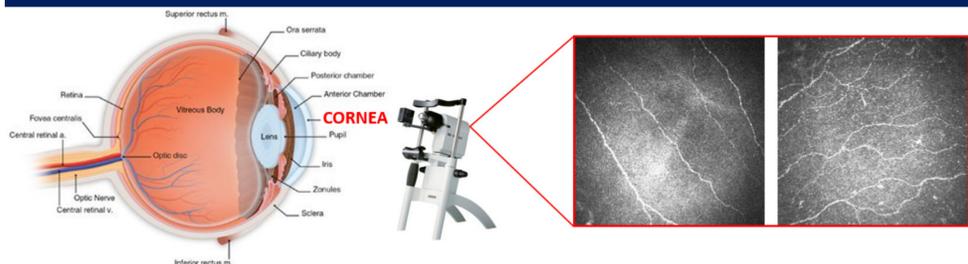


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Abstract

We present a novel method for classifying corneal nerves images in 4 levels of tortuosity. We use multi-scale features and a new multi-window algorithm for curvature estimation. A wrapper using logistic ordinal regression or an embedded method based on random forests is applied for feature and scale selection. Tested with 90 images classified by 3 clinicians, the accuracy of our system is 88.89%, 76.67%, 77.22% against each observer, outperforming the best one hold out (76.67%, 76.67%, 75%, respectively).

Clinical Motivation



- Corneal fibres appear QUALITATIVELY more tortuous in some diseases (e.g. keratoconic corneas [1,2], dry eyes [3]);
- Tortuosity significantly higher in Diabetic Retinopathy (DR), one of the leading pathological causes of blindness among working-age people in developed countries [4].

Technical Motivation

MAIN ISSUE: QUALITATIVE assessment leads to high inter-observer and intra-observer variability.

GOAL: to obtain an objective and reproducible tortuosity evaluation.

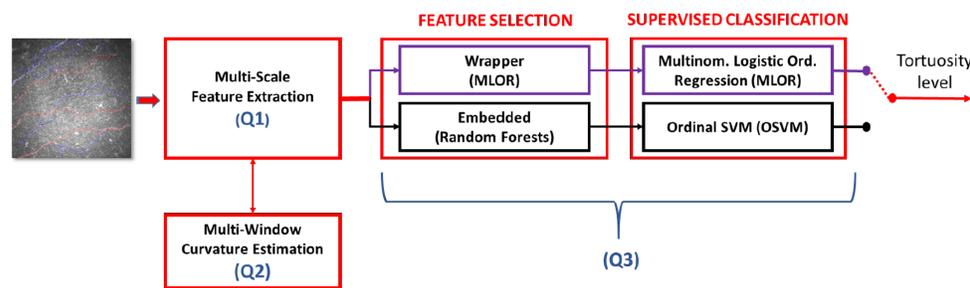
Q1. Does scale play a role?

Q2. Curvature seems a good feature: how accurately can it be estimated?

Q3. Previous work: is this the right approach?

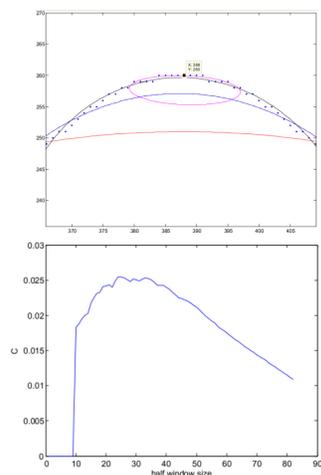
Proposed Approaches

IDEA: tortuosity is likely to be based on ophthalmologist's experience and it is hardly captured by a formula – hence classifier:



A Multiple-Window Approach for Digital Curvature Estimation

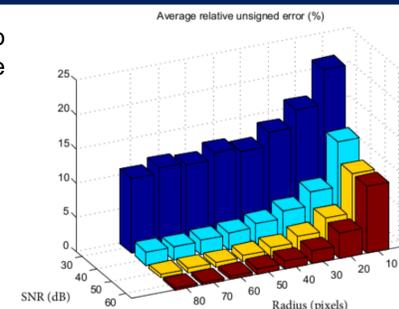
1. At each pixel, apply local ellipse fitting and line fitting using the smallest window size in a pre-defined range $R = [w_m, w_M]$;
2. Choose the best fitting function (ellipse-arc or line) based on the sum of squared errors;
3. If ellipse-arc is the best fitting function, compute the curvature using analytical derivatives on the estimated ellipse;
4. Repeat 1.-3. for all windows in R ;
5. Select the maximum estimated curvature over all windows after median filtering to eliminate small, spurious peaks.



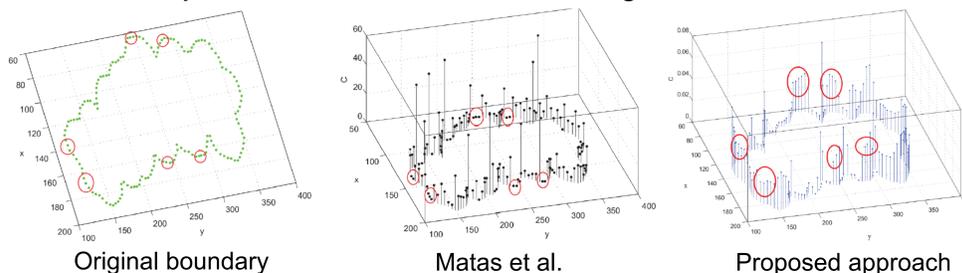
Experiments: Curvature Estimation

- Discretised circles with radii ranging from 10 to 80 pixels are corrupted by radial additive white Gaussian noise;
- Performance is quantified using the ARUE:

$$ARUE = \frac{1}{N} \sum_{i=1}^N \frac{\left| \frac{1}{r} - C_{est}(i) \right|}{\frac{1}{r}}$$



Comparison with Matas et al. method using fixed window size



Experiments: Corneal Nerves Images Classification

- Data set: 100 images, 4 levels of tortuosity, 3 ophthalmologists;
- Poor inter-observer agreement (< 50%), the consensus ground truth (CGT – 90 images) is used instead;
- 3 experiments:

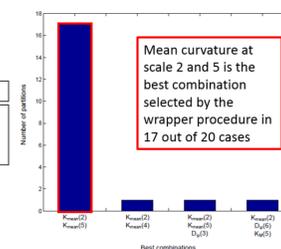
Association with CGT

Performance measures	MLOR	OSVM
Acc	84.44%	80.56%
Se	69.77%	61.94%
Sp	89.50%	86.86%
Ppv	69.75%	62.61%
Npv	89.48%	86.84%
MSE	0.3444	0.4222
MAE	0.3222	0.4000

Association with individual GT (Accuracy)

	AK	PH	SA	MLOR
AK	100%	76.67%	75%	88.89%
PH	76.67%	100%	73.89%	76.67%
SA	75%	73.89%	100%	77.22%

Are multiple scales effective? (MLOR)



Conclusions

- Trained with CGT and tested against each observer, our MLOR-based approach outperforms the best observer hold out (benchmark);
- Scale seems to play a role and a multi-scale approach is effective;
- Supervised approach instead of single formula for tortuosity estimation;
- New approach for digital curvature estimation;
- First to propose an automatic method capable of predicting more than 3 tortuosity levels.

References

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- [2] Niederer R. L., Perumal D., Sherwin T., McGhee C. N. "Laser scanning in vivo confocal microscopy reveals reduced innervation and reduction in cell density in all layers of the keratoconic cornea". *Investigative ophthalmology & visual science*, 49(7), 2964-2970 (2008).
- [3] Cruzat A., Pavan-Langston D., Hamrah P. "In vivo confocal microscopy of corneal nerves: analysis and clinical correlation". *In Seminars in ophthalmology*, vol. 25, No. 5-6, pp. 171-177, New York: Informa Healthcare (2010).
- [4] De Cillá S., Ranno S., Carini E., Fogagnolo P., Ceresara G., Orzalesi N., Rossetti L. M. "Corneal subbasal nerves changes in patients with diabetic retinopathy: an in vivo confocal study". *Investigative ophthalmology & visual science*, 50(11), 5155-5158 (2009).