Retinal Vascular Geometry: Novel Biomarkers of Progression from Diabetes to Diabetic Retinopathy

Georgios Leontidis

Computer and Data Scientist

School of Computer Science
University of Lincoln, UK

Correspondence email: gleontidis@lincoln.ac.uk

UNIVERSITY OF LINCOLN

Introduction

- Diabetic retinopathy (DR) remains a major cause of blindness in the developed countries [1].

- Geometric and Haemodynamic features are still not widely investigated, especially as biomarkers of progression to DR.

- Most studies rely on disease vs control design, which introduces errors and limitations, given the diversity of the retinal vascular geometry (small and large vessels).

- Our studies have mainly focused on investigating the vascular changes within the same patients during a four year period that includes the last three years of pre-DR and 1st year of DR (onset).

[1]. G. Leontidis, B. Al-Diri, and A. Hunter, " Diabetic retinopathy: current and future methods for early screening from a retinal hemodynamic and geometric approach". Expert Review of Ophthalmology, 2014, 9(5), 431-442.

Investigated Features

Geometric

- Widths
- Angles
- Tortuosity
- CRVE/CRAE and AVR
- Branching coefficient
- Angle-to-BC ratio
- Asymmetry index
- Fractal dimension
- FD-to-Lacunarity ratio
- Lacunarity

Haemodynamic

- Blood flow velocity
- Blood flow rate
- Reynolds number
- Wall shear stress
- Pressure
- Descriptive statistics of the above

UNIVERSITY OF LINCOLN

Tools and Methods

- Automated tools for the segmentation and the extraction of the investigated features [2].

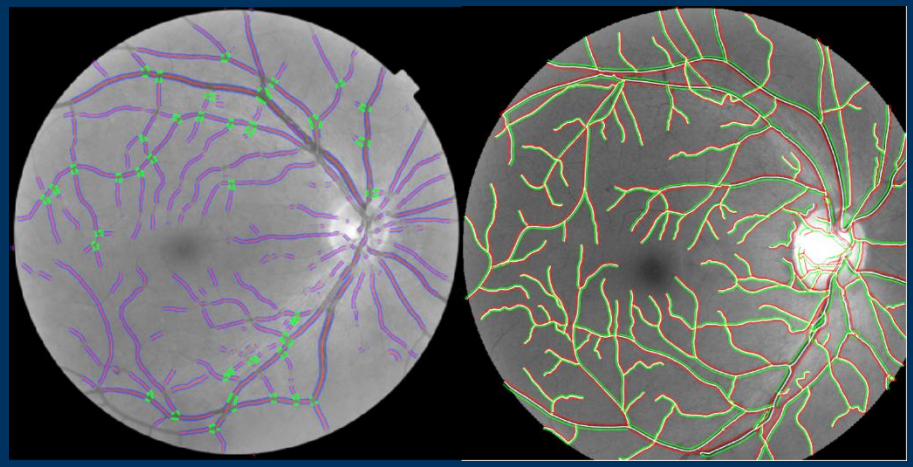

Figure 1. Two segmented retinal images.

- Mathematical modelling (0D lumped models) in order to simulate and estimate haemodynamic parameters [3].

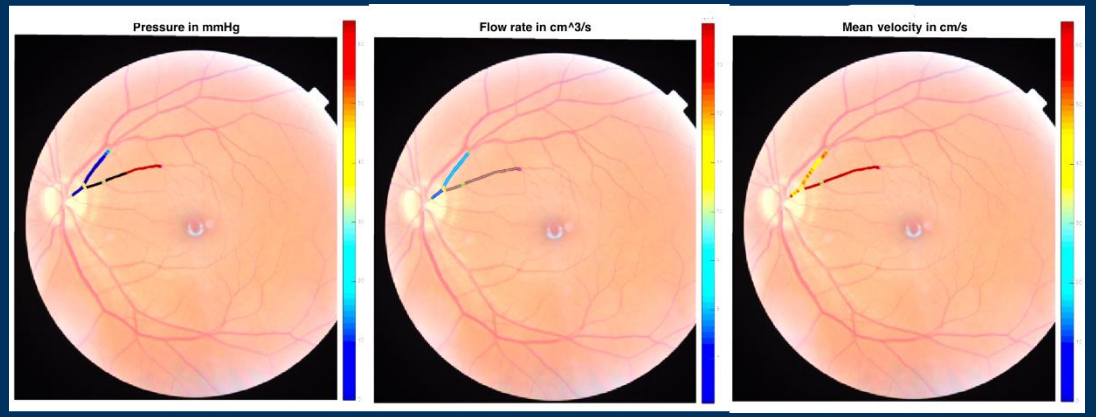

Figure 2. Example of the tool for the estimation of haemodynamic parameters in vascular trees.

[2]. B. Al-Diri, A. Hunter, and D. Steel. "An active contour model for segmenting and measuring retinal vessels." IEEE Transactions on Medical imaging 28.9 (2009): 1488-1497.

[3]. F. Caliva, G. Leontidis, L. Antica, A. Hunter and B. Al-Diri. “Hemodynamics in the retinal vasculature during the progression of diabetic retinopathy”. Journal for modeling in Ophthalmology. (2016). Under review.

UNIVERSITY OF LINCOLN

Tools and Methods

- Extraction of arterial and venular bifurcations and modeling in connected trees.

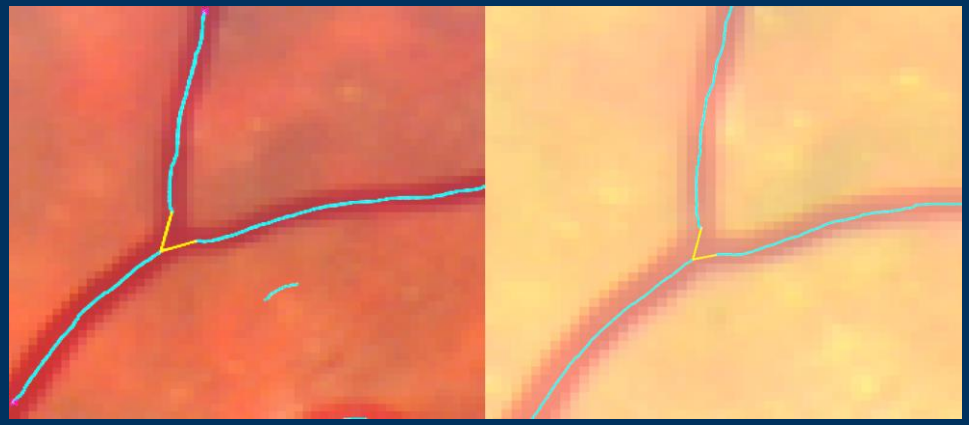

Figure 3. Example of connected bifurcation

- Areas of Interest [4] for individually studying some of the geometric features (widths, angles and tortuosity).

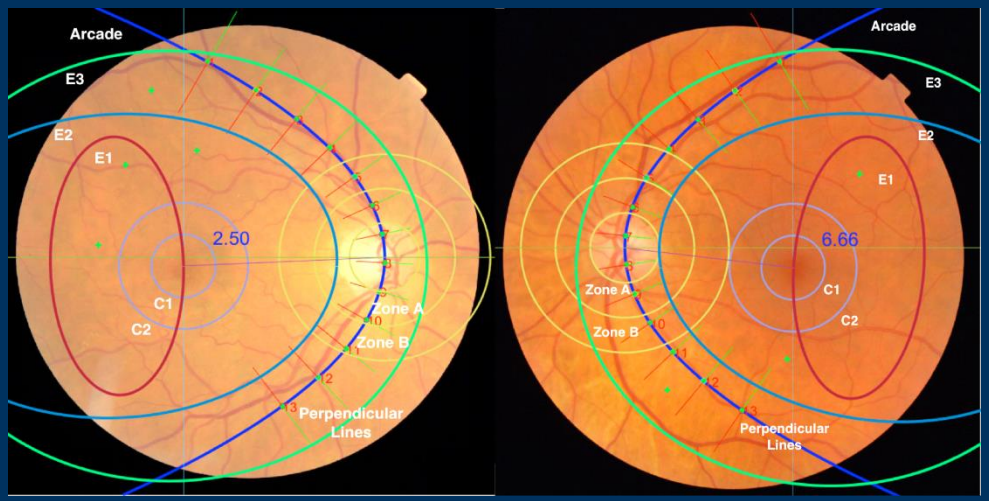

Figure 4. Partition of the Retina into various areas of interest.

[4]. M. N. Hove, J.K Kristensen, T. Lauritzen, T. and T. Bek. "Quantitative analysis of retinopathy in type 2 diabetes: identification of prognostic parameters for developing visual loss secondary to diabetic maculopathy (2004)". Acta Ophthalmologica Scandinavica, 82(6), 679-685.

UNIVERSITY OF LINCOLN

Tools and Methods

- Statistical evaluation based on linear mixed effects models – metric based on AIC, BIC, log-likelihood and p-values (full vs restricted models [5].

- Machine learning (Elastic-net logistic regression and random forests) for the feature selection and classification process [5].

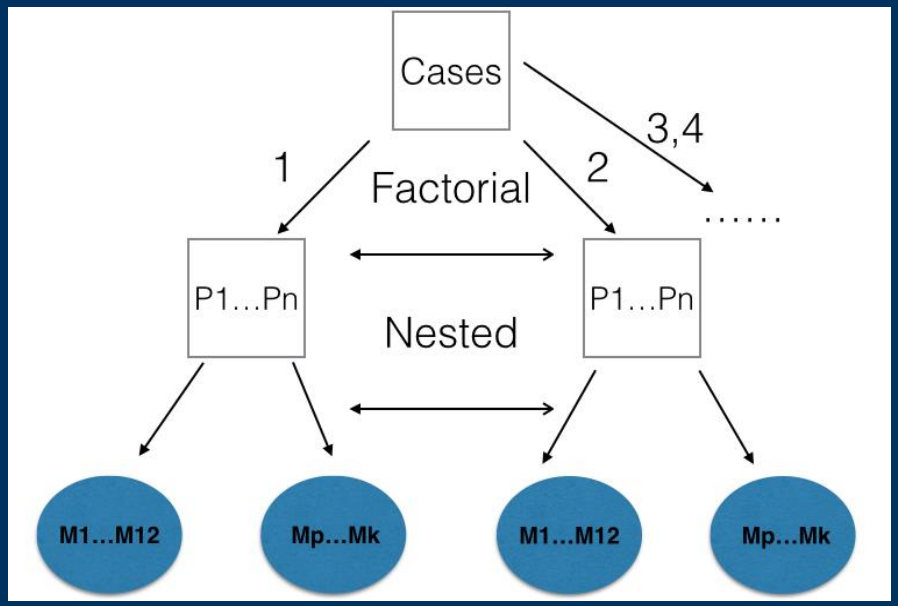

Figure 5: Mixed model design for the statistical analysis of each feature, using a Hierarchical/Factorial repeated measures approach.

[5].G. Leontidis, B. Al-Diri, J. Wigdahl and A. Hunter. "Evaluation of geometric features as biomarkers of diabetic retinopathy for characterizing the retinal vascular changes during the progression of diabetes". In 2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (pp. 5255-5259). IEEE.

Results

- Arterial and venular widths, tortuosity, fractal dimension, blood flow velocity, blood flow rate, pressure and wall shear stress were found to significantly differ across the whole four year period.

- Post-hoc comparisons showed that the changes are primarily found for the combination “three years pre-DR and 1st year of DR”.

- Classification models created for various combinations, such as 3y/2y/1y pre-DR vs 1st year of DR (onset), patients with diabetes vs DR patients and progressors vs non-progressors vs DR patients.

UNIVERSITY OF LINCOLN

Results

- Best five features for the discrimination of the classes within all the combinations of the classification models are SD of arterial angles, CRVE [6], CRAE [6], Angle-to-BC ratio and venular pressure.

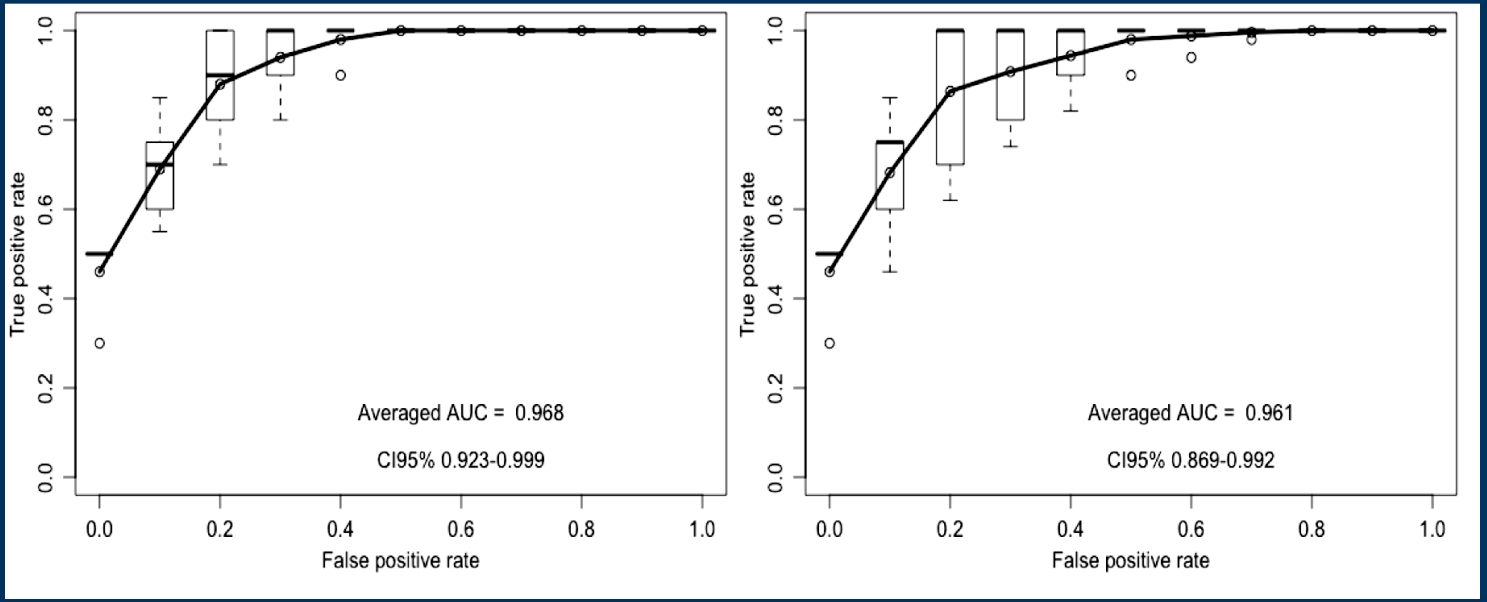

Figure 6: Area under the Receiver operating characteristic (ROC) curve (AUC) for the combination “non-progressed patients with diabetes vs DR patients”.

[6]. G. Leontidis, B. Al-Diri, and A. Hunter. "Summarising the retinal vascular calibres in healthy, diabetic and diabetic retinopathy eyes." Computers in biology and medicine 72 (2016): 65-74.

UNIVERSITY OF LINCOLN

Summary

- Early screening of diabetic retinopathy, before any lesions appear, can be identified, relying on geometric and haemodynamic features.

- Robust statistical analysis is crucial for identifying the biomarkers that can be used in classification models.

- Machine learning techniques for the feature selection process and for the classification models can help to identify the progression to DR.

- This can be used as an indication of the progression (or not) of the disease (within each patient's annual retinal screening) and possibly investigate the condition further, if needed.

CREDITS

Retinal Vascular Modelling, Measurement and Diagnosis

https://revammad.blogs.lincoln.ac.uk

Research supported by a Marie Skłodowska-Curie grant from the European Commission in the framework of the REVAMMAD ITN Project number 316990.

UNIVERSITY OF LINCOLN

QUESTIONS

THANK YOU FOR YOUR ATTENTION

UNIVERSITY OF LINCOLN