

Nerve fiber tracing in bright-field images of human skin using deep learning

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TU Delft

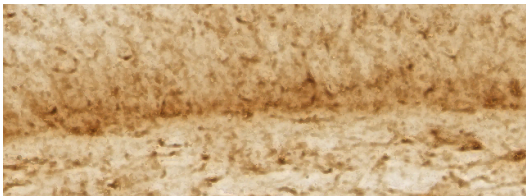
July 10, 2018

Introduction

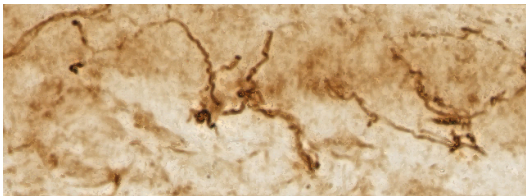
Small Fiber Neuropathy

- ▶ Caused by damaged small unmyelinated nerve fibers.
- ▶ Affects an estimated 15-20 million people in the USA.
- ▶ Symptoms include abnormal sensations of numbness, burning, cold, and prickling.

Small Fiber Neuropathy

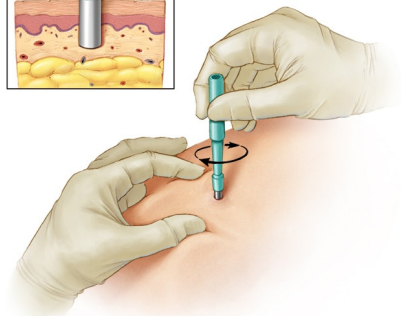
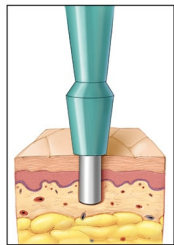


(a) Patient



(b) Healthy volunteer

Skin biopsy



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- ▶ Skin biopsy is often used as investigation tool by determining the skin innervation[1].
- ▶ Immunostaining is used to make nerves visible under a bright-field microscope.

Skin biopsy

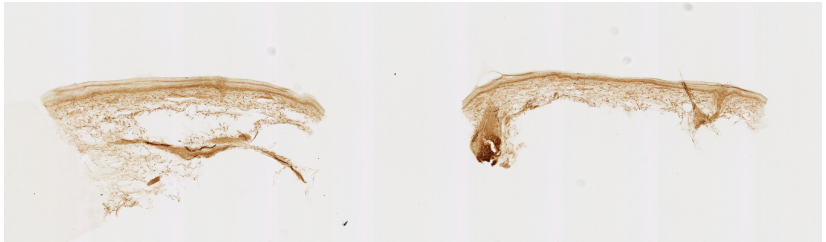


Figure: Two scanned slices

Skin biopsy

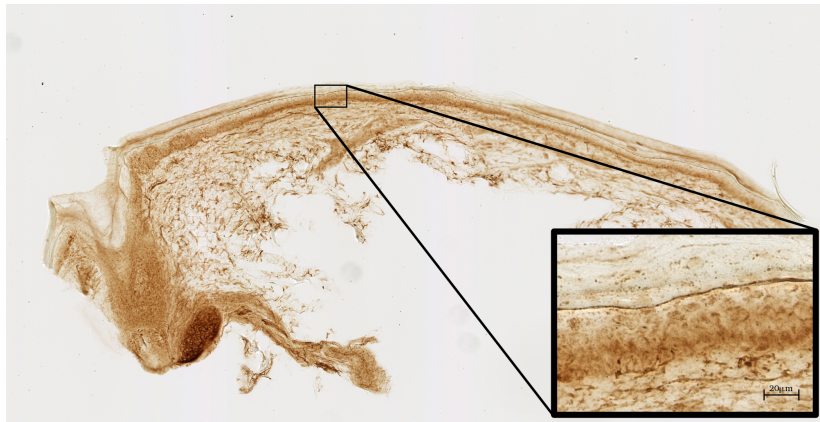
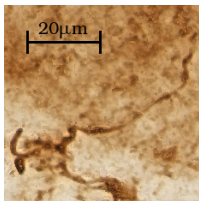


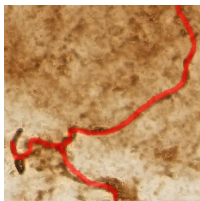
Figure: A region of interest

Skin biopsy

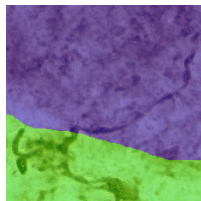
- ▶ *Intra-Epidermal Nerve Fiber Density* (IENFD) is the dermis/epidermis nerve crossing density.



(a) Original image



(b) Nerve



(c) Junction

Problem difficulty

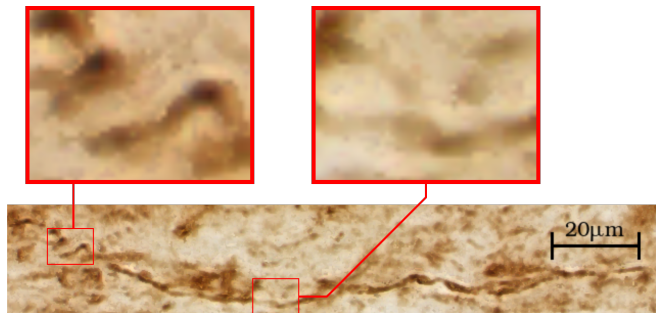
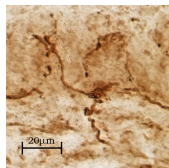


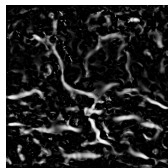
Figure: Discontinuities in the imaged nerve

Conventional method

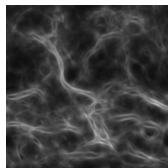
- ▶ Pontenagel [2] developed an automated nerve fiber detection technique using conventional tools in 2017.



(a) Input image



(b) Frangi filter



(c) Tensor voting



(d) Skeleton

What is deep learning

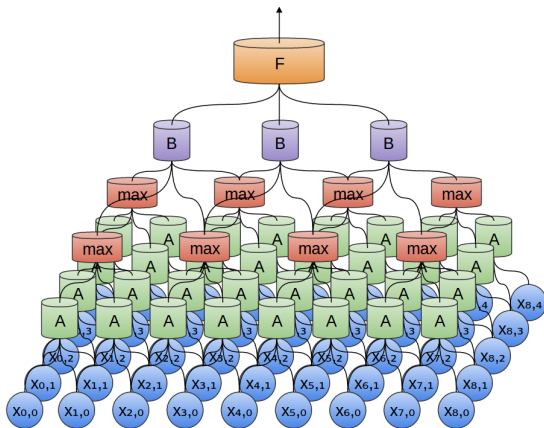


Figure: A miniature computation graph (colah.github.io)

What is deep learning

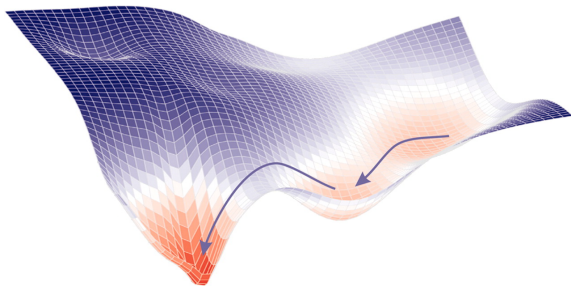


Figure: Gradient descent

What is deep learning

An excellent book on this topic: I. Goodfellow, Y. Bengio, and A. Courville, *Deep learning*. MIT Press, 2016,
<http://www.deeplearningbook.org>.

Deep learning advances

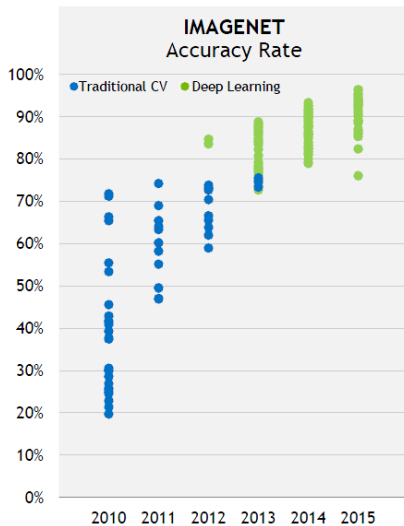


Figure: Advance of deep learning in image classification (slideshare.net/NVIDIA/nvidia-ces-2016-press-conference)

Deep learning advances

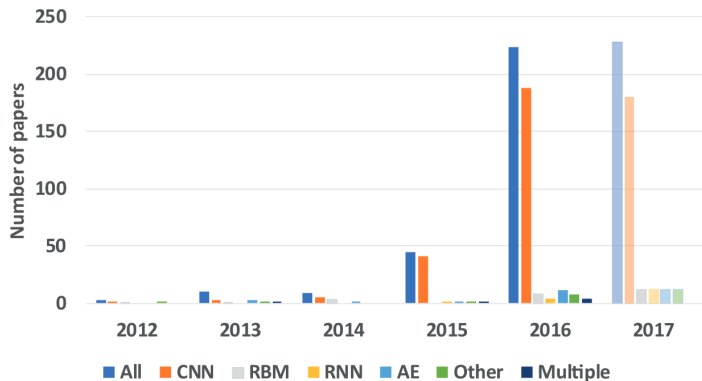
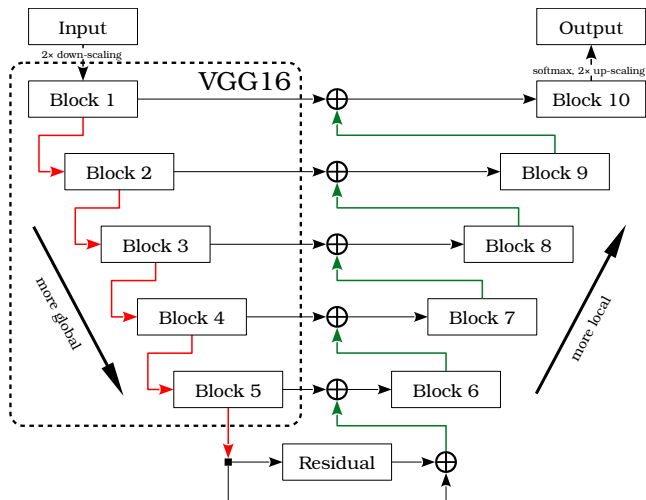


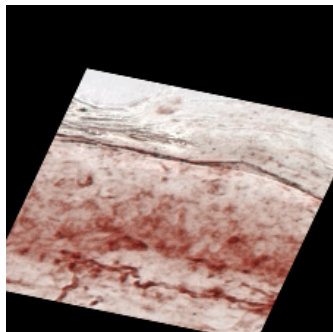
Figure: Deep learning in medical image analysis[4].

Methods

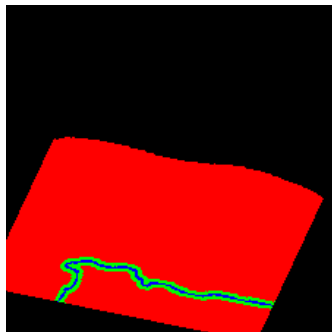
Neural network model



Learning target



(a) Transformed image patch



(b) Ground-truth

Training

	All data (96 images of 640x448)					
	1	2	3	4	5	6
Network 1	Val.	Train				Test
Network 2	Train	Val.	Train			Test
Network 3	Train		Val.	Train		Test
Network 4	Train			Val.	Train	Test
Network 5	Train				Val.	Test

Figure: Division of the available data to train five networks.

Spatial distance metric

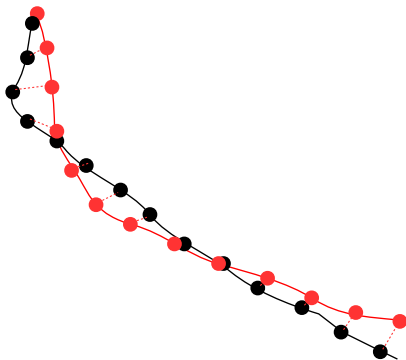


Figure: Two imaginary nerves.

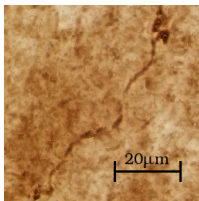
Spatial distance metric

$$D(A, B) = \text{average} \{ \text{Distances from A to B} \}$$

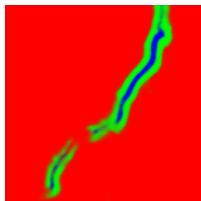
$$SD(\text{Pred}, \text{Truth}) = \frac{D(\text{Pred}, \text{Truth}) + D(\text{Truth}, \text{Pred})}{2}$$

Results

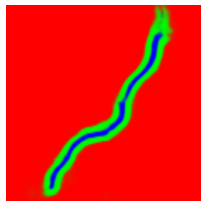
Training results



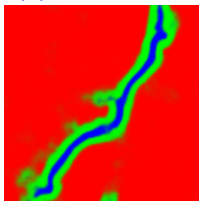
(a) Input image



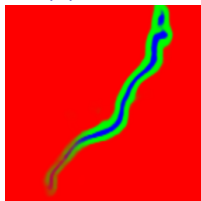
(b) CNN 1



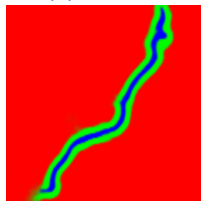
(c) CNN 2



(d) CNN 3

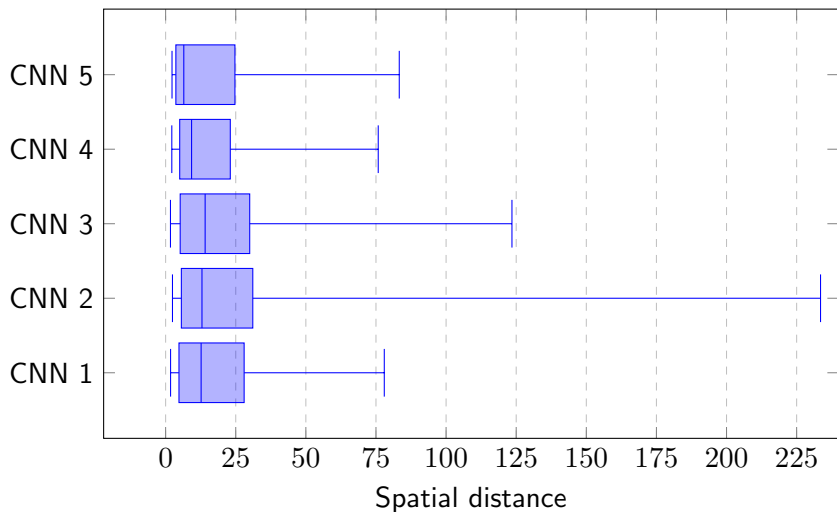


(e) CNN 4

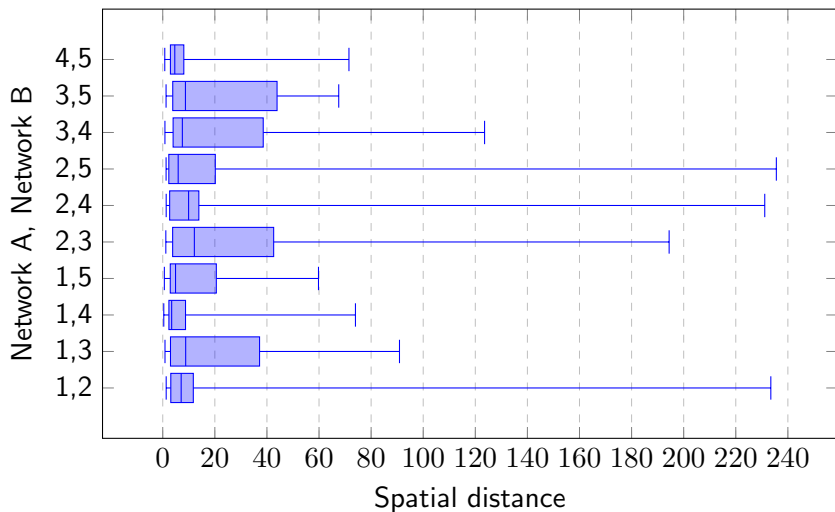


(f) CNN 5

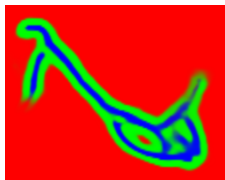
Cross-validation



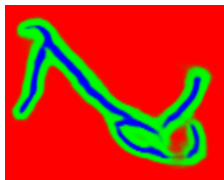
Cross-validation



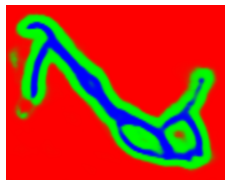
Median prediction



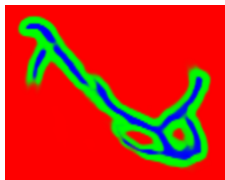
(a) CNN1



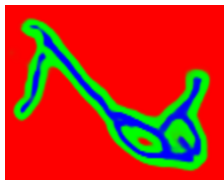
(b) CNN2



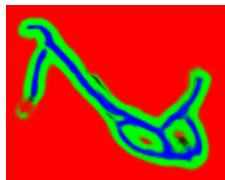
(c) CNN3



(d) CNN4

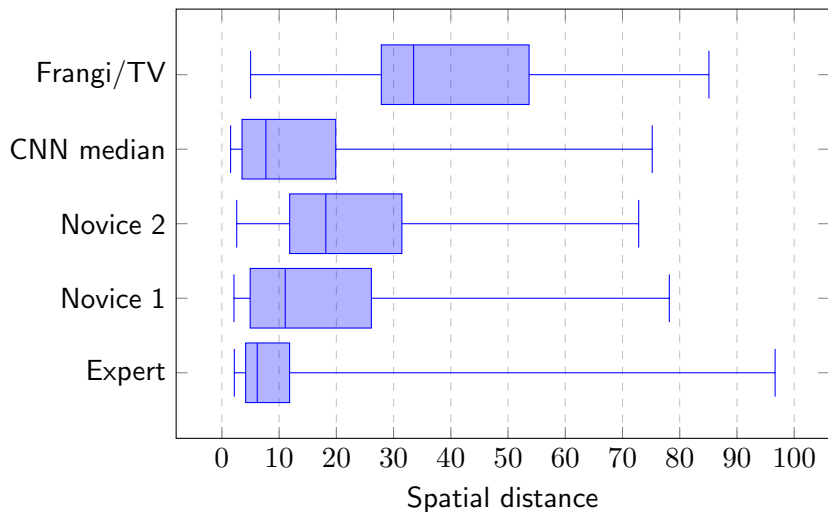


(e) CNN5



(f) Median

Final results



Further work

- ▶ Improve training data quality and quantity

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- ▶ Reduce model size by removing unused filters

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- ▶ Improve training data quality and quantity
- ▶ Reduce model size by removing unused filters
- ▶ Integrate results in secondary neural network for counting

Questions

For a PDF file of the slides and thesis, visit:

<http://bit.ly/bergwerf2018>

(these documents will also be uploaded to the TU Delft research repository)

References

-  G. Lauria, R. Lombardi, F. Camozzi, and G. Devigili, “Skin biopsy for the diagnosis of peripheral neuropathy,” *Histopathology*, vol. 54, no. 3, pp. 273–285, Jul. 2008.
-  P. Pontenagel, “Towards automated quantification of intra-epidermal nerve fibers for diagnosis of small-fiber neuropathy in brightfield microscopy,” *Master’s thesis*, Erasmus MC, TU Delft, Feb. 2017.
-  I. Goodfellow, Y. Bengio, and A. Courville, *Deep learning*. MIT Press, 2016, <http://www.deeplearningbook.org>.
-  Litjens Geert, Kooi Thijs, Bejnordi Babak Ehteshami, Setio Arnaud Arindra Adiyoso, Ciompi Francesco, Ghafoorian Mohsen, van der Laak Jeroen A.W.M., van Ginneken Bram, and Sánchez Clara I., “A survey on deep learning in medical image analysis,” *Medical Image Analysis*, vol. 42, pp. 60–88, 2017.