EuroRV3: EuroVis Workshop on Reproducibility, Verification, and Validation in Visualization (2016)
K. Lawonn, M. Hlawitschka, and P. Rosenthal (Editors)

Uncertainty and Reproducibility in Medical Visualization

Lars Linsen[1], Ahmed Al-Taie[1], Gordan Ristovski[1], Tobias Preusser[1,2], and Horst K. Hahn[1,2]

[1] Jacobs University, Bremen, Germany
[2] Fraunhofer MEVIS, Bremen, Germany

Abstract

The medical visualization pipeline is affected by various sources of uncertainty. Many errors may occur and several assumptions are made in the various processing steps from the image acquisition to the rendering of the visualization output, which induce uncertainty. High uncertainty leads to low robustness of the algorithms impacting reproducibility of the results. We present how uncertainty can be mathematically described in the medical context. Moreover, in medical applications, the visualization is typically based on a segmentation of the medical images. We propose a method to capture uncertainty in image segmentation and present extensions to ensemble and multi-modal image segmentation.

1. Introduction

The medical visualization pipeline ranges from medical imaging over several data processing steps to the final rendering. Each of these steps introduce a certain amount of uncertainty based on errors or assumptions. The rendered images typically omit this information and allude to the fact that the shown information is the only possible truth. Medical doctors may base their diagnoses and treatments on these visual representations. However, many decisions made in the visualization pipeline are sensitive to small changes, i.e., the robustness of the approach is low. To allow for a proper assessment of the data by the medical experts, the uncertainty that is inherent to the displayed information needs to be revealed.

A crucial step in the medical visualization pipeline is the segmentation step, which classifies each voxels in the medical image. Many different approaches exist and they often lead to different results due to the errors in image acquisition and assumptions in image (pre-)processing, We present an approach to capture these uncertainties. When applying many different segmentation approaches to find a best combined result, one uses the concept of ensemble segmentations. We generalize our approach to also capture the uncertainty in ensemble segmentations. This naturally extends to multi-modal image segmentation uncertainties.

2. Uncertainties in the Medical Context

We first develop a mathematical description to capture uncertainty in medical visualization. We adopt the concept of random fields. Let $(\Omega, \mathcal{A}, \mu)$ denote a complete probability space with a set of events Ω, where an event is a set of outcomes, a sample space $\mathcal{A}$, which is a set of all possible outcomes, and a function μ that assigns to each event a probability. In the context of spatially sampled data, it has become popular to describe uncertain quantities by stochastic fields (or random fields), which roughly speaking are random variables indexed by a spatial location. If $D \subset \mathbf{R}^n$ is a set of spatial locations and $B(D)$ is a Banach space of functions over D (e.g., scalar or vector-valued functions on D), then a random field is a random variable $X(\cdot;x) : \Omega \to \mathbf{R}$, which is indexed by $x \in D$ and such that $X(\omega,\cdot) \in B(D)$ for all possible events $\omega \in \Omega$.

In the medical visualization pipeline, several processing steps are applied, each of which introduces uncertainty. After data acquisition, processing steps including image reconstruction, correction of noise, bias fields, partial volume effects, and patient motion, and possibly registration all make assumptions to compensate for imaging errors. Such uncertainties impact the image segmentation step, which is crucial to all further visualization tasks. There is a wide variety of segmentation procedures that can be applied. Their typical outcome is a list of n segments, where each voxel is assigned to one segment. When capturing the uncertainty in this step, we obtain for each voxel an n-dimensional probability vector that indicates the probability that the respective voxel belongs to one of the n segments. Fuzzy segmentation procedures, such as the fuzzy c-means [BEF84] or modified fuzzy c-means [MAF99], or some Bayesian algorithms, such as the maximum a posteriori or Markov random fields [HGM09], capture these vectors. In the context of the partial volume effect, the type of uncertainty that is being captured by such probabilistic segmentation algorithms is a discrete 3D random field with categorical events. We have derived a complete taxonomy of uncertainties occurring in medical visualization according to the presented mathematical description and classified the different uncertainty typed [RPHL14].

3. Uncertainty in Image Segmentation

To capture the uncertainty in medical image segmentations, we propose an information-theoretical measure applied to fuzzy (or

DOI: 10.2312/eurorv3.20161107

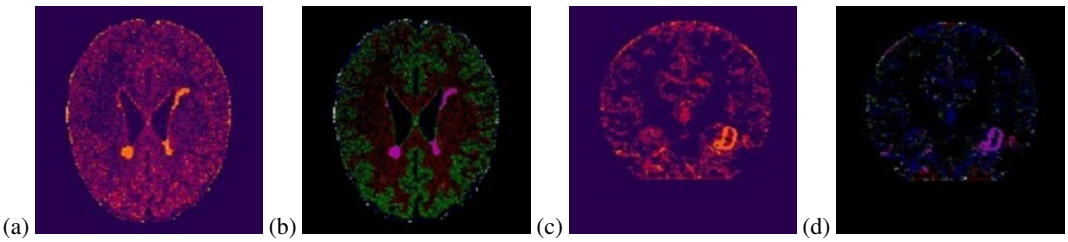

Figure 1: *(a) Uncertainty visualization of multi-modal image segmentation (high uncertainties in brighter colors). (b) Improved segmentation of multi-modal image with multiple sclerosis tumor segmented from high-uncertainty regions in (a). (c) Uncertainty visualization of time-varying image segmentation. (d) Segmentation of tumor growth area from high-uncertainty regions in (c).*

probabilistic) segmentation results. Given two probability vectors $P = (P_1, \ldots, P_c)$ and $Q = (Q_1, \ldots, Q_c)$ of dimensionality c, the Kullback-Leibler divergence is defined as $D_{KL}(P\|Q) = \sum_{i=1}^{c} P_i \log_2 \frac{P_i}{Q_i}$, which measures the difference between the two probability vectors or the information loss when Q is used to approximate P. P represents the true distribution of data,

We use the Kullback-Leibler divergence to compute the uncertainty $U(v)$ associated with a voxel v based on the probability vector P_v that has been computed using a probabilistic segmentation algorithm, i.e., the i-th entry of vector P_v denotes the probability that voxel v belongs to the i-th segment, where the number of segments is c. Following the definition, we use the Kullback-Leibler divergence to measure the amount of the deviation of the probability vector P_v from the minimum uncertainty vector P_{min}. Minimum (i.e., no) uncertainty is obtained when one entry of the probability vector is 1 and all the others 0. Hence, we set $P_{min} = \{1, 0, \ldots, 0\}$. Maximum uncertainty is obtained when a voxel is equally likely to belong to all segments, i.e., $P_{max} = \{\frac{1}{c}, \ldots, \frac{1}{c}\}$ Consequently, the uncertainty for voxel v is defined by $U_{KL}(v) = \frac{D_{KL}(P_{min}\|P_v)}{D_{KL}(P_{min}\|P_{max}))}$. Results for uncertainty visualization are presented in [AHL14b].

4. Uncertainty in Ensemble Segmentations

In order to easily reproduce medical visualizations, the segmentation step needs to be robust, i.e., similar inputs shall lead to similar outputs. For a more robust (and improved) segmentation, ensemble of classifiers can be introduced. For ensemble segmentation, instead of using the probabilities obtained by a single classifier, the probability values of all classifiers compete to determine the winner as the final ensemble decision. Different combining rules can be used. We extended them to the probabilistic setting and observed that the majority rule performs best. Here, the i-th entry of the probability vector of the probabilistic ensemble segmentation result (for L classifier) at each voxel x can be computed by $P_i(x) = \frac{\sum_{j=1}^{L} \Delta_{ij}}{\sum_{k=1}^{c} \sum_{j=1}^{L} \Delta_{kj}}$, where Δ_{ij} is a binary vote being 1 if P_{kj} is the maximum among all P_{ij}, $i = 1, \ldots, c$, and 0 otherwise. Our empirical studies showed that the ensemble sementations can reduce uncertainty [AHL14a].

5. Ensemble Diversity

The success of an ensemble segmentation is based on its diversity. A classifier ensemble is considered to be diverse, if the classifiers make no coinciding errors. We propose a local diversity measure given by the normalized entropy $D(P_v) = \frac{H(P_v)}{\log_2(c)}$, where $H(P_v)$ is the entropy of the probability vector P_v, i..e, $H(P_v) = -\sum_{i=1}^{c} P_{v_i} \log_2 P_{v_i}$. Global diversity can be estimated as the average local diversity. The local diversity is 0 when all classifiers agree on one decision and it is 1 when all classes have equal probability. We show the advantages of our local diversity measure for uncertainty visualization in [AHL15a].

6. Uncertainty in Multi-modal Image Segmentations

The ensemble segmentation can also be used in the context of multi-modal segmentations, where classifiers are applied to different modalities of a multi-modal image. When using different modalities, tumors show up with different intensities. Hence, when using a majority vote rule, the votes do not not concur in tumor regions leading to high uncertainties. Figure 1 shows an example where T1-weighted, T2-weighted, and PD-weighted magnetic resonance images of a head scan (data source: Brain Web) were combined. The tumors show up as high-uncertainty regions (a) and can be segmented robustly based on these estimates (purple regions in (b)). Figure 1(c) shows how our approach is applied to time-varying data, where T1-weighted magnetic resonance images where taken at two points in time. The example shows that the segmentations do not occur in region of tumor growth, i.e., the uncertainty is high. Figure 1(d) shows the respective tumor growth area (in purple) derived using our uncertainty-based approach, More details are provided in [AHL15b].

7. Conclusion

Reproducibility of medical visualization results is impaired by the choice of many parameters in the medical visualization pipeline, especially in the crucial segmentation step. Uncertainty sources in the pipeline accumulate and lead to a challenging segmentation task. Probabilistic segmentations try to capture the uncertainty in the approach. We presented an uncertainty measure in probabilistic segmentation and showed how an ensemble of classifiers can be used to reduce the uncertainty. This step relies on a diversity of the ensemble. We also showed how this concept can be used in a multi-modal setting to obtain reliable segmentations of features (tumors in our case) that can only be extracted using all modalities. This was based on our uncertainty measure.

References

[AHL14a] AL-TAIE A., HAHN H. K., LINSEN L.: Uncertainty-aware ensemble of classifiers for segmenting brain MRI data. In *Eurographics Workshop on Visual Computing for Biology and Medicine, VCBM 2014, Vienna, Austria, 2014. Proceedings* (2014), pp. 41–50. URL: http://dx.doi.org/10.2312/vcbm.20141182, doi:10.2312/vcbm.20141182. 2

[AHL14b] AL-TAIE A., HAHN H. K., LINSEN L.: Uncertainty estimation and visualization in probabilistic segmentation. *Computers & Graphics 39* (2014), 48–59. URL: http://dx.doi.org/10.1016/j.cag.2013.10.012, doi:10.1016/j.cag.2013.10.012. 2

[AHL15a] AL-TAIE A., HAHN H. K., LINSEN L.: Point-wise diversity measure and visualization for ensemble of classifiers - with application to image segmentation. In *VISAPP 2015 - Proceedings of the 10th International Conference on Computer Vision Theory and Applications, Volume 1, Berlin, Germany, 11-14 March, 2015.* (2015), pp. 569–576. URL: http://dx.doi.org/10.5220/0005309605690576, doi:10.5220/0005309605690576. 2

[AHL15b] AL-TAIE A., HAHN H. K., LINSEN L.: Uncertainty estimation and visualization for multi-modal image segmentation. In *Eurographics Workshop on Visual Computing for Biology and Medicine, VCBM 2015, Chester, UK, September 14-15, 2015.* (2015), pp. 21–30. URL: http://dx.doi.org/10.2312/vcbm.20151205, doi:10.2312/vcbm.20151205. 2

[BEF84] BEZDEK J., EHRLICH R., FULL W.: FCM: The fuzzy c-means clustering algorithm. *Computers & Geosciences 10*, 2-3 (1984), 191–203. 1

[HGM09] HU, GROSSBERG, MAGERAS: Survey of recent volumetric medical image segmentation techniques. *Biomedical Engineering Carlos Alexandre Barros de Mello Ed* (2009), 321–346. 1

[MAF99] MOHAMED N. A., AHMED M. N., FARAG A.: Modified fuzzy c-mean in medical image segmentation. In *in Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing* (1999), pp. 3429–3432. 1

[RPHL14] RISTOVSKI G., PREUSSER T., HAHN H. K., LINSEN L.: Uncertainty in medical visualization: Towards a taxonomy. *Computers & Graphics 39* (2014), 60–73. URL: http://dx.doi.org/10.1016/j.cag.2013.10.015, doi:10.1016/j.cag.2013.10.015. 1