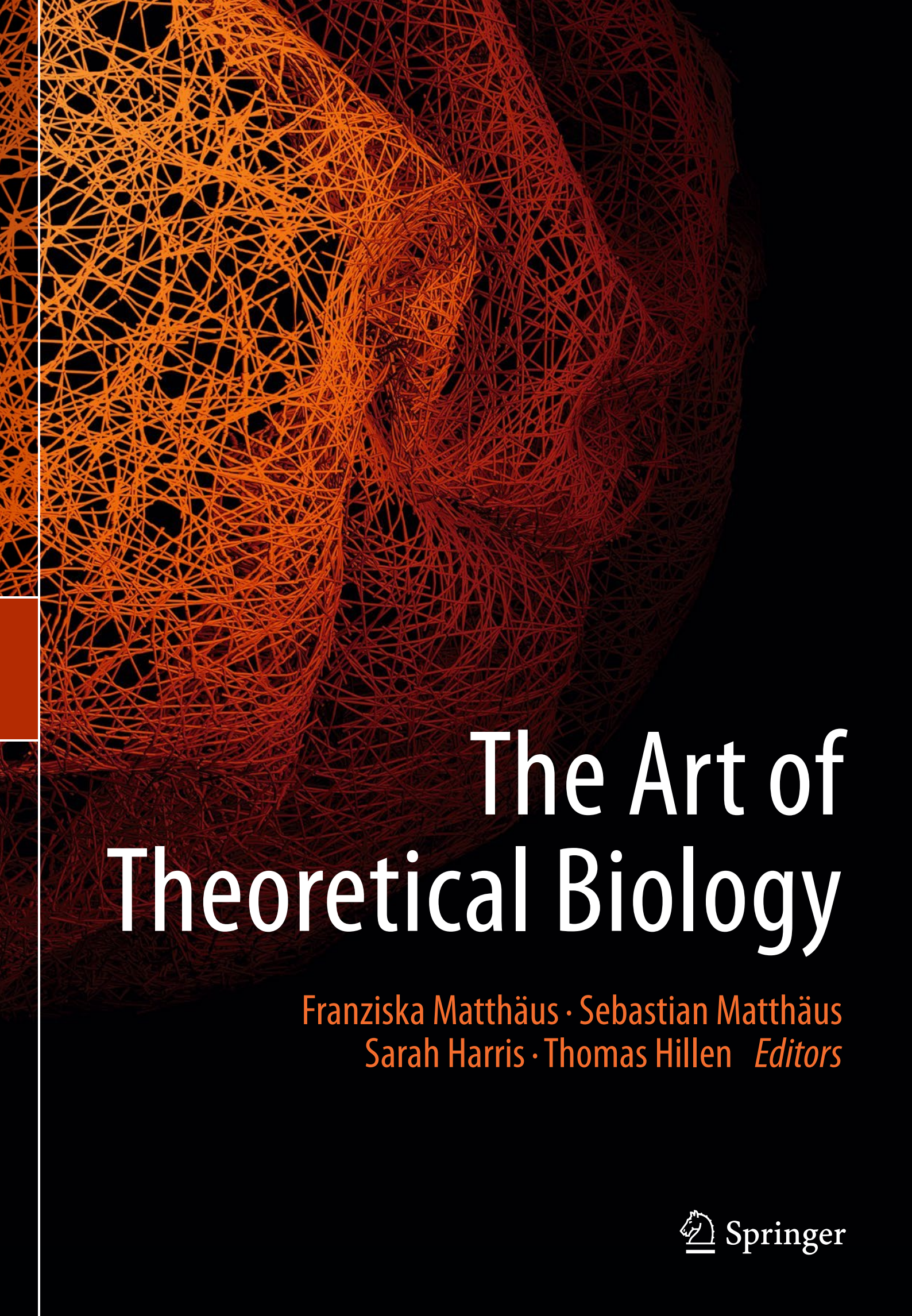

The Art of Theoretical Biology

Franziska Matthäus · Sebastian Matthäus
Sarah Harris · Thomas Hillen *Editors*

Springer

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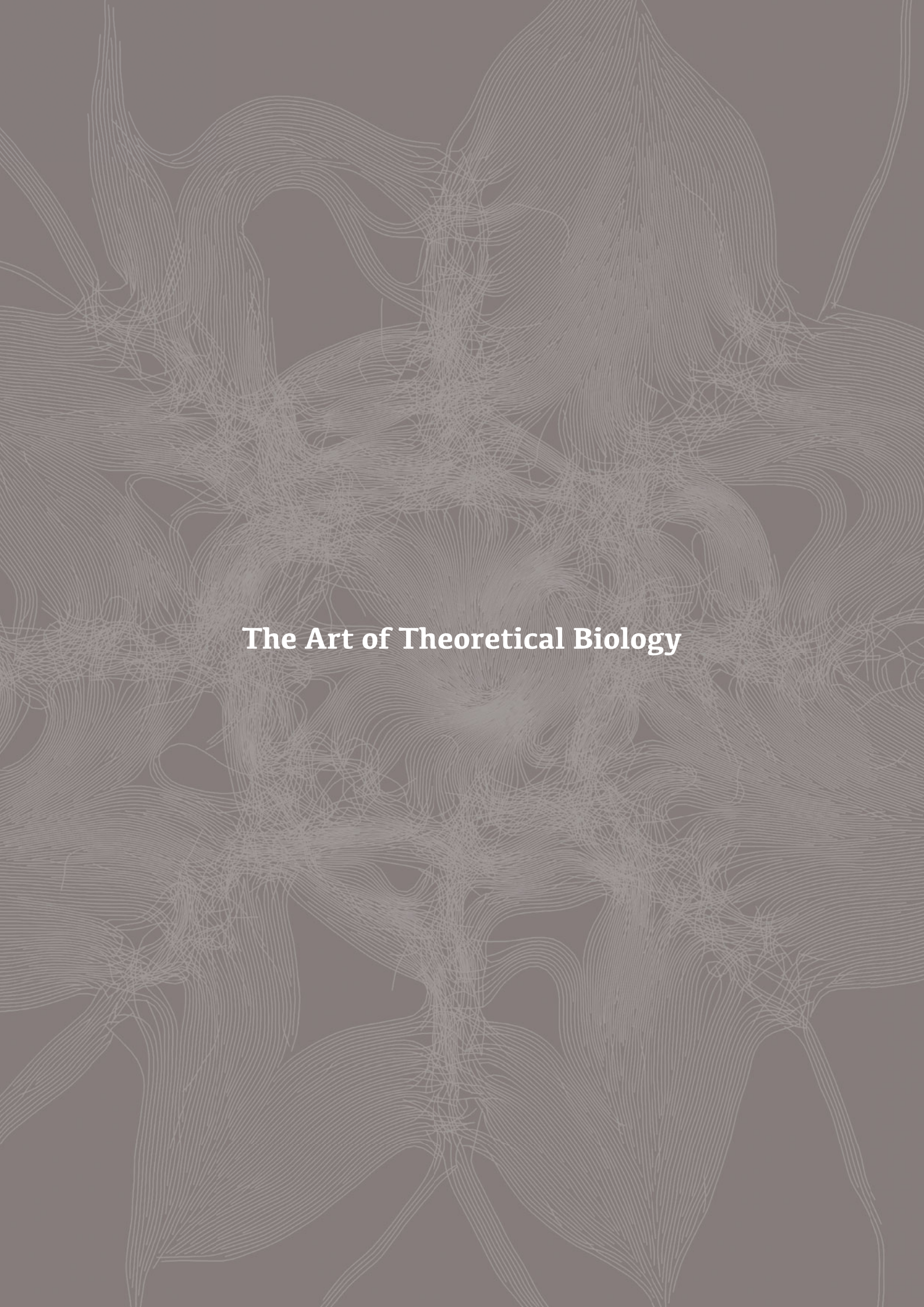

The Art of Theoretical Biology

Preface

Every image in this book was created for a purely scientific purpose. The images were obtained using mathematical modelling and simulations to explore and understand biological or medical concepts. The images were chosen since they touched the scientists on a different level. They inspire further thought, they showcase disturbing facts, express confusion, or are simply aesthetically beautiful. By being included in this collection, they have won the honourable title of "art".

Some think this accolade must be reserved for works created out of the sheer joy of creativity alone. These images, however, all share a fundamental purpose, they are based on research in theoretical biology.

Each contributing author has provided a personal explanation of the underlying science they were exploring. Many of them describe why their chosen image was so striking to them. This indication of purpose adds resonance to the pictures, rather than taking away their mystery. The images show how beauty can arise in the darkest of places, such as in the breakdown of cell function during cancer, and how complexity generates richness in unexpected ways. Each picture provided their creators with an inspiration distinct from the purely scientific results they originally intended. Therefore, we view the book as a superposition of art and science; each separate image is an act of scientific research, but the whole collection is a work of art.

The field of Theoretical Biology has made some fundamental contributions to our understanding of nature, biology, and medicine. Within our community we study the impact of global warming on polar bears, reindeer populations, migrating birds, and mountain pine beetles. We study the spread of diseases and advise governments about vaccination strategies, we develop pharmaceutical drugs, medical procedures and optimize cancer treatments, we visualize brain tumours, bones and organs, and we help to understand how individual cells move, how they polarize and divide, how they react to signals from their environment and how it is possible for individual cells to produce a living, conscious species such as humans. Theoretical Biologists use advanced tools from mathematics and computational sciences, which are targeted to the biological problem at hand.

Several of the contributions relate to active research in Oncology. Cancer is a devastating illness and many of us have had first hand experience with this disease. The cancer related contributions of this special issue are chosen to show our deep respect to all people that are affected by cancer. The contributions showcase the combined efforts of the research community to better understand the effects of cancer and to design more effective treatments. Each of the contributors is driven by the goal to make a substantial impact on cancer treatment, to reduce cancer related death, and to improve the quality of patients' lives. The contributions also show that cancer researchers are simply humans, people who deeply care and who appreciate some form of beauty in an otherwise disturbing research topic.

This book is comprised of 71 contributions, involving more than 120 authors. The big adventure of bringing the book into existence would not have been possible without the enthusiasm, support and, not the least, the patience of all of our authors, for which we would like to thank them deeply. Since the first discussion of the editorial team in the early spring of 2016 several years passed, during which we issued repeated calls for contributions, went through selection rounds and collected abstracts. We also address our deepest thanks to Jan-Philip Schmidt (SpringerNature Publishing), who supported the project during the entire period. And last, but not least, having the collection and a publishing house, we still faced the challenge of bringing all these different images into one coherent product. This involved formatting of all images for book print, design aspects of how to present the images, as well as their variety, in an optimal way, and the creation of a layout for the text parts and the book cover. Fortunately, Sebastian Matthäus, head of a graphic design agency located in Berlin, Germany, agreed to support us with his expertise.

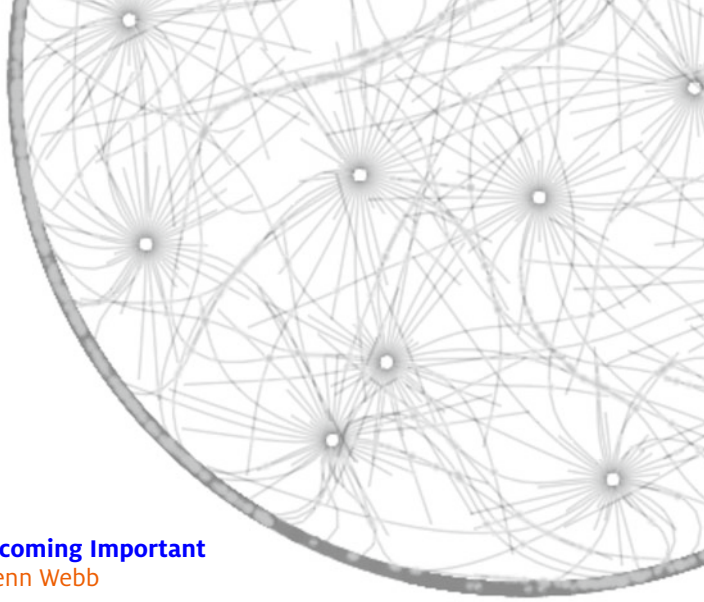
With his help we organized an exhibition, starring a subset of our images, at the Riedberg Campus of the University of Frankfurt in June and July, 2018. This exhibition was only possible due to generous financial support from the Frankfurt Institute for Advanced Studies, allowing us to display large-scale printouts on the occasion of the Frankfurt Night of Science. Further exhibitions will follow.

For each of our images you can find a description of the scientific context and some scientific publications are listed. The author's affiliations are provided as well at the back of this book. Feel free to contact any of them if you would like to learn more about a specific topic, or if you would like to offer your support. Our authors are happy to respond.

Enjoy browsing through these images. Stop at anything that touches you and speculate what it could mean. Then read the description. Enjoy.

Franziska Matthäus, Sebastian Matthäus,
Sarah Harris & Thomas Hillen

Content



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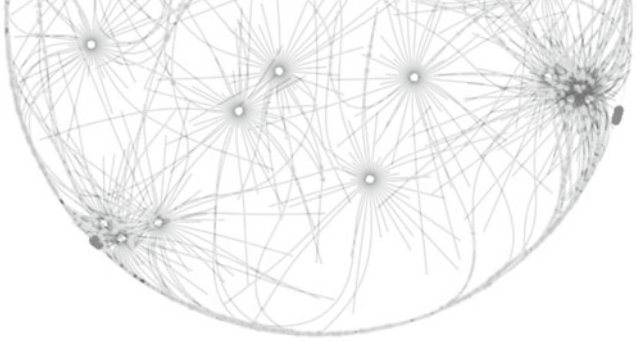

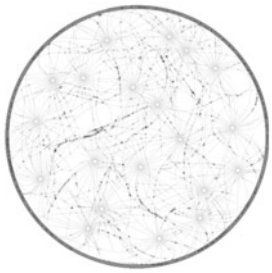

It makes you wonder …

The Deadly Beauty of Cancer

By Bartlomiej Waclaw & Martin Nowak

The research story

Cancerous tumours are not a uniform mass of identical cells but can be very heterogeneous [1]. Cells from different parts of the tumour harbour different genetic mutations. These mutations affect how fast cancer cells are able to grow, whether they can invade the surrounding healthy tissue, or how sensitive they are to chemotherapy. Heterogeneity not only makes tumours more difficult to eradicate but also to diagnose, because a small biopsy sample may not be representative of the entire tumour. We were interested in what biological processes determine how heterogeneous tumours are. We developed a computer model that simulated a population of cancer cells that replicate, die, migrate, and mutate. We varied the strength of these processes and measured the level of heterogeneity.

The image

The image shows a simulated tumour with a low level of migration. Cells are represented by small dots. The tumour shown in the foreground has about 10 million cells, smaller tumours in the background are snapshots of the same tumour from earlier times. Cells have been colour-coded depending on what mutations they carry in addition to the first cancer-initiating mutation. Cells with similar mutations have been assigned similar colours. A huge diversity of colours means that the tumour is genetically heterogeneous. This is typical for our simulation. Only when migration is very fast or cells rapidly die and are replaced by other cells, tumours become more homogeneous. The sequence of images has been created using a published computer algorithm [2].

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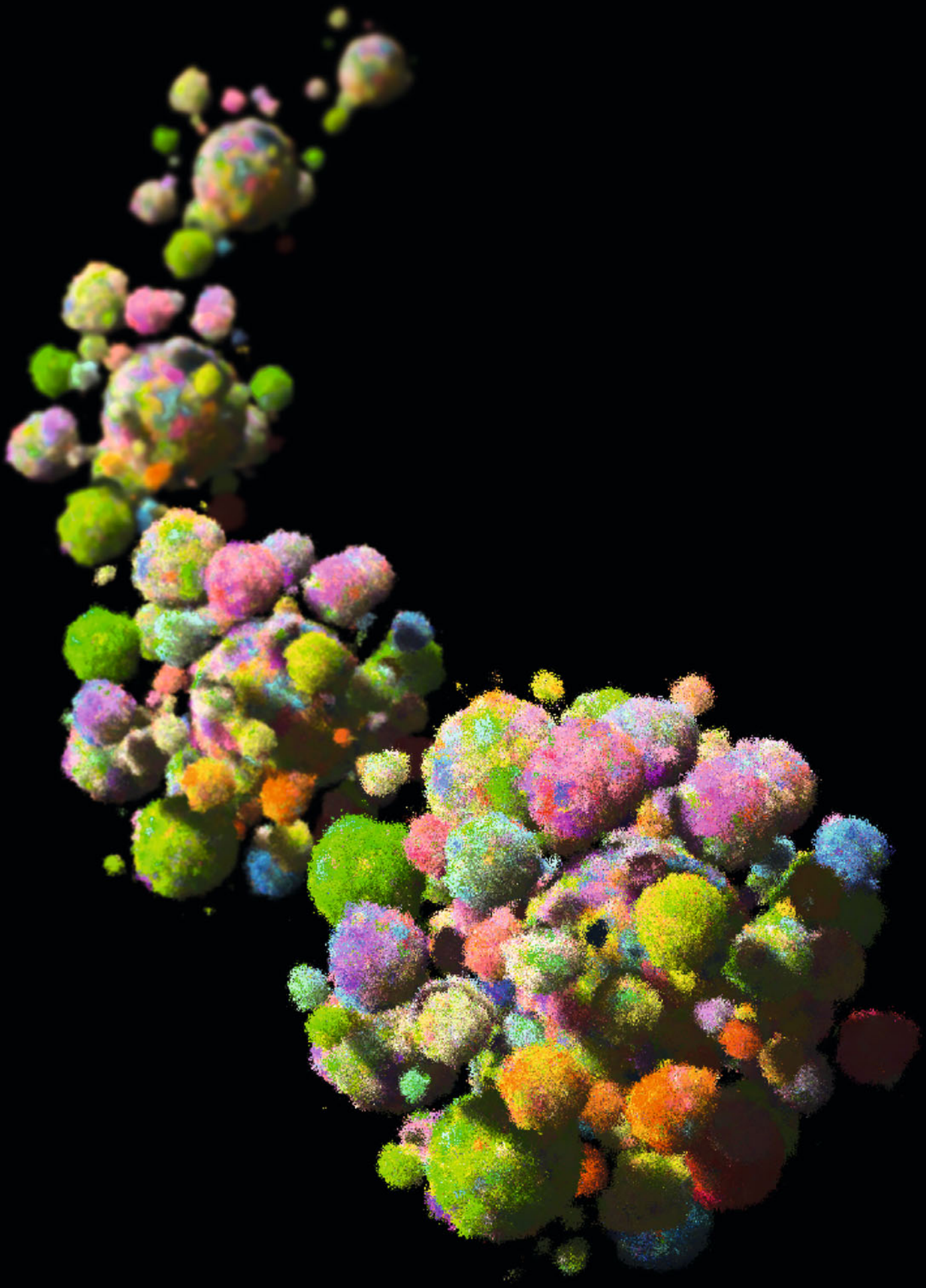

Cellular Connections

By Roeland Merks

The research story

"Cellular Connections" shows a computer simulation of the growth of blood vessels. Endothelial cells, the building blocks of blood vessels, collectively form networks of blood vessels, much like ants work together to form their nests. In the centre of the image, the cells are sufficiently close together such that they feel one another and manage to interconnect. The cells at the periphery are too far away and wander around aimlessly.

The image

The tiny blood vessels that we simulate are formed early in embryonic development, and they continue to grow throughout our lives. Cells can stimulate adjacent blood vessels to form side branches as a healthy response to lack of oxygen, for example during wound healing and menstruation. Unfortunately, cancer cells can hijack this process, and attract blood vessels for their own benefit. By figuring out the rules that endothelial cells use to construct a blood vessel, we hope to find new ways to control blood vessel growth. Through this computer simulation we found out that the cells form particularly realistic networks if we let them assume an elongated shape, and we let them attract one another through a signal that they emit into the environment. The simulations are performed on a square grid through stereotypic algorithmic steps. Yet they generate life-like forms. This is due to the biological model rules and a pinch of mathematically-generated unpredictability.

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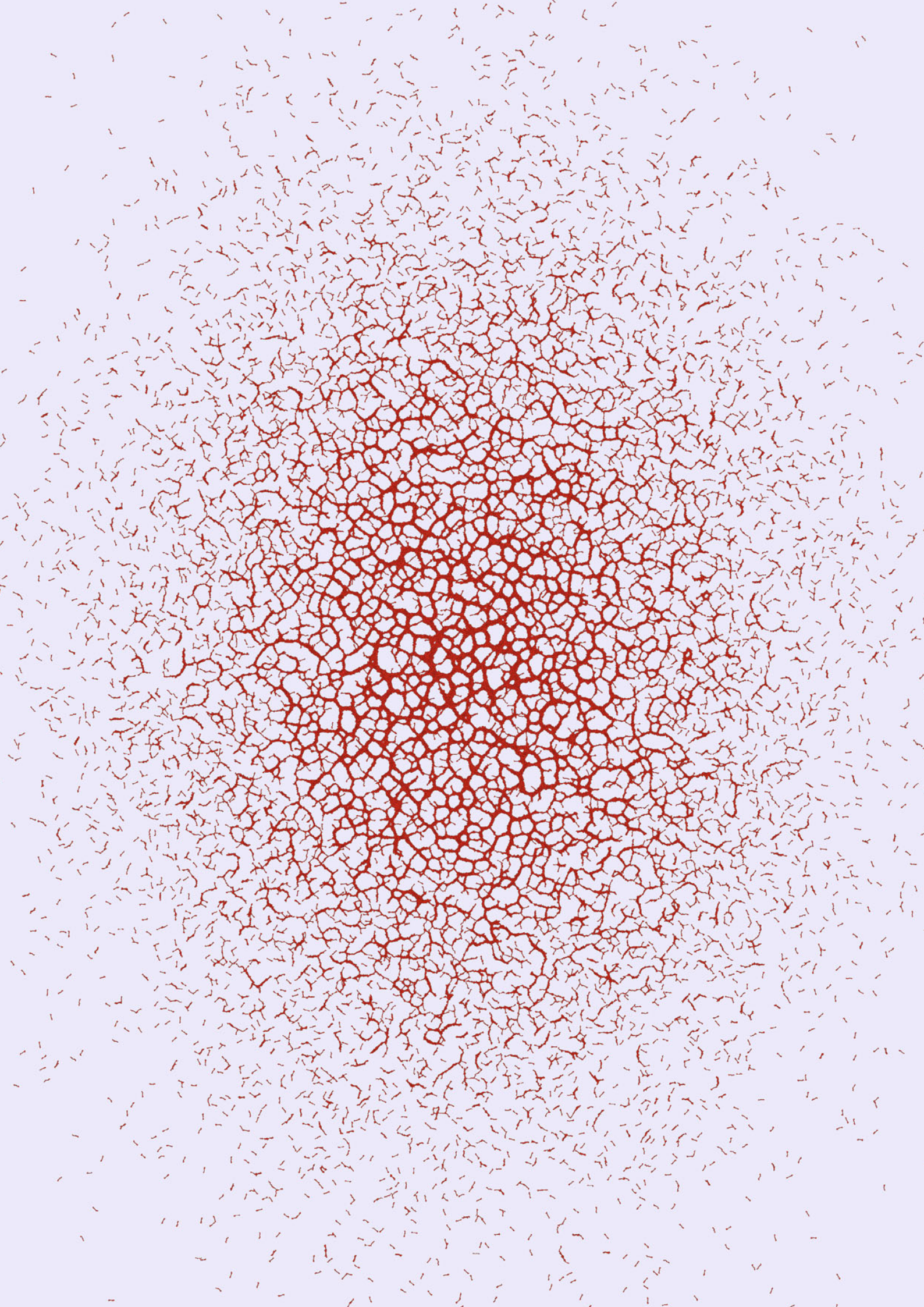

Annealing Party

By Maximilian Strobl & Daniel Barker

The research story

A phylogeny shows the pattern of relationships for a set of species – their family tree. Traditionally used in taxonomy and evolutionary biology, the algorithms used to reconstruct phylogenies from DNA sequencing data are now also finding applications in cancer research and epidemiology. However, inferring a phylogeny is a challenging optimisation problem: Out of the many possible ways in which the species might be evolutionarily related, one must identify the most plausible one. This is analogous to trying to climb to the top of the highest peak in a large mountain range, in fog, without access to a map of the area. In this project, we studied how the simulated annealing algorithm tackles this problem, to learn more about the algorithm and the topography of the search landscapes.

The image

Shown here is an attempt to map the path of the algorithm for one data set. Each point represents one candidate phylogeny considered by the algorithm, and its colour indicates if it was considered early (red) or late in the search (blue). Distance reflects the similarity between two phylogenies. The data was collected by running a modified version of the LVB phylogeny reconstruction software, and visualised using the treesetviz package for Mesquite [1]. One can nicely see how the search starts by exploring disconnected regions, but then converges to a final plateau. Redrawn from Strobl and Barker (2016) [2].

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