Tortuosity Classification of Corneal Nerves Images Using a Multiple-Scale-Multiple-Window Approach

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MARIE CURIE ACTIONS

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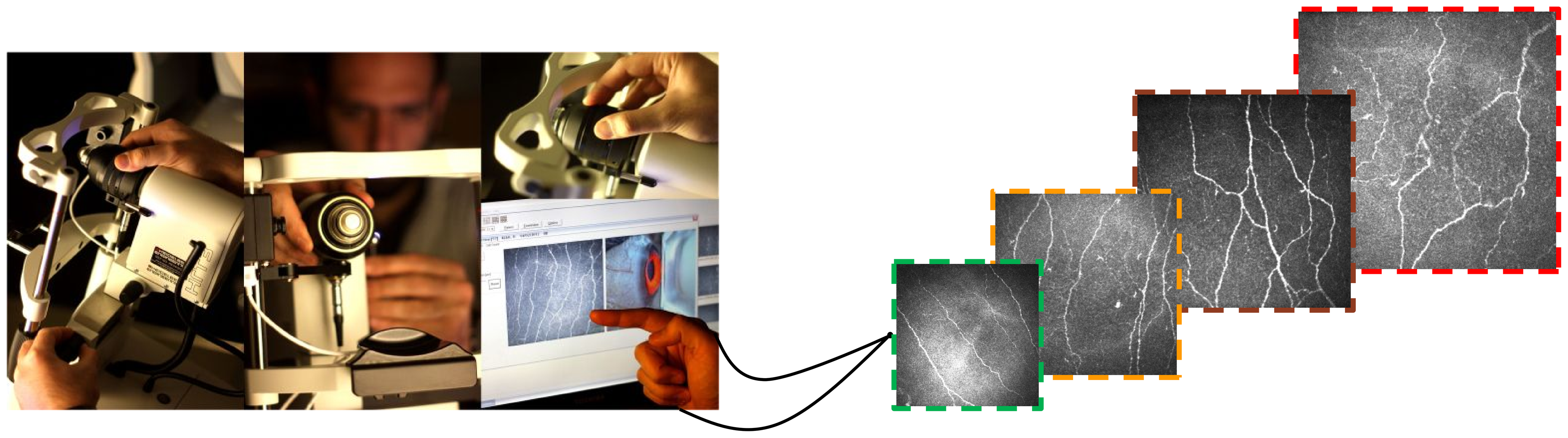
Abstract

Classification of tortuosity of corneal subbasal nerves by *in vivo* confocal microscopy (IVCM) images is complicated by the presence of variable numbers of nerve fibres with different tortuosity levels. Instead of designing a function combining manually selected features into a single coefficient, as done by other groups, we propose a supervised approach which selects automatically the most relevant combination of shape features from a pre-defined dictionary.
To the best of our knowledge, we are the first group to consider features at different spatial scales and show experimentally their relevance in tortuosity modelling. Our results, obtained with a set of 100 images and 20 fold cross-validation, suggest that multinomial logistic ordinal regression, trained on consensus ground truth from 3 experts, yields an accuracy indistinguishable, overall, from that of experts when compared against each other.

Main Contributions

- Multiscale analysis of nerve fibre tortuosity features;
- New, highly accurate numerical curvature estimation applied to corneal nerve fibres
- Automatic identification of most relevant set of scale-space features
- Supervised approach for combining features as opposed to hand-crafted tortuosity definitions
- Dataset:
  - 100 images, 3 independent annotators
  - noisy labels (i.e. modest agreement among annotators)
  - 4 levels of tortuosity to be assessed

Clinical Motivation



- Corneal nerve fibres appear *qualitatively* more tortuous in some diseases (e.g. keratoconic corneas, dry eyes);
- Tortuosity significantly higher in diabetic Retinopathy (DR), one of the leading pathological causes of blindness among working-age people in developed countries.

Technical Motivation

MAIN ISSUE: *qualitative* tortuosity assessment, the current gold standard, leads to high inter-observer and intra-observer variability.

GOAL: to obtain an objective and reproducible corneal nerve fibres tortuosity estimate.

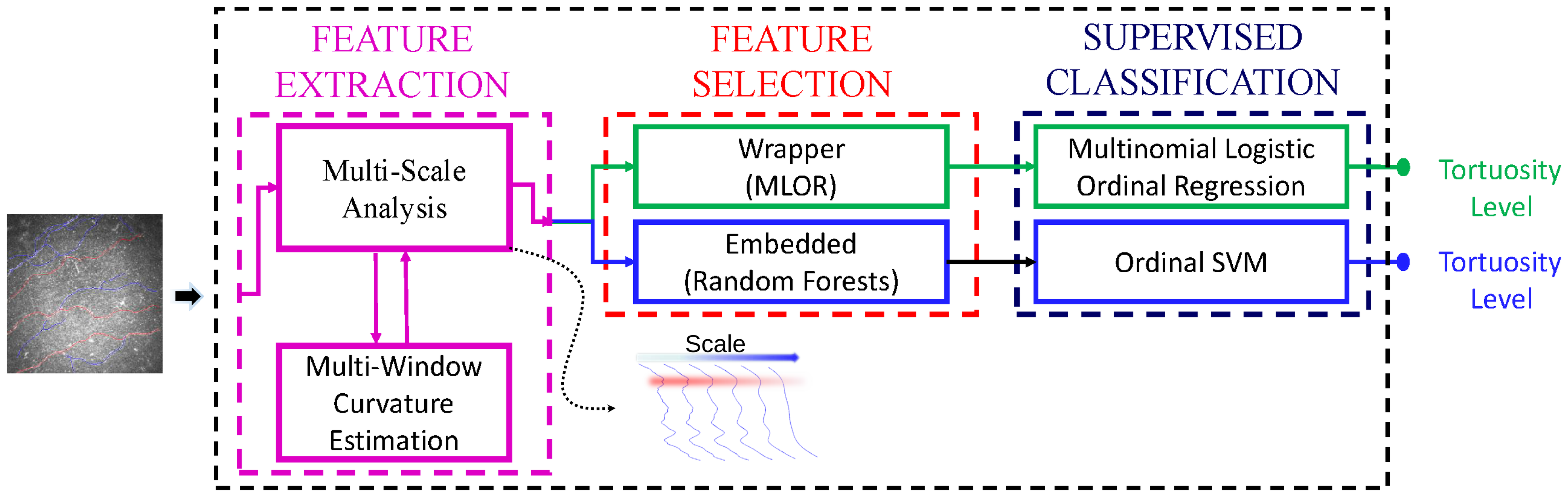
Q1. Does scale play a role?

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

Q3. Previous work: hand-crafted feature selection and tortuosity definition. Can relevant features be identified automatically?

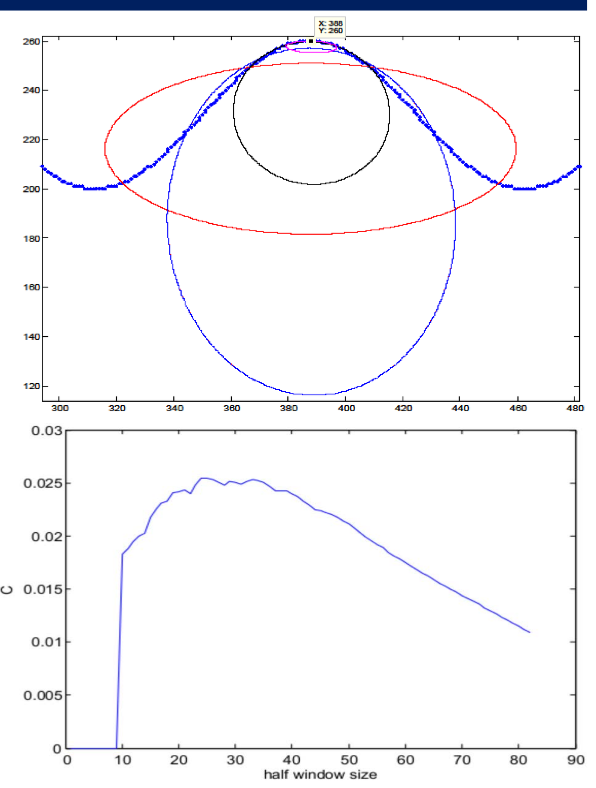
Proposed Approach

IDEA: corneal nerve fibre 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: Classifying Corneal Nerve Images

- Modest inter-observer agreement (< 50%), so we use Consensus Ground Truth (CGT - 90 images).

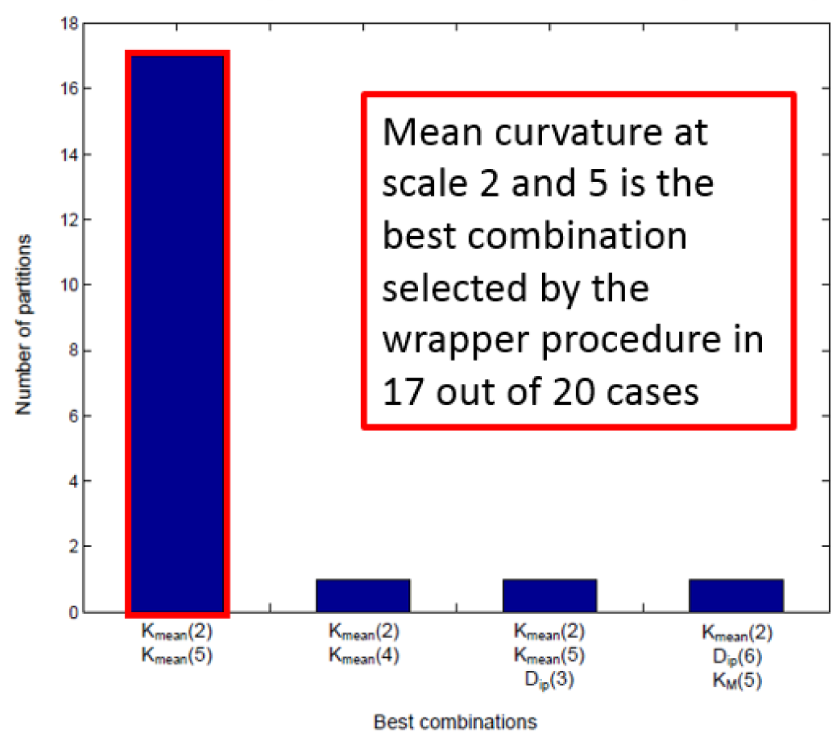
Association with CGT

Perfomance 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

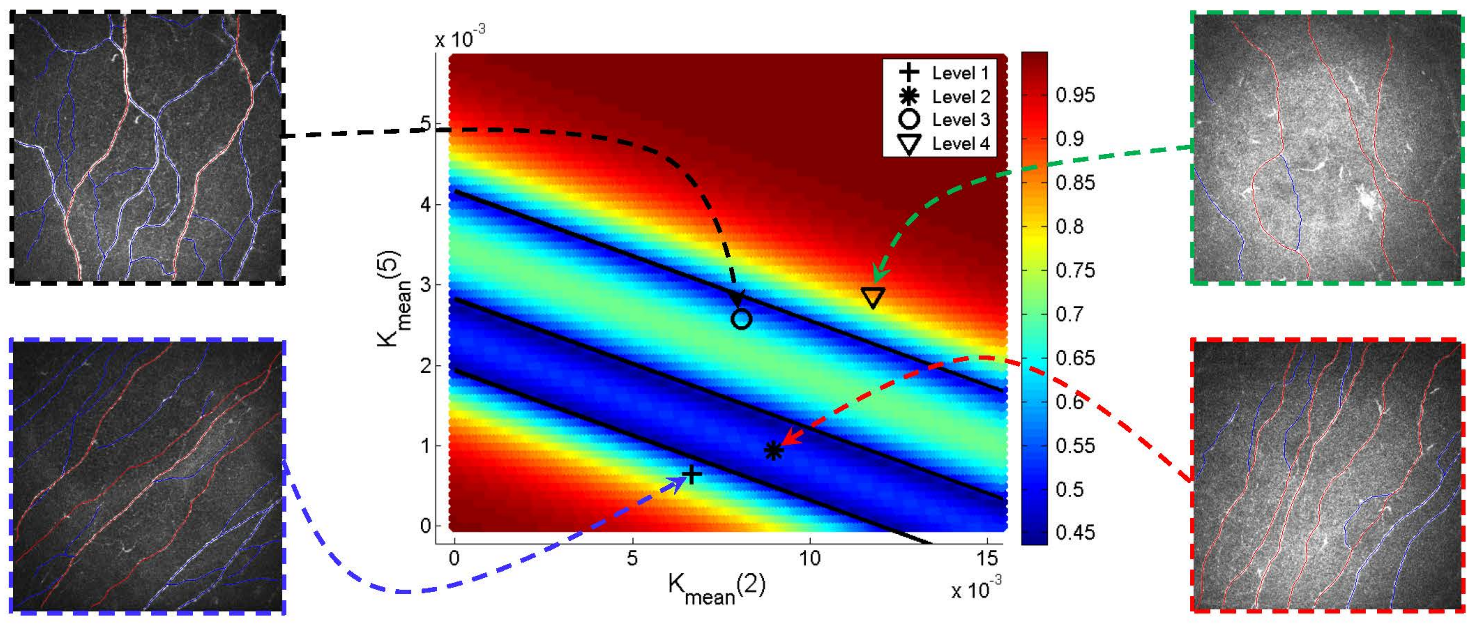
Association with individual GT (Accuracy)

	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)



Examples of predictions on the "tortuosity plane"



Each image is represented as a point on the plane generated by $K_{mean}(2)$ and $K_{mean}(5)$. Different markers are used for images with (actual) different tortuosity levels (CGT). Colour is a visual measure of predictive confidence: high confidence (red), low confidence (blu). Black lines are predicted decision boundaries.

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;**
- **Automatic feature selection, instead of intuitively choosing them, gives promising results;**
- **Supervised approach instead of single formula for tortuosity estimation;**
- **New approach for digital curvature estimation applied to corneal nerve fibres;**
- **First to propose an automatic method capable of predicting more than 3 tortuosity levels.**