- 1. Our entry is based on the following two published literatures:
 - a) Optimizing a Medical Image Analysis System Using Mixed-Integer Evolution Strategies. R. Li, M.T.M. Emmerich, J. Eggermont, E.G.P. Bovenkamp, T. Bäck, J. Dijkstra, and H. Reiber. Book chapter in Evolutionary Image Analysis and Signal Processing, 91-112, Springer, ISBN: 978-3-642-01635-6, July 2009. (http://springerlink.com/content/3033r6642j453p10/?p=d1299d788bab495f82854a4ff059de70&pi=5)
 - b) Mixed-Integer Evolution Strategies for Parameter Optimization and Their Applications to Medical Image Analysis. R. Li, PhD Thesis, Leiden University, ISBN: 978-90-9024665-9, October 2009. (https://openaccess.leidenuniv.nl/handle/1887/14049)
- 2. The names of the authors of both publications (in alphabetical order):
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4. Abstracts:

Book chapter abstract:

We will discuss Mixed-Integer Evolution Strategies (MIES) and their application to the optimization of control parameters of a semi-automatic image analysis system for Intravascular Ultrasound (IVUS) images. IVUS is a technique used to obtain real-time high-resolution tomographic images from the inside of coronary vessels and other arteries. The IVUS image feature detectors used in the analysis system are expert-designed and the default parameters are calibrated manually so far. The new approach, based on MIES, can automatically find good parameterizations for sets of images, which provide in better results than manually tuned parameters. From the algorithmic point of view, the difficulty is designing a black-box optimization strategy that can deal with nonlinear functions and different types of parameters, including integer, nominal discrete and continuous variables. MIES turns out to be well suited for this task. The results presented in this contribution will summarize and extend recent studies on benchmark functions and the IVUS image analysis optimization problem

PhD thesis abstract:

The original idea of our work is to extend the canonical Evolution Strategies (ES) from traditional real-valued parameter optimization domain to mixed-integer parameter optimization domain. This is necessary because there exist numerous practical optimization problems from industry in which the set of decision variables simultaneously involves continuous, integer, and nominal discrete variables. Furthermore, objective functions of this type of problems could be based on large-scale simulation models or the structure of the objective functions may be too complex to be modeled. From this perspective, optimization problems of this kind are classified into the black-box optimization category. For them, classic optimization techniques, which come from the Mathematical Programming (MP) research field, cannot be easily applied, since they are based on the assumption that the search space can always be efficiently explored using a divide-and-conquer scheme. Our new proposed algorithm, the so-called Mixed-Integer Evolution Strategies (MIES), by contrast, is capable of yielding good solutions to these challenging black-box optimization problems by using specialized variation operators tailored for mixed-integer parameter classes.

The contents of this dissertation consist of three major parts: (1) the introduction and theoretical study of the newly proposed optimization algorithm; (2) Its application to the real-world applications, that is, parameter optimization for medical image analysis; (3) advanced topics, such as niching techniques. More specifically, in the theoretical part the state-of-the-art MIES algorithms are introduced, and then they are tested on several carefully designed artificial landscapes, for instance, generalized NK landscapes.

The real-world application part mainly focuses on parameter optimization problems from the medical research field. More specifically, we apply MIES to the optimization of control parameters of a semi-automatic image analysis system for Intravascular Ultrasound (IVUS) [4] and Computed Tomography Angiography (CTA) [3] images which show the inside of coronary or other arteries. These medical images are difficult to interpret which causes manual segmentation to be highly sensitive to intra- and inter-observer variability [2]. Thus, the development of feature detection systems for medical images has received much attention in medical and computer science research. However, the performance of most

systems depends on a large number of control parameters that are hard to optimize manually and may differ for different interpretation contexts. Moreover, these parameters are subject to change when something changes in the image acquisition process. Compared to other approaches, with MIES the system developer can search for optimized parameter settings automatically and likely will obtain parameter settings that lead to significant higher accuracy of the feature. The results show the parameters optimized by the MIES algorithms are equal or better than human-optimized parameters.

In the third part, some advanced techniques, which can be used in combination with MIES, are investigated to further improve the performance of our algorithms, for example, Metamodel-Assisted Optimization, Niching Techniques and Bayesian Learning.

5. Criterion: E, F, and G

- (e) The result is equal to or better than the most recent human-created solution to a long-standing problem for which there has been a succession of increasingly better human-created solutions.
- (f) The result is equal to or better than a result that was considered an achievement in its field at the time it was first discovered.
- (g) The result solves a problem of indisputable difficulty in its field.

6. Rationale:

One of the highest targets in image analysis is the realization of intelligent fully automatic image interpretation. However, especially in medical imaging, this has proven to be very hard due to the complexities of the scenes, poor image quality, variability of objects, artefacts, and occlusion. Often complex and variable structures, such as calcified plaques in arteries, are to be detected and modelled in images or sequences of images.

Despite it receiving much attention in medical and computer science research, the performance of most systems still depends on a large number of control parameters. Nowadays, the setting of these control-parameters is done by means of an educated guess or manual tuning following a tedious trial and error approach which often leads to suboptimal settings. In addition, given the frequent changes in image processing technologies (e.g., IVUS, CTA, and MRI) this manual tuning has to be carried out again and again. Each time this will occupy the valuable time of experts

For the Savage-project (Self-Adaptive Vision Agents using Genetic Evolution, NWO project 612.066.408) we proposed a truly self-learning system that can bridge this "knowledge gap" automatically by learning such knowledge from examples and user-interactions. We applied this system to different contexts, all related to cardiovascular disease detection. As cardiovascular disease is the leading cause of death in the world (30%) [1], it is important to have reliable systems to detect the calcified plagues that cause this disease. A state-of-the-art multi-agent system for analysing image data of coronary vessels has been developed by researchers of the LKEB/LUMC [2]. We restated the problem of finding an optimal configuration of the system as a high dimensional mixed integer programming optimization task. The solution of this system is accomplished by a newly developed self-adaptive evolutionary algorithm, the Mixed-Integer Evolution Strategy (MIES). More advanced problems that deal with data from different patient groups, are solved by a multi-island evolutionary algorithm called Dynamic Fitness Based Partitioning (DFP) that uses the MIES as a subroutine [3].

In order to validate our approach we applied it to different image processing systems (IVUS [4], CTA [3]) and compared the solutions of the optimized systems to those of a system optimized by experts and using out-of-the-box optimization approaches. Whereas the manually found solutions often led to misclassifications on the validation data (> 200 images for IVUS, > 630 images for CTA), the configurations found by MIES/DFP technique yielded a reliability of 100%. Our flexible MIES/DFP module is now also used for parameter optimization of MRI segmentation algorithms, which will be used in a commercial package distributed by the LUMC in the near future.

7. Full citations:

- [1] World Health Organization (2004). "Annex Table 2: Deaths by cause, sex and mortality stratum in WHO regions, estimates for 2002". *The world health report 2004 changing history*. (http://www.who.int/whr/2004/annex/topic/en/annex 2 en.pdf)
- [2] User-Agent Cooperation in Multiagent IVUS Image Segmentation, E.G.P. Bovenkamp, J. Dijkstra, J.G. Bosch, J.H.C. Reiber, IEEE Transaction on Medical Imaging, 94-105, 28(1), 2009.
- [3] Optimizing Computed Tomographic Angiography Image Segmentation using Fitness Based Partitioning. J. Eggermont, R. Li, E.G.P. Bovenkamp, H. Marquering, M.T.M. Emmerich, A.v.d. Lugt, T. Bäck, J. Dijkstra, and H. Reiber. Proceedings of the 10th European workshop on evolutionary computation in image analysis and signal processing (EvolASP), 275-284, LNCS 4974, Springer, 2008. (Best Paper Award)
- [4] Mixed-Integer Evolution Strategies and their Application to Intravascular Ultrasound Image Analysis. R. Li, M.T.M. Emmerich, E.G.P. Bovenkamp, J. Eggermont, T. Bäck, J. Dijkstra, and H. Reiber. Proceedings of the 8th European workshop on evolutionary computation in image analysis and signal processing (EvolASP), 415-426, LNCS 3907, Springer, 2006 (Best Paper Award Nomination).
- Any prize money is to be divided equally among the two research groups involved (LKEB, Leiden University Medical Center and LIACS, Leiden University) and will be used to support PhD students or PostDocs in international travel to present their results at conferences.
- 9. Statement of why the judges should consider the entry as "best" in comparison to other entries that may also be "human-competitive"

Cardiovascular disease has been reported by the WHO as the leading cause of death in the world (30%) [1]. Modern medical image processing technologies, such as MRI and CTA scans, bear the promise that they can detect the disease in time and with minimal intervention. Such systems are of great importance as the number of well-trained physicians (experts) on this subject is low and the automated detection of structures can relieve them from routine tasks and spend more time on patient-care. The software used for supporting these technologies, however, is still in its infancy. Non-sharp images, occlusion, complexities in scenes, etc., make it difficult to optimize such systems purely by hand.

Our self-learning software configuration approach based on MIES/DFP provides a solution for this problem, by completely taking over the time consuming task of configuring and parameterizing the systems from the expert. Moreover, it provides more reliable results than manual tuning, thereby increasing quality of the medical image analysis software and eventually the therapeutically success. Therefore, the system is directly used to help humans

when it comes to the discovery, identification and treatment of (often serious) diseases and it has an impact on society as a whole – improving the quality and speed of medical image based diagnosis significantly.

Our MIES/DFP system turned out to be surprisingly flexible and versatile: It proved to be human-competitive not only in the most extensively studied domain of IVUS and CTA image feature detection, but also it could be easily adopted for MRI images, where it is now used in practise and will be part of a software package distributed by LUMC. We expect our approach to be applicable also in feature detection domains outside the cardiovascular diagnosis. The vision of a generic, self-learning image analysis system has come closer.