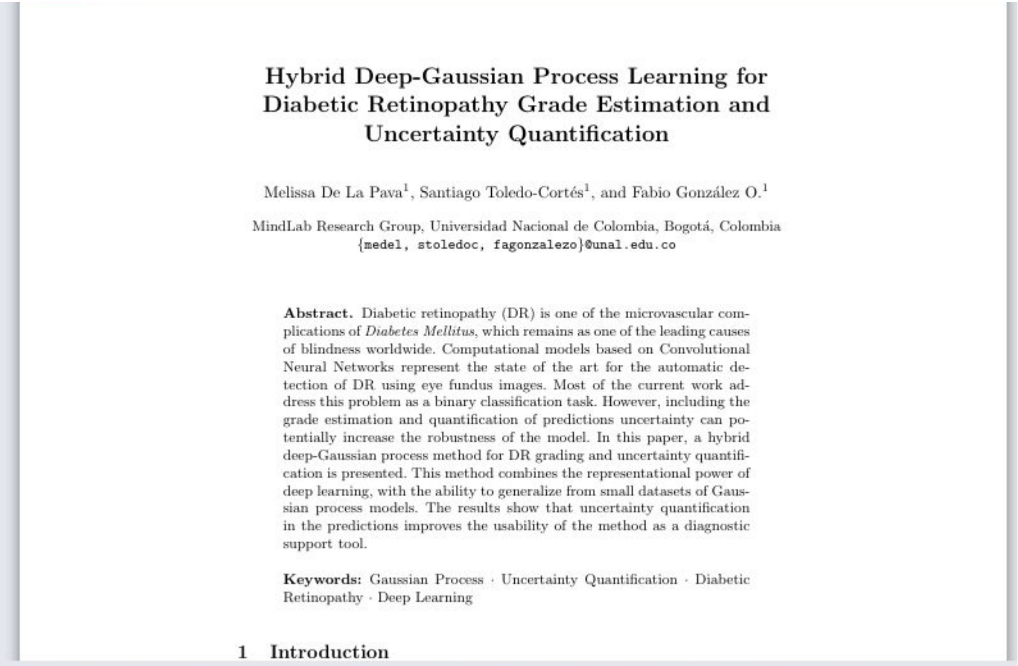


A1.1 Creation of Multimodal Datasets

A1.2 Preprocessing

A1.3 Representation Models

Done



Hybrid Deep-Gaussian Process Learning for Diabetic Retinopathy Grade Estimation and Uncertainty Quantification

Melissa De La Pava[1], Santiago Toledo-Cortés[1], and Fabio González O.[1]

MindLab Research Group, Universidad Nacional de Colombia, Bogotá, Colombia
{medel, stoledoc, fagonzalezo}@unal.edu.co

Abstract. Diabetic retinopathy (DR) is one of the microvascular complications of *Diabetes Mellitus*, which remains as one of the leading causes of blindness worldwide. Computational models based on Convolutional Neural Networks represent the state of the art for the automatic detection of DR using eye fundus images. Most of the current work address this problem as a binary classification task. However, including the grade estimation and quantification of predictions uncertainty can potentially increase the robustness of the model. In this paper, a hybrid deep-Gaussian process method for DR grading and uncertainty quantification is presented. This method combines the representational power of deep learning, with the ability to generalize from small datasets of Gaussian process models. The results show that uncertainty quantification in the predictions improves the usability of the method as a diagnostic support tool.

Keywords: Gaussian Process · Uncertainty Quantification · Diabetic Retinopathy · Deep Learning

1 Introduction

MICCAI 2020 Lima PERU

- Deep Learning for feature extraction
- Gaussian Process for DR grading.

Done

Hybrid Deep-Gaussian Process Learning for Diabetic Retinopathy Grade Estimation and Uncertainty Quantification

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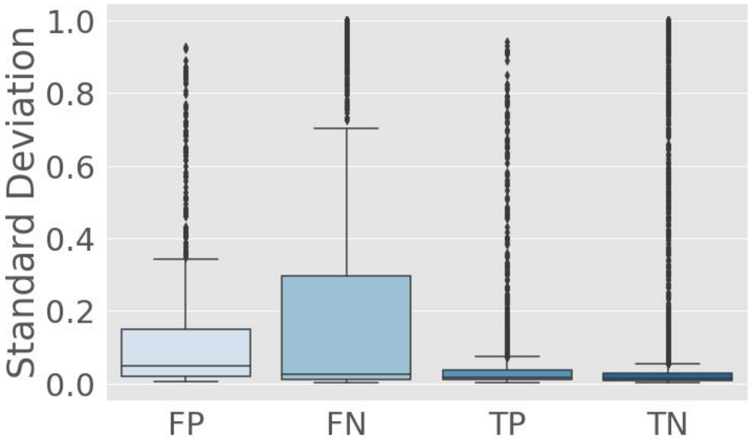
23rd INTERNATIONAL CONFERENCE ON MEDICAL IMAGE COMPUTING & COMPUTER ASSISTED INTERVENTION

- Deep Learning for feature extraction
- Gaussian Process for DR grading.

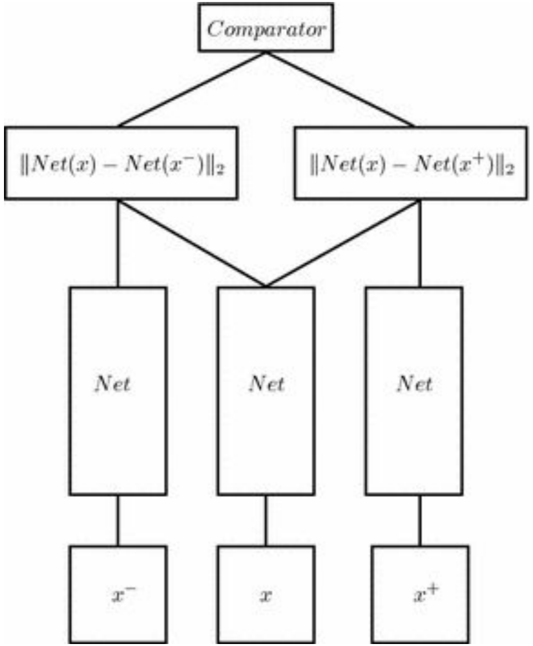
Done

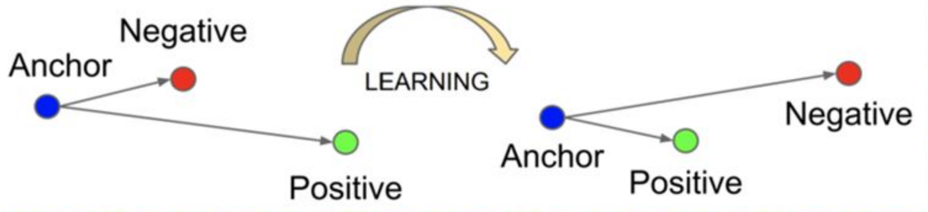


Performance for binary classification in Messidor-2

Description	Sensitivity	Specificity	AUC
Voets 2019	0.818	0.712	0.853
Gulshan 2016	**0.967**	0.84	0.974
Gargeya 2017	0.93	0.87	0.94
Inception-V3 *Model-3*	0.6974	0.8977	0.8713
DGP-DR Binarization	0.9316	0.91	0.9619
GPC	0.5135	**0.998**	**0.9812**

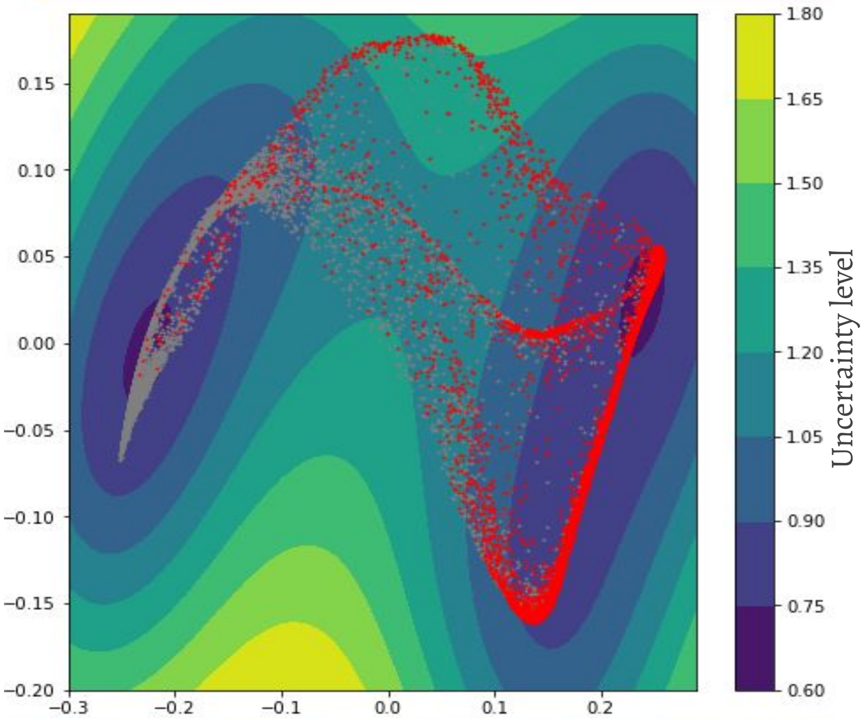
Triplet Network - Metric Learning





$$Loss = \sum_{i=1}^{N} \left[\| f_i^a - f_i^p \|_2^2 - \| f_i^a - f_i^n \|_2^2 + \alpha \right]_+$$

Metric Learning - Visualization



Diabetic Retinopathy
(Kaggle Dataset)

Non-Referible

Referible

Multimodal datasets

	1. Select Images →	2. Write Reports
Responsable	Researcher MindLab & Supra-Specialist in Retina FON	Supra-Specialist in Retina FON
Description	Balance regarding: ● Quality ● Lesions	Descriptive report of the examination, with information on lesions, location, and morphometrical description of structures of the retina.

Budget

Concept	Source	Cost
Laptop	Self funded	$2'000.000
High performance equipment	Research group MindLab	$20'000.000
Investigator salary	Google	$150'000.000
Advisor salary	Universidad Nacional de Colombia	$95'000.000
Office supplies	Self funded	$1'500.000
Conference travels	Self funded / Universidad Nacional de Colombia	$30'000.000
Bibliography	Universidad Nacional de Colombia	$3'000.000
		Total: $287'500.000

LARA
Latin America
Research Awards 2019

This certificate is awarded by Google to

Primary investigator:
Fabio Gonzalez

Student:
Santiago Toledo-Cortés

University: **Universidad Nacional de Colombia**
Country: **Colombia**

For their winning project:

Computational Learning Model for the Eye Fundus Analysis to Support Medical Diagnosis

Google

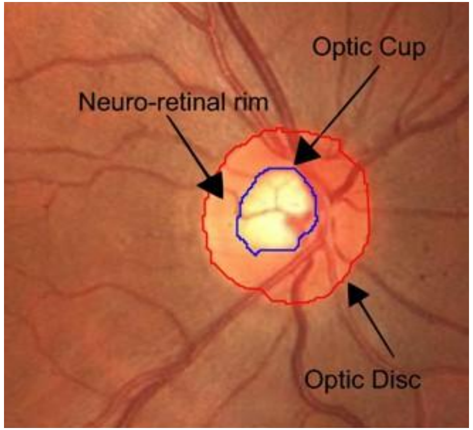
Questions?

Proposed Disease Severity Level	Findings Observable upon Dilated Ophthalmoscopy	Derivation from ETDRS Levels	Risk Assessment	Management Options*
No apparent Retinopathy	€ No abnormalities	Levels 10: DR absent		Optimize medical therapy of glucose, blood pressure and lipids
Mild Non-Proliferative Diabetic Retinopathy	Microaneurysms only	Level 20: Very mild NPDR		Optimize medical therapy of glucose, blood pressure and lipids
Moderate Non-proliferative Diabetic Retinopathy	More than just microaneurysms but less than Severe NPDR	Levels 35,43: moderate NPDR less than 4:2:1	One year early PDR: 5.4 – 11.9% One year high risk PDR:1.2-3.6%	Refer to an ophthalmologist Optimize medical therapy of glucose, blood pressure and lipids
		Level 47: moderate NPDR less than 4:2:1	One year early PDR 26.3% One year High Risk PDR: 8.1%	Refer to an ophthalmologist Optimize medical therapy of glucose, blood pressure and lipids

Severe Non-Proliferative Diabetic Retinopathy	Any of the following: € Extensive (>20) intraretinal hemorrhages in each of 4 quadrants € Definite venous beading in 2+ quadrants € Prominent IRMA in 1+ quadrant € And no signs of proliferative retinopathy	53A-E: severe to very severe NPDR, 4:2:1 rule	One year risk for early PDR: 50.2% (severe NPDR) One year High Risk PDR: 14.6% (severe NPDR) – 45.0% (very severe NPDR)	Consider scatter (panretinal) laser treatment for patients with type 2 diabetes Optimize medical therapy of glucose, blood pressure and lipids
Proliferative Diabetic Retinopathy	One or more of the following: € Neovascularization € Vitreous/preretinal hemorrhage	Levels 61, 65, 71,75, 81,85: PDR, high-risk PDR, very severe or advanced PDR		Strongly consider scatter (panretinal) laser treatment, without delay for patients with vitreous hemorrhage or neovascularization within one disc diameter of the optic nerve head Optimize medical therapy of glucose, blood pressure and lipids

Glaucoma Diagnosis

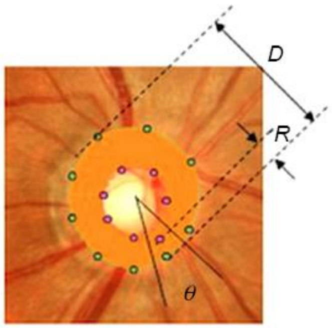
- **Patient history** to determine any symptoms the patient is experiencing and if there are any general health problems and family history that may be contributing to the problem.
- **Visual acuity measurements**
- **Tonometry**
- **Pachymetry**
- **Visual field testing**, also called **perimetry**.
- **Evaluation of the retina of the eye**
- **Supplemental testing**



Source: American Optometric Association (AOA)

Disc Damage Likelihood Scale (DDLS)

		The thinnest width of the rim (Rim Disc Ratio)		
	Stage	**Small disc <1.50 mm**	**Average size disc 1.50–2.00 mm**	**Large disc >2.00 mm**
Normal	0a	0.5	0.4 or more	0.3 or more
	0b	0.4 up to 0.5	0.3–0.4	0.2–0.3
At Risk	1	0.3 up to 0.4	0.2–0.3	0.1–0.2
	2	0.2 up to 0.3	0.1–0.2	0.05–0.1
Glaucoma damage	3	0.1 up to 0.2	0.01–0.1	0.01–0.05
	4	0.01–0.1	No rim <45 degrees	No rim <45 degrees
	5	No rim <45 degrees	No rim 45–90 degrees	No rim 45–90 degrees
Glaucoma disability	6	No rim 45–90 degrees	No rim 91–180 degrees	No rim 91–180 degrees
	7	No rim >90 degrees	No rim >180 degrees	No rim >180 degrees



$$\text{Rim disc ratio} = \frac{R}{D}$$

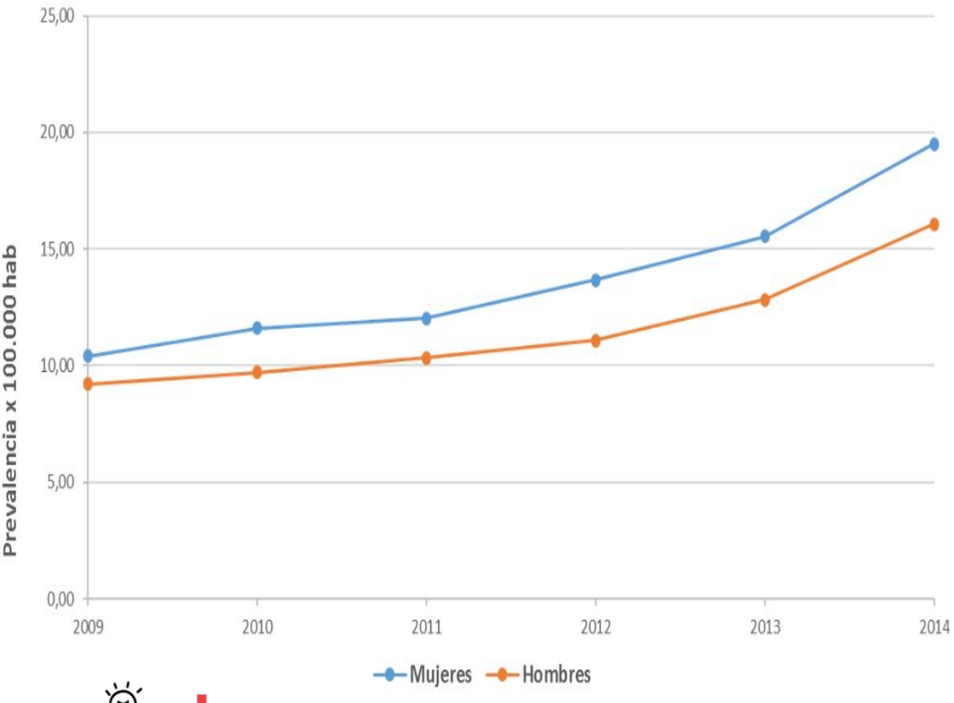
Figure 1 Normogram of the disc damage likelihood scale.
Notes: The disc damage likelihood scale: a method of estimating the risk of glaucomatous damage of the optic nerve head. Figure courtesy of Kowa Company Ltd., Tokyo, Japan.

What is “good” for a representation map?

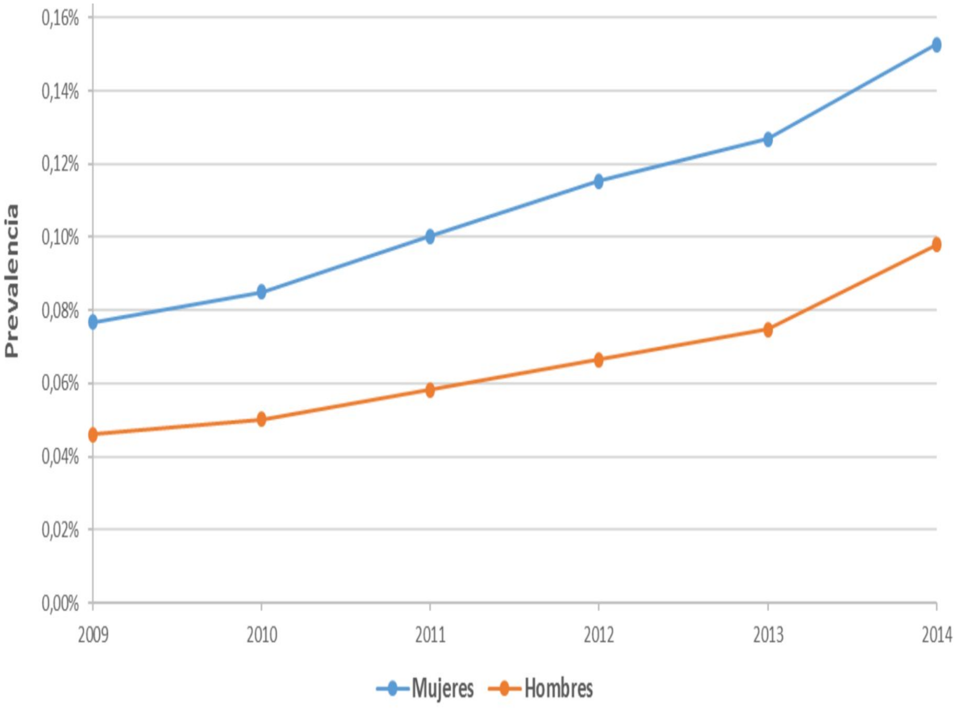
The a priori parameters for evaluation will be those given by Bengio et al. in [7], evaluating factors such as:

- smoothness,
- space-time coherence,
- sparsity of the feature mapping.

Prevalence of DR in Colombia

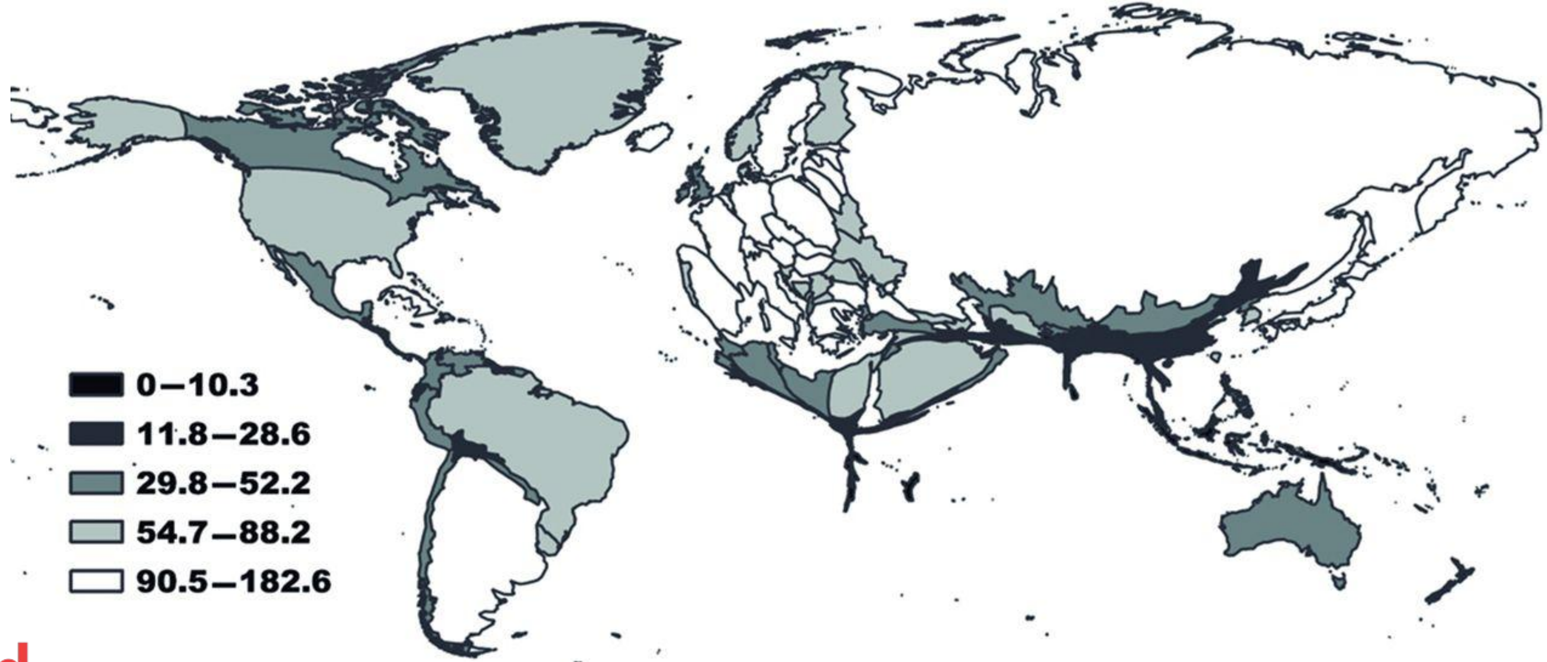


Prevalence of Glaucoma in Colombia



Source: MinSalud Colombia 2016

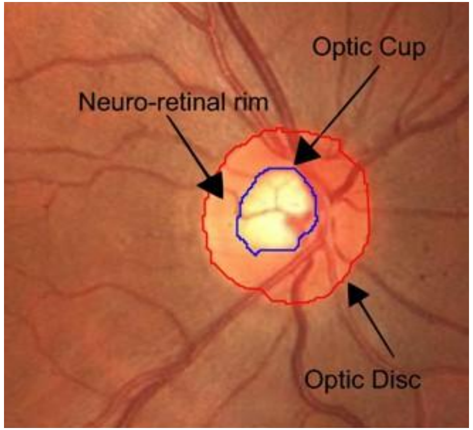
Global distribution of the ophthalmologist density (the number of ophthalmologists per million) population.



Resnikoff S, Lansingh VC, Washburn L, et al. 2020

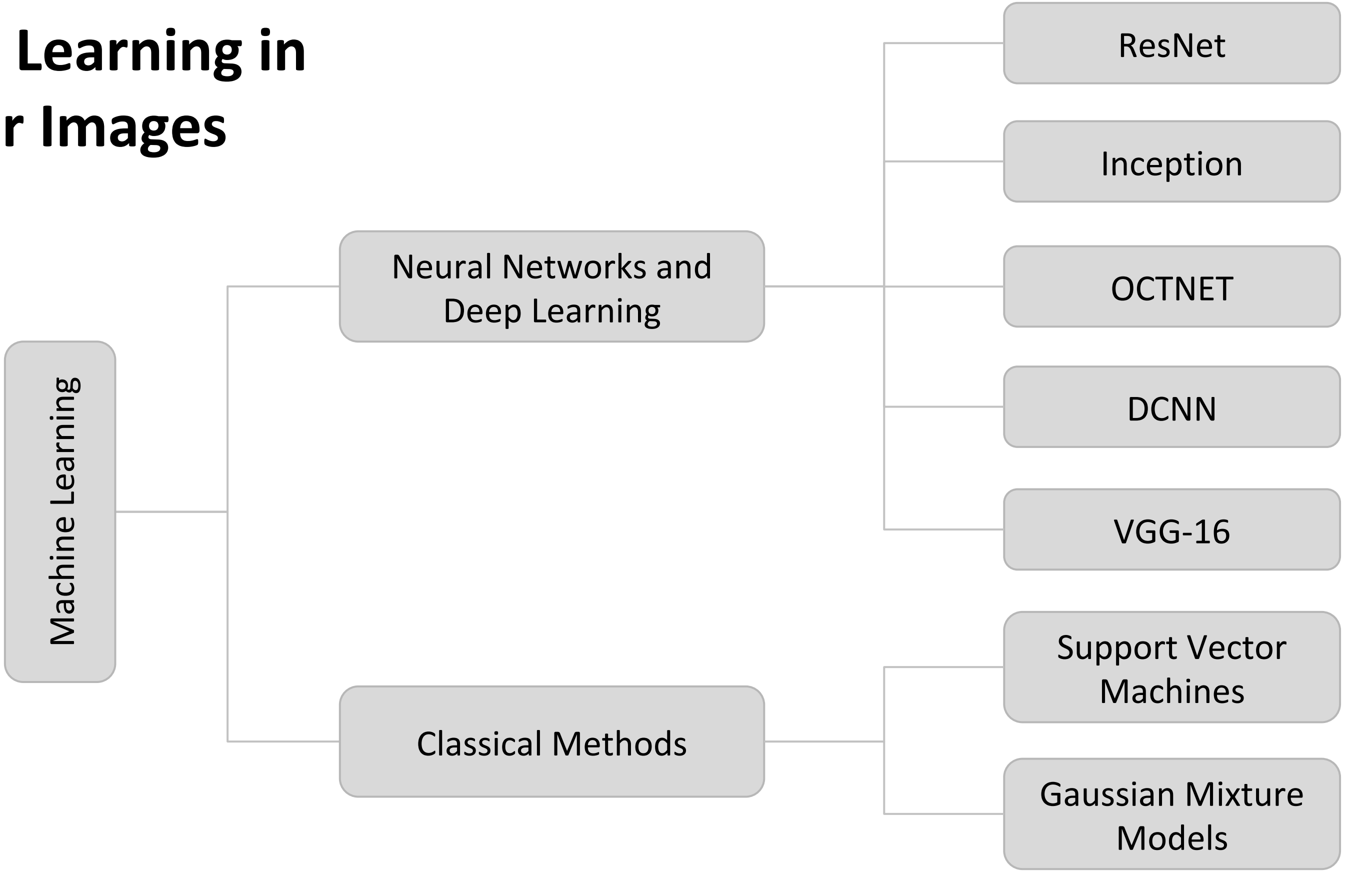
Glaucoma Diagnosis

- **Patient clincal history** to determine any symptoms the patient is experiencing and if there are any general health problems and family history that may be contributing to the problem.
- **Visual acuity measurements**
- **Tonometry**
- **Pachymetry**
- **Visual field testing**, also called **perimetry**.
- **Evaluation of the retina of the eye**
- **Supplemental testing**



Source: American Optometric Association (AOA)

Machine Learning in Ocular Images



Examen de Calificación

What is the main hypothesis to expect that the method that will be developed will be suitable to support the diagnosis of a wide variety of eye-diseases, and is there a risk that such method can fail for some particular eye diseases?

Prof. Luis Fernando Niño

¿Cuáles enfermedades son las que se podrían tratar en la tesis?
¿Cuál es la metodología que se empleará para recolectar los datos junto con la Fundación Oftalmológica Nacional? Y ¿Cuáles son las múltiples fuentes de datos que menciona en el documento?

Prof. Cesar Augusto Pedraza Bonilla

¿Cuáles son las características que se han considerado para la base de datos multimodal, cómo será su proceso de construcción, y cómo se usará tanto en el diseño del sistema de apoyo al diagnóstico de las enfermedades como en la validación de dicho sistema.

Prof. Flavio Augusto Prieto Ortiz

Ocular diseases

- Diabetic Retinopathy
  - 15 public datasets
  - FON data
  - FON retina specialist
- Glaucoma
  - 11 public datasets
  - FON data
  - FON glaucoma specialist
- Age-Related Macular Degeneration
  - 11 public datasets
  - FON data
  - FON retina specialist
- Diabetic Macular Edema
  - 6 public datasets
  - FON data
  - FON retina specialist

Multiple Data sources

- Visual:
  - Eye Fundus Images
  - Optical Coherence Tomography
  - Angiograms
- Non Structured
  - Medical Reports
- Structured
  - Clinical Records - Formats
    - Type of diabetes
    - Time since first diagnosis
    - Last hemoglobin test
    - Previous eye surgery

Multimodal datasets

	1. Select Images →	2. Write Reports
Responsable	Researcher MindLab & Supra-Specialist in Retina FON	Supra-Specialist in Retina FON
Description	Balance regarding: • Quality • Lesions	Descriptive report of the image, with information on lesions, location, and morphometrical description of the structures of the retina.

Multimodal datasets

- FON example:

  Foto a color de polo posterior de ojo derecho, medios transparentes, disco de bordes bien definidos con mínimas palidez, RCD de 0.4, se observa un adelgazamiento generalizado del árbol arterial, con relación arteriovenosa de 1.0:2.0, se observa en la región macular escasas lesiones amarillentas y múltiples lesiones en punto rojizas. Impresión diagnóstica Retinopatía diabética no proliferativa la leve, drusas maculares.

DR Lesions

- Microaneurysms
- Haemorrhages
- Venous beading
- Vascular abnormalities
- Hard exudates
- Cotton-wool spots

DME Lesions

- Exudates
- Macular thickening

DR Lesions

- Microaneurysms
- Haemorrhages
- Venous beading
- Vascular abnormalities
- Hard exudates
- Cotton-wool spots

DME Lesions

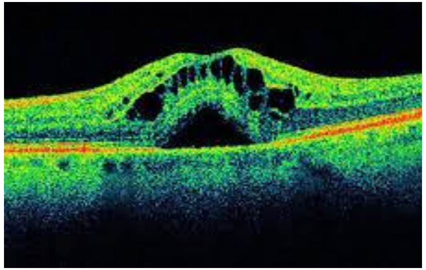
- Exudates
- Macular thickening

DR Lesions

- Microaneurysms
- Haemorrhages
- Venous beading
- Vascular abnormalities
- Hard exudates
- Cotton-wool spots

DME Lesions

- Exudates
- Macular thickening



Visual

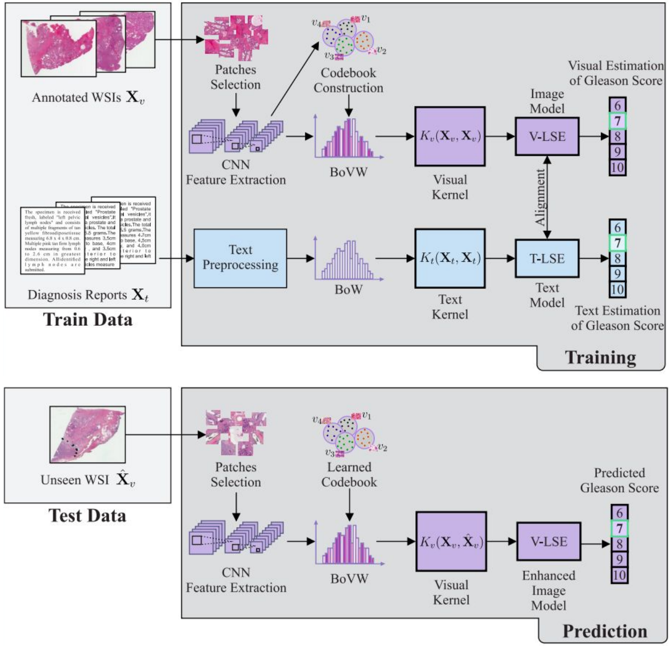
- Preprocessing
- Feature extraction
  - Neural Networks
  - Kernels
  - Generative Models
  - Manifold Learning

Text

- Preprocessing
- NLP
  - Topic Modeling (TD-IDF)
    - Latent Dirichlet Allocation
    - Non-negative Matrix Factorization
  - Deep Learning
    - Learned Features
      - Distributed Representations
        - Word2Vec
        - Med2Vec
    - Named Entity Recognition
    - Transformers

Validate model capacities on:

- Co-learning
- Translation
- Alignment



Validate model capacities on:

- Co-learning
- Alignment
- Translation

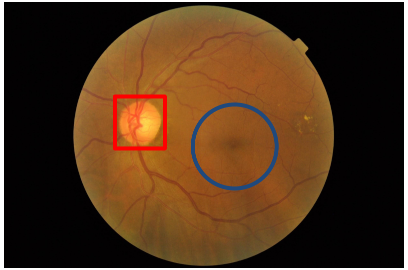


Foto a color del polo posterior del ojo izquierdo, Medios claros, disco de coloración normal, bordes definidos, ligera creciente escleral peripapilar temporal, RCD 0.4. Vasos con distribución normal, ligera tortuosidad venosa, cruces arteriovenosos, relación AV 1.0:2.0. En el área macular se observan múltiples lesiones puntiformes rojizas asociado a depósitos amarillentos intrarretinianos con tendencia a la confluencia localizadas en el aspecto temporal. Impresión diagnóstico Retinopatía diabética no proliferativa moderada OI

Validate model capacities on:

- Co-learning
- Alignment
- Translation

Foto a color de polo posterior de ojo izquierdo, medios claros, disco ligeramente pálido, Neovasos que ocupan toda el área del disco, bordes ligeramente borrados, no se puede definir RCD, vasos con distribución normal, arterias con ligera tortuosidad, relación AV 1.0:2.0. Se observa en el área macular coloración grisácea de la fóvea, brillo en celofán, asociados a múltiples lesiones puntiformes rojizas y depósitos amarillentos intraretinianos yuxtafoveales nasales. Por fuera de las arcadas vasculares temporales se observan manchas blanco algodonosas y aparente proliferación fibrovascular sobre arcada vascular temporal superior. Impresion diagnostica Retinopatía diabética proliferativa de alto riesgo OI, Edema macular diabético presente severo OI

Foto a color de polo posterior del ojo izquierdo, Medios claros, disco con ligera palidez temporal, bordes definidos, RCD 0.3, vasos con distribución normal, relación AV 1.5:2.0. En el área macular se observan múltiples lesiones puntiformes rojizas. Por fuera de las arcadas temporales se observan lesiones puntiformes rojizas en punto y mancha, asociado a depósitos amarillentos intraretinianos con tendencia la confluencia. Impresion diagnostica Retinopatía diabética no prolifetativa moderada OI

Foto a color del polo posterior del ojo izquierdo, Medios claros, disco de coloración normal, bordes definidos, ligera creciente escleral peripapilar temporal, RCD 0.4. Vasos con distribución normal, ligera tortuosidad venosa, cruces arteriovenosos, relación AV 1.0:2.0. En el área macular se observan múltiples lesiones puntiformes rojizas asociado a depósitos amarillentos intraretinianos con tendencia a la confluencia localizadas en el aspecto temporal. Impresion diagnostico Retinopatía diabética no proliferativa moderada OI

Foto a color del polo posterior del ojo derecho, medios claros, disco de coloración normal, bordes definidos, ligera creciente escleral temporal, RCD 0.6. Vasos con distribución normal, ligera tortuosidad arterial y venosa, estrechamiento arteriolar focal, hilos de cobre y cruces arteriovenosos. En el área macular se observan lesiones puntiformes rojizas asociado a depósitos amarillentos intraretinianos con tendencia a la confluencia localizados en el aspecto temporal y superior. Finalizando el trayecto de la arcada vascular temporal superior se observa una manchas blanco algodonosas y hemorragias en llama. Impresion diagnostica Retinopatía hipertensiva OD, Secuelas de oclusión de rama venosa superotemporal OD, Excavación aumentada OD

Foto a color del polo posterior del ojo izquierdo, leve a moderada opacidad de medios, disco con palidez temporal, bordes definidos, ligera creciente escleral temporal y RCD 0.3. Vasos con distribución normal, marcada congestión y tortuosidad venosa, tortuosidad capilar a nivel macular, cruces Arteriovenosos, hilos de cobre y relación AV1.0: 2.5. En el área macular se observan múltiples lesiones puntiformes rojizas asociado a depósitos amarillentos intra retinianos que se localizan en el área yuxtafoveal temporal y en el aspecto inferior y temporal de la mácula. Impresion diagnostica Retinopatía hipertensiva OI, Retinopatía diabética no proliferativa moderada OI

What is the difference between multi-view learning and multi-modal learning and, in the proposed research, what are the main challenges of applying multimodal learning?

Prof. Luis Fernando Niño

Siendo la fusión una de las posibles estrategias usadas en el aprendizaje multimodal, a la luz de trabajos similares (diagnóstico de enfermedades) reportados en la literatura, cuáles serían las ventajas y desventajas de usar esta estrategia en el desarrollo de la tesis?

Prof. Flavio Augusto Prieto Ortiz

"Multi-view learning is the branch of machine learning concerned with the analysis of multi-modal data, i.e. patterns represented by different sets of features extracted from multiple data sources."

SERRA, Angela ; GALDI, Paola ; TAGLIAFERRI, Roberto: Multiview learning in biomedical applications. In: *Artificial Intelligence in the Age of Neural Networks and Brain Computing* (2018), Nr. June, S. 265–280. ISBN 9780128154809

Search

multimodal learning

5,706 document results

TITLE-ABS-KEY (multimodal AND learning) AND (LIMIT-TO (SUBJAREA , "COMP"))

Search

multiview learning

722 document results

TITLE-ABS-KEY (multiview AND learning) AND (LIMIT-TO (SUBJAREA , "COMP"))

"In recent years, a great many methods of learning from multi-view data by considering the diversity of different views have been proposed. These views may be obtained from **multiple sources** or different feature subsets."

XU, Chang ; TAO, Dacheng ; XU, Chao: A Survey on Multi-view Learning. (2013), S. 1–59

"We frame the task as a multi-view learning problem to induce semantic information from a multimodal model into our acoustic-only network using a contrastive loss function."

AGUILAR, Gustavo ; ROZGIC, Viktor ; WANG, Weiran ; WANG, Chao: Multimodal and Multi-view Models for Emotion Recognition. (2019), S. 991–1002. ISBN 9781950737482

"Multi-view learning aims to **learn one function to model each view and jointly optimizes** all the functions to improve the generalization performance."

"A naive solution for multi-view learning considers **concatenating all multiple views into one single view** and applies single-view learning algorithms directly."

ZHAO, Jing ; XIE, Xijiong ; XU, Xin ; SUN, Shiliang: Multi-view learning overview: Recent progress and new challenges. In: *Information Fusion* 38 (2017), S. 43–54. – ISSN 15662535

"A simple way to convert from a single view to multiple views is to split the original feature set into different views at random, and there indeed a number of experiments in multi-view learning employing this trick."

"In image classification problems, the classifiers could learn to distinguish the domestic animals from the wild animals and also to classify the object in the image to be a cat or a dog, while the different views could be the distinct poses of the same animal."

ZHENG, Lecheng ; CHENG, Yu ; HE, Jingrui: Deep multimodality model for multi-task multi-view learning. In: *SIAM International Conference on Data Mining, SDM 2019* (2019), S. 10–16. ISBN 9781611975673

Challenges

- **Representation Learning**
- **Fusion**

Representation Learning

- Representation learning is a research field by itself in the machine learning community.

- Success of machine learning algorithms generally depends in data representation.

Representation Learning

Different representations may entangle and hide different explanatory factors.

¿What is a good representation?

Needs to capture the latent representation of the data → In a way that exploits the complementarity and redundancy of multiple modalities

Depends on the model, but...

There are some general parameters:

- Smoothness
- Multiple explanatory factors
- Natural Clustering

In medical applications...

- Electronic Health Records have a unique structure

Temporally ordered

but

The medical codes within a visit may form an unordered set

- Learned representations should be interpretable

It also depends on:

- **Joint representations:** projects unimodal representations together into a multimodal space
    - Mostly used when multiple sources are available in training ***and*** in prediction.
    -
- **Coordinated representation:** learn representations separately but coordinate them through a constraint

Fusion Advantages

- More information
- Complementary information
- Co-learning
- Robustness
- Possibility to operate even in absence of some modality.

Fusion Disadvantages

- More complexity
- Increasing risk of bias (as more variables can interfere)
- It is necessary to explore and learn the importance of each modality.

Advantages and disadvantages mostly depends on how and when the fusion is made.

Advantages	Disadvantages

Early Fusion

Advantages	Disadvantages
● Exploit low level features of each modality ● Only requires training of a single model	● Needs parallel info ● Lacks of flexibility ● Heterogeneous spaces

Late Fusion

Advantages	Disadvantages
● Flexibility: allows different models for each modality ● Allows predictions when some modality is missing	● Ignores low level interactions between modalities ● Only requires training of a single model

More Facts

- **Preprocessing times are different** for each modality.
- Different modalities have **different confidence levels.**
- Correlation between modalities should be explored
- Having too many modalities makes difficult to learn **cross-correlation** among heterogeneous features
- A proper synchronization between modalities is needed

¿Por favor describa los riesgos potenciales del uso del uso de herramientas computacionales de predicción en ambientes clínicos para la estimación de una condición particular, y cómo se pueden mitigar estos riesgos?

¿Por favor describa cuales son algunos de los aspectos éticos más relevantes a considerar en el desarrollo de herramientas computacionales que soportan el diagnóstico de pacientes?

Prof. Francisco Gómez

Risks

- Bias
- Over-reliance on annotations
- Non-clinically meaningful algorithms
- Reducing Skills of Physicians
- Intrinsic Uncertainty in Medicine
- Focus on text and the Demise of Context
- Interpretability
- Ethics

Risks

- Bias
  - PROBAST
  - Identify target population
  - Socioeconomically diverse healthcare systems for testing.
  - Include key variables
  - Test potential discriminatory behaviour
- Over-
- Non-
- Redu

CELIE, Karel-Bart ; PRAGER, Kenneth ; CHAET, Danielle ; JOHNSTON, Carolyn ; YARMOLINSKY, Rachel: AMA Journal of Ethics®. In: *Clinical Ethics* 18 (2016), Nr. 5, S. 473–563

GIANFRANCESCO, Milena A. ; TAMANG, Suzanne ; YAZDANY, Jinoos ; SCHMAJUK, Gabriela: Potential Biases in Machine Learning Algorithms Using Electronic Health Record Data. In: *JAMA Internal Medicine* 178 (2018), Nr. 11, S. 1544–1547. – ISSN 21686106

WOLFF, Robert F. ; MOONS, Karel G. ; RILEY, Richard D. ; WHITING, Penny F. ; WESTWOOD, Marie ; COLLINS, Gary S. ; REITSMA, Johannes B. ; KLEIJNEN, Jos ; MALLETT, Sue: PROBAST: A tool to assess the risk of bias and applicability of prediction model studies. In: *Annals of Internal Medicine* 170 (2019), Nr. 1, S. 51–58.

Risks

- Bias
- Over-reliance on annotations

- Ensure interdisciplinary approach and continuous human involvement.
- Conduct follow up studies to ensure that results are meaningful

ANDERSON, Michael ; ANDERSON, Susan L.: How should AI Be developed,validated and implemented in patient care? In: *AMA Journal of Ethics* 21 (2019), Nr. 2, S. 125–130. – ISSN 23766980

Risks

- Bias
- Over-reliance on annotations
- Non-clinically meaningful algorithms
    - Focus on clinically important improvements rather than performance metrics
    - Impose human values in algorithms at the cost of efficiency

GIANFRANCESCO, Milena A. ; TAMANG, Suzanne ; YAZDANY, Jinoos ; SCHMAJUK, Gabriela: Potential Biases in Machine Learning Algorithms Using Electronic Health Record Data. In: *JAMA Internal Medicine* 178 (2018), Nr. 11, S. 1544–1547. – ISSN 21686106

Risks

- Reducing Skills of Physicians

CABITZA, Federico ; RASOINI, Raffaele ; GENSINI, Gian F.: Unintended consequences of machine learning in medicine. In: *JAMA - Journal of the American Medical Association* 318 (2017), Nr. 6, S. 517–518. – ISSN 15383598

Risks

- Bias
- Over-reliance on annotations
- Non-clinically meaningful algorithms
- Reducing Skills of Physicians
- Intrinsic Uncertainty in Medicine → Inter Observer Variability

JUNGO, Alain ; MEIER, Raphael ; ERMIS, Ekin ; BLATTI-MORENO, Marcela ; HERRMANN, Evelyn ; WIEST, Roland ; REYES, Mauricio: On the effect of inter-observer variability for a reliable estimation of uncertainty of medical image segmentation. In: *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)* 11070 LNCS (2018), S. 682–690. – ISBN 9783030009274

Risks

- Bias
- Over-reliance on annotations
- Non-clinically meaningful algorithms
- Reducing Skills of Physicians
- Intrinsic Uncertainty in Medicine
- Focus on text and the Demise of Context

CABITZA, Federico ; RASOINI, Raffaele ; GENSINI, Gian F.: Unintended consequences of machine learning in medicine. In: *JAMA - Journal of the American Medical Association* 318 (2017), Nr. 6, S. 517–518. – ISSN 15383598 de Bruijne, Marleen: Machine learning approaches in medical image analysis: From detection to diagnosis. In: *Medical Image Analysis* 33 (2016), S. 94–97. – ISSN 13618423

Cabitza, Federico ; Rasoini, Raffaele ; Gensini, Gian F.: Unintended consequences of machine learning in medicine. In: *JAMA - Journal of the American Medical Association* 318 (2017), Nr. 6, S. 517–518. – ISSN 15383598

Risks

- Interpretability
- Ethics

Many efforts have been made to develop methods that automatically give explanations and/or interactive visualization tools

Risks

Ethics

Celie, Karel-Bart ; Prager, Kenneth ; Chaet, Danielle ; Johnston, Carolyn ; Yarmolinsky, Rachel: AMA Journal of Ethics®. In: *Clinical Ethics* 18 (2016), Nr. 5, S. 473–563

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Ethical Challenges for ML in Medicine

- ML should be committed to fairness
- ML should satisfy transparency standards
- Data sourcing in ML must adhere to data protection and privacy requirements

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Unrepresentative sets can lead to biased models

Racism (Glaucoma)

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  - Interpretability for whom?
    - Data Scientist?
    - Patients?
    - Physicians?
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