



## Habilitation Thesis Reviewer's Report

### Masaryk University

#### Faculty

Faculty of Informatics

#### Procedure field

Informatics

#### Applicant

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#### Habilitation thesis

Object Tracking in Bioimage Data

#### Reviewer

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Habilitation thesis “*Object Tracking in Bioimage Data*” submitted by Martin Maška contains a collection of selected articles – 9 journal publications and 3 conference contributions – representing Dr. Maška's research interests and scientific results since receiving his Ph.D. degree. The collection is introduced by a comprehensive commentary (26 pages) summarizing the topic of object tracking, its relevance and specificities in automated biomedical image analysis, with a particular focus on the relevance of reliable quantitative performance assessment of the available algorithms. Dr. Maška's own contributions to the state of the art are briefly overviewed in a well structured summary: Chapter 2 focuses on the task of particle tracking (P1-Nature Methods 2014, P2-ECCVW 2017), Chapter 3 highlights the contributions to cell tracking (P3-TMI 2013, P4-Bioinformatics 2014, P5-PLoS ONE 2015, P6-PLoS ONE 2017, P7-Nature Methods 2017), whereas Chapter 4 elaborates on Dr. Maška's work on filopodia tracking (P8-ISBI 2013, P9-TMI 2018, P10-TMI 2019, P11-Bioinformatics 2019, P12-ICIP 2019). Chapter 5 offers the Author's view on some possible future research directions.

The Commentary provides a well written summary of the main research challenges addressed by Dr. Maška's work, highlighting specificities of biomedical image analysis characterized by high diversity and complexity of huge (and continuously increasing) amount of high-dimensional data, imposing necessity of automated analysis, while at the same time critically limiting availability of ground truth annotations relevant for algorithm development and evaluation, as well as quantitative assessment of the final bioimage analysis results obtained by the available approaches. On a negative side, let me comment that the illustrations included in the commentary are of rather limited informative content, being taken out of the context of the respective original publications, while not being suitably explained in the text (or captions). Figures 2.2 and 3.4 are most representative examples of this type. Further, I find Chapter 5 too brief, considering its relevance. I would prefer to read a more elaborate outlook, with some well argued for inspiring research questions to be addressed in the future, stemming from Dr. Maška's recent or current work.

## Overall Assessment of the Included Selection of Works

Dr. Maška's contribution to the research field is multi-folded. It includes **(1) development and application of novel algorithms** for robust and fully automatic tracking of particles, cells, and filopodial protrusions in multidimensional bioimage data (P3, P6, P8, P10) **(2) proposals of novel tools – quality measures and high quality synthetic data simulators** – which enable development and performance evaluation of (particle, cell, and filopodia) tracking algorithms (P2, P5, P9, P11, P12) and **(3) preparation of rigorous evaluation protocols** to be conducted in several community-wide efforts (**challenges**) to identify potential and limitations of the available approaches, as well as promising directions for further development of the field (P1, P4, P7).

In my opinion, such a broad range of contributions, which respond to diverse needs of the bioimage analysis community, is highly beneficial for reaching scientific maturity, expanding own collaborative networks and gaining experience of team-work, while having close and continuous insight in state-of-the-art of the field and its development, and frequently contributing to its own high quality results.

I have no doubts that Dr. Maška's experience gained from challenge organization is highly valuable, and that the related publications (P1, P4, P7) are of high relevance for the (biomedical) image analysis community as a whole, and in particular for its part focused on object tracking. However, this activity/contribution is a result of a joint effort of several very well established research groups, leading to publications with 30-40 co-authors. Whereas the list of co-authors, as well as the quality of the journals where the papers are published, strongly speak for high relevance of the research output, a confident assessment of any individual contribution of the co-authors is hardly possible. Quite naturally, this type of collaboration does not promote independence. Furthermore, the number of citations of these publications is strongly related to the type of publication (comparison of a selection of competing, and “winning”, algorithms), and is in my opinion, a poor (unsuitable) indicator of the impact of Martin's scientific work. I therefore find this particular aspect of Dr. Maška's work of lower relevance for assessment of his own scientific contribution.

On the other hand, Dr. Maška's original results related to the development and evaluation of object tracking algorithms confirm, with no doubts, both high quality and relevance, but also Author's independence and high level of responsibility for the conducted research and published results.

### Contributions to Method Development

*P3-TMI 2013* proposes a novel approach to cell tracking in 2D and 3D time-lapse series, based on model evolution. Methodological contributions ensure fast computation, as well as simultaneous multiple cell tracking, with excellent tracking performance; alternative considered formulations enable a trade-off between accuracy and speed. Dr. Maška's contribution to this study is crucial. *P6-PLoS ONE 2017* illustrates successful application of these developed methods in a real scenario, where Dr. Maška had responsibility for the image analysis part of the performed biomedical research.

**P8-ISBI 2013** presents a first fully automatic approach to quantitatively analyzing filopodial protrusions of migrating cells in 3D+t fluorescence microscopy image data. The limitations of this initial study are addressed in **P10-TMI 2019**, resulting in a pioneering approach to robustly analyzing the 3D morphology and dynamics of arbitrarily oriented filopodial structures for cells embedded in three-dimensional microenvironments, with high generalizability to different realistic scenarios. This extensive study builds on several other Authors' results, and relies on deep learning approaches, reaching high performance.

### **Contributed Tools for Quantitative Evaluation and Benchmarking**

**P5-PLoS ONE 2015** proposes a novel tracking accuracy measure that penalizes all types of errors in tracking results and aggregates them into a single value, accounting for all important cellular events (migration, division, death, and transit), within a single evaluation protocol. The measure assesses the difficulty of transforming a computed acyclic oriented graph into a given ground-truth reference. Both the theoretical properties and performance evaluation of the proposed measure are elaborated on, indicating its robustness, relevance and applicability. **P2-ECCVW 2017** presents a simplified version of the measure, applicable to particle tracking (with a reduced range of relevant events), where linear oriented graphs are used as a more suitable model. Both measures were extensively used in evaluation of the contributions submitted to the organized challenges. Dr. Maška's contribution to these results is crucial.

**P9-TMI 2018** introduces FiloGen, a simulation system for generating 3D+t sequences of motile cells with filopodia, enabling user-controlled diversity and variability of filopodia's structural and temporal attributes. Due to the reached high level of similarity (structural, visual, and quantitative) of the generated synthetic data to the original counterpart (and with the benefit of inherently generated reference annotations), this system is of a highest relevance for (filopodia tracking) method development and evaluation, with a particular focus on deep learning-based approaches. Dr. Maška significantly contributed to all aspects of this work, including its overall supervision. FiloGen simulator is made publicly available through its integration into CytoPacq, a web-interface presented in **P11-Bioinformatics 2019**, and developed for generating synthetic benchmark datasets of various cytology-centric 3D digital phantoms in diverse imaging scenarios. Dr. Maška co-supervised this initiative which confirms his devotion to open science and user-friendly applicable software solutions, suitable for a broad and diverse interdisciplinary audience. This work is further extended and complemented by the provided new benchmark dataset, FiloData3D, designed for performance assessments of 3D filopodium segmentation and tracking algorithms, as presented in **P12-ICIP 2019**, where its relevance is confirmed by indicating superiority of 3D+t analysis over the, by then prevailing, 2D-selection-oriented protocols. Dr. Maška significantly contributed to all aspects of this work.

### **Reviewer's questions for the habilitation thesis defence**

1. What are the possible/envisioned directions forward in challenge organization which may promote general, theoretically well-founded, reliably evaluated, and well performing bioimage analysis methods which advance the field, support open science, and ensure

trustworthy bioimage analysis results? What are the main observed obstacles, and what are the identified approaches to overcome them? Are there any particular issues related to deep learning approaches, considering their often low level of explainability (interpretability)?

2. Why is the fact that the novel tracking quality measures (P2 and P5) lead to re-ranking of a large number of the considered algorithms (participating in the challenges) seen as an evidence for the quality of the measure? How does that relate to the relevance (quality) of the initial challenge results?
3. Could you elaborate on relevant emerging research questions in biomedical image analysis, in particular related to your current research interests? What are your 5-10 year research and career goals and what are the immediate steps towards them?
4. What is the future of data simulation, having on mind both its high relevance and a challenge to synthesize high quality data with required variability, in particular considering the increasing number of imaging techniques/modalities (reaching e.g., several tens of different types of microscopy)? What are the alternatives, in particular w.r.t. data annotation?

## Conclusion

Dr. Martin Maška has confidently documented his high quality, and respectable in volume, scientific contribution to the field of object tracking in bioimage data. His co-authored publications in some of the top-ranked journals (TMI, PloS ONE, Nature Methods, Bioinformatics) and at conferences highly relevant for this scientific field (ISBI, ECCV-W, ICIP), respectable number of citations, and established collaborative networks including leading international research groups, give very strong evidence of Dr. Maška's strong and independent research profile and enable me to conclude that:

The habilitation thesis entitled “*Object Tracking in Bioimage Data*” by Dr. Martin Maška *fulfils* the requirements expected of a habilitation thesis in the field of Informatics.

In Uppsala,  
on November 30 2020