## Calculation of sum-of-angles metric

The sum-of-angles metric (SOAM) was calculated following Bullitt et al. (Bullitt et al., 2003). $n$ points $(p)$ with 1 mm distance from each other are identified along the optimized vessel path with sub-voxel accuracy. For any point $p_{k}$ the linear sections between the previous and the subsequent point define the vectors

$$
\begin{gather*}
v_{1}=p_{k}-p_{k-1} \text { and }  \tag{1}\\
v_{2}=p_{k+1}-p_{k} \tag{2}
\end{gather*}
$$

with $p_{0}$ being the start point of the vessel path. The in-plane angle in radian between these two vectors is given by

$$
\begin{equation*}
\theta_{k}=\cos ^{-1}\left(\left(\frac{v_{1}}{\left|v_{1}\right|}\right) \cdot\left(\frac{v_{2}}{\left|v_{2}\right|}\right)\right) \tag{3}
\end{equation*}
$$

where $\theta_{k} \in[0, \pi]$ and $\left|v_{1}\right|$ and $\left|v_{2}\right|$ are the lengths of the vectors $v_{1}$ and $v_{2}$, respectively. SOAM is calculated by summing up the angles between adjacent sections of a vessel segment and dividing the result by the length of the vessel segment, which is represented by the cumulative length of the sections used:

$$
\begin{equation*}
S O A M=\frac{\sum_{k=1}^{n-2} \alpha_{k}}{\sum_{k=1}^{n-1}\left|p_{k}-p_{k-1}\right|} \tag{4}
\end{equation*}
$$

Any remaining piece of the vessel path within 1 mm of the last point $p_{n}$ was not considered in the analysis. Only vessel segments with at least two sections were analyzed.

## Reference

Bullitt, E., Gerig, G., Pizer, S.M., Lin, W.L., and Aylward, S.R. (2003). Measuring tortuosity of the intracerebral vasculature from MRA images. IEEE Trans. Med. Imaging 22, 1163-1171. doi: 10.1109/TMI.2003.816964

