Making the invisible visible: exploring host–microbiome interactions across different taxa using data-driven 3D visualization

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The importance of microbiome research is rapidly gaining momentum for understanding its role in development, evolution, ecology, health and disease. Recent progress in community and single-cell genomic approaches has provided an unprecedented amount of information on the abundance and ecology of microbes in different host organisms and turned them into metaorganisms. A metaorganism is a host and its complete microbial community which is commonly referred to as the microbiome. Over half the cells in a human body are not human but belong to the multitude of species that compose our microbiome. However, linkages between metaorganisms from different taxa and their *in situ* level of intraspecific dependence (be it growth, division or metabolic activity) are much more scarce. Visualization therefore is crucial for understanding host–microbe interactions as well as overarching concepts in different host organisms. Here we introduce an innovative user-friendly method for interactive visualization of microbiome multi-omics data. The new communication format combines science and visual communication design. Interactive media are used to transform scientific findings on host–microbe interactions in an intuitive way. The method provides access to additional layers of information that cannot be visualized using a traditional platform. We demonstrate the usefulness of this visualization approach using the interactive scientific poster 'Digital Meta', which is designed to support not only interdisciplinary co-working but also communication with the general public.

Background

Microbial communities are complex ecosystems with important impacts on human health and on the environment. The research on microbial communities inhabiting plant, animal and human epithelia and organs has progressed at a spectacular rate over the past decade. This progress is due in large part to the application of 'metagenomic' methods: a series of experimental and computational approaches that allow a microbial community's composition to be defined by DNA sequencing without having to culture its members. This work has yielded catalogues of microbial species, many previously unknown and belonging to all three domains of life, as well as lists of millions of microbial genes collectively known as our 'microbiome'. Research on host–microbe interactions has become an emerging cross-disciplinary field. The Collaborative Research Centre 'Origin and Functioning of Metaorganisms' (CRC1182; https://www.metaorganism-research.com/) is a multidisciplinary group of biological, mathematical and clinical scientists who deeply explore the role that symbiotic microorganisms play in determining health and disease in host organisms ranging from plants to animals to humans.

Recent advances in sequencing technologies and computational methods have enabled the study of microbial communities and host–microbe interactions at unprecedented resolution. However, these advances in data generation have presented novel challenges to researchers attempting to analyse and visualize these

data. There is a rich library of software platforms for microbiome data analytics implementing various visualization techniques. Most of these platforms provide access to self-contained standalone tools or web servers enabling users to perform a number of analyses accompanied with interactive visualizations. Here our goal is different. Our working hypothesis is that the inherent complexity of host–microbiome data, and the need to relate these many layers of information to an interdisciplinary dialogue, will necessitate the development of more intuitive user interfaces for visual exploration and analysis. We present a new and innovative interdisciplinary tool to gain a holistic understanding of findings describing complex host–microbiome interactions that was developed in a team of scientists and media designers.

Our goal was to develop a communication format that combines both science and media design to transform scientific findings in an intuitive way. Since existing techniques are inadequate when it comes to 3D visualization of host–microbe interactions, we were concerned to improve visualization of the hundreds of thousands of species of microorganisms which make up the microbiome in diverse host organisms to better understand the host–microbiota complexity. Next to that we also wanted to achieve user friendliness which allows to inform and engage the public to participate in some aspects of this research – and thus contribute to clearing misunderstandings about, e.g., the use of antibiotics and hygiene measures in the context of the microbiome. The ultimate goal of our approach is to enable a biologist inexperienced in programming to interpret and analyse the experimentally obtained microbiome data without any complex installation requirements.

How to make the invisible visible (methods and technical implementation)

To create a common ground on which scientists from various fields and with different levels of knowledge can communicate with each other we developed an interactive platform, the so-called interactive scientific poster 'Digital Meta' (Figure 1). The novelty of the interactive scientific poster lies in the combination of different media in one interactive application. Thus, the combination of data visualizations, detailed 3D animated models and coherent formulated texts creates a new communication format that enables scientists to present and discuss their research in a comprehensible and multi-faceted way to foster new ideas and make complex findings easier to understand. For undergraduate students the interactive poster serves as baseline to gain a deep understanding of the overarching concepts that are crucial for the

Figure 1. Interactive scientific poster 'Digital Meta'. Students interacting with the poster and getting engaged with microbiome research.

understanding of microbiome research. This is to our knowledge the first time that an interactive, strongly visual platform was developed in an interdisciplinary team of scientists, designers and programmers to both better understand and communicate the complexity of host–microbe interactions in different organisms.

In a first step it was necessary to transform the various scientific data, such as microbiome sequencing data, into one overarching and common visual language to make them comparable and also accessible to everyone. To achieve this, media designers and scientists looked deep into the data and concepts of microbiome research and engaged in intensive conversations with each other to translate common scientific data visualizations into a new consistent visual language. The outcome was a selection of data and according findings to convey the information in a consistent visual language, more precisely into data-driven animations.

Data visualization as a kind of new microscope

The challenge was to develop an overall visual language that was easy to understand, appealing but at the same time scientifically correct. In our visualizations, we placed great emphasis on a 3D representation, because this allows the viewing angles to be varied enormously. At the same time, a very realistic model of structures, ratios and proportions was created. By using different zoom levels, it is possible to zoom from a holistic overview to an accurate detail in a 3D model, conceptually very similar in using a microscope with different magnification settings to explore samples. For example, we show the entire organism of the freshwater polyp hydra in its natural environment and, at a very close zoom level, the interaction of hydra's epithelia with the microorganisms on the surface (see Figure 2). Hence, data visualization becomes a modern form of microscope allowing zooming into data and making them come alive with the help of 3D visualization and animation. That is why we attach great importance to a brilliant and high-resolution representation in the data-driven visualizations. We like to call this a 'cinematic style', as such animations are familiar from elaborately produced motion pictures and at the same time are remembered because they evoke emotions.

In addition to this spatial representation of microbiome research, it was crucial to display the original research data into the same visual context to enable discussion among scientists. For this the original data plots were transformed applying principle design rules to enhance readability and thus make them better comparable (Figure 3).

How to tell the story?

One important element in visual science is the conception of a key visual. Here, in 'Digital Meta' the key visual is the visualization of the millions of microorganisms that are living on and inside plant, animal or human hosts. For this we used computer-generated particle animations to show what one usually cannot see in real life: the buzzing and whirring microorganisms colonizing every inch of this world. Within each of the brilliant and highly rendered 3D models of flatworm, hydra, wheat, sponge and human we display new findings from the scientific community, always showing not only what the naked eye would see (the model organism) but also the scientific findings and knowledge from microorganism research. Through this stylization we not only create a new, holistic image of a particular host organism but also make different hosts comparable with each other by choosing the same representation mode. Similarities and differences become so very clearly.

To structure the selected data and findings we used a storytelling approach as communication method.

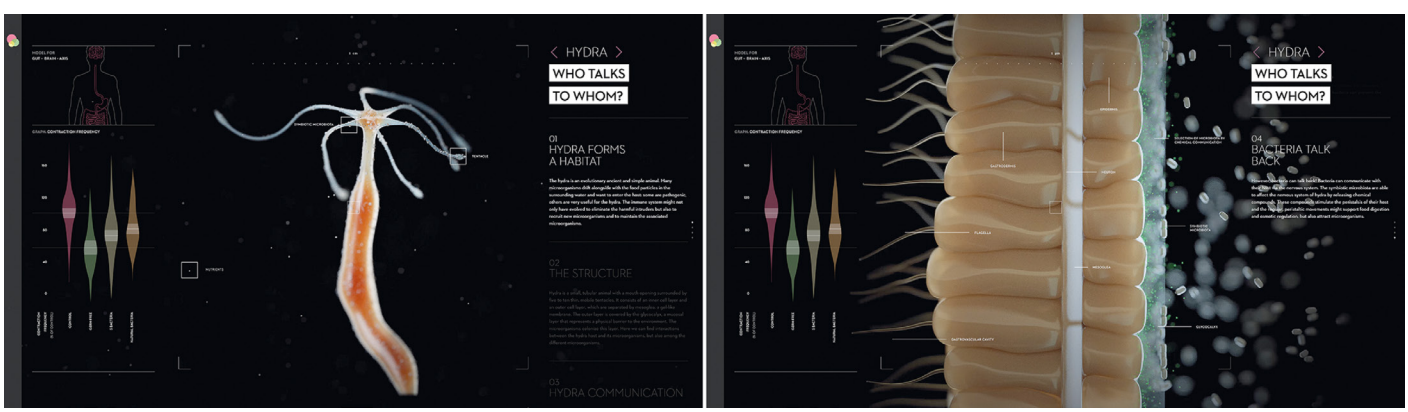

Figure 2. Close-ups of model organism hydra. Left: In its natural environment, surrounded by microbes. Right: Interaction of hydra with the microorganisms on the surface, showing newest findings of microbiome research.

Figure 3. Consistent usage of visual language in data visualization: this enhances the comparability and readability of the oftentimes complex microbiome research.

Designers, conceptionists and scientists transformed scientific data into stories: each of the topics was scripted into a narration to support the understanding of the complex topics, ranging from colonization patterns, dysbiosis and potential health consequences, communication between microorganisms and with their host to the implications of lack of microorganisms for agriculture and food safety. Using narration can facilitate the understanding of scientific knowledge, as listening to stories lies in our human nature and activates certain areas in the brain so that a listener turns the story into their own idea and experience. The usage of the pinch gesture navigates through the content, again using the metaphor of the microscope. Ultimately, this turns the interaction into an experience and a journey of discovery.

Conclusion and perspectives

Here we present a novel interactive communication platform allowing collaborative work and discussion on host–microbiome interactions in different host organisms from plants to animals to humans. The new visualization tool also can be used in the field of digital learning. To illustrate the utility of the approach, we include two examples.

1. Interactive poster 'Digital Meta': Our experience when presenting the digital interactive poster (Figures 1 and 2) indicates that lay people were interested immediately and willing to understand the complexity of host–microbiome research. Especially the brilliant and detailed 3D visuals help to convey the researchers' fascination for their research. At events such as the annual Darwin Day at the Christian Albrechts University in Kiel, the interactive poster was a real crowd puller. "The visually beautiful, 3D animated models capture the attention of students in a way no other media support can. The students immediately get engaged in the topic. Also, exploring this cutting-edge interactive poster makes them experience that microbiome research is an up-to-date, highly relevant, and rapidly progressing research field" (citing Dr Katja Dierking, a scientist at Kiel University highly engaged in teaching). Researchers were able to explain their work much better with the interactive visuals than with conventional presentations. One of the project's findings is that the interactive data-driven visualizations are to be further developed for teaching and school lessons. To do this, the previous development must be accessible on a web-based platform, which is a challenge in view of the large data volumes of the high-resolution visualizations and animations. Likewise, the modularity is to be increased so that the latest findings and research results can also be integrated into the application. For this purpose, the development team of the Science Communication Lab has joined forces with specialists in education in the natural sciences in order to be able to integrate the latest findings in educational research.

2. Science to science communication in multi-disciplinary research teams: Another finding from the development of the interactive poster is that scientists are also able to communicate their research projects better and more comprehensibly to colleagues through the precise presentation of data-driven visuals (Figure 3). In the words of Hinrich Schulenburg, professor at Kiel University and authority in *Caenorhabditis elegans* research: "The interactive poster is a fantastic tool to better explain the dynamics of microbial community changes during the lifetime of our model organism, *C. elegans*. This particular topic is rather abstract and theoretical and often difficult to understand. However, the visuals directly illustrate the processes involved. The interactive poster is thus a true eye-opener!" With a look into the future, it will be necessary to transfer current data sets onto the 3D visualizations and compare them. A temporal progression, which is also stored, should also document the research steps and show when significant discoveries have led to new insights. Ideally, we are aiming for a visual presentation tool that will become more and more comprehensive through collaborative interactions and will depict the entire research activities within a multi-disciplinary research team such as a Collaborative Research Centre.

Together, these examples emphasize both the challenges faced when analysing microbiome data and the shortcomings of a discipline-specific approach. They demonstrate that we can broaden and change our understanding of how plants, animals and humans interface with the world via the microbiome by fostering interactions and discussions between disciplines that normally do not speak with each other. In conclusion, to understand and to communicate the biochemistry of the dialogue between hosts and their microbes we will need to incorporate 3D visualization of the high-dimensional datasets in a way which is both intelligible and comprehensive. ■

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Further reading and viewing

- Collaborative Research Center "Origin and Function of Metaorganisms" https://www.metaorganism-research.com
- Web documentation on "digital Meta": https://phase1.metaorganism-research.com/sciposter/
- Video documentation on "digital Meta" on YouTube: https://www.youtube.com/watch?v=V-Dyp_CjXSs&t=2s
- Science Communication Lab: https://www.scicom-lab.com

On microbiome research:

- McFall-Ngai, M., Hadfield, M., Bosch, T., et al. (2013) Animals in a bacterial world, a new imperative for the life sciences. *Proc. Natl. Acad. Sci. U.S.A.* **110**, 3229–3236. DOI: 10.1073/pnas.1218525110
- Bosch, T.C.G., Guillemin, K. and McFall-Ngai, M. (2019) Evolutionary "experiments" in symbiosis: the study of model animals provides insights into the mechanisms underlying diversity of host-microbe interactions. *BioEssays* **41**, e1800256 DOI: 10.1002/bies.201800256
- Rausch, P., Rühlemann, M., Hermes, B.M. et al. (2019) Comparative analysis of amplicon and metagenomic sequencing methods reveals key features in the evolution of animal metaorganisms. *Microbiome* **7**, 133. DOI: 10.1186/s40168-019-0743-1
- Sieber, M., Pita, L., Weiland-Bräuer, N., et al. (2019) Neutrality in the metaorganism. *PLoS Biol.* **17**, e3000298. DOI: 10.1371/journal.pbio.3000298
- Jaspers, C., Fraune, S., Arnold, A.E., et al. (2019) Resolving structure and function of metaorganisms through a holistic framework combining reductionist and integrative approaches. *Zoology* **133**, 81–87. DOI: 10.1016/j.zool.2019.02.007

On data visualization from the design perspective:

- Drucker, J. (2014) Graphesis : Visual Forms of Knowledge Production. Cambridge, Massachusetts: Harvard University Press.
- Duscher, T., Sachs, S. and Schulz, M. (2017) *Sensing the Ocean - A Collaboration between Art, Design and Science*. Revolver Publishing, Berlin..

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Further reading (*Continued*)

- Kirk, A. (2016) *Data Visualisation: A Handbook for Data Driven Design*. SAGE, London.
- Steele, J., and Iliinsky, N. (2010) *Beautiful Visualization*. O'Reilly Media, Sebastopol.
- Tufte, E. (2001) *The Visual Display of Quantitative Information*. Second edition. Graphics Press. Cheshire.

On data visualization from the scientist's perspective:

- Gehlenborg, N., O'Donoghue, S.I., Baliga, N.S. et al. (2010) Visualization of omics data for systems biology. *Nat. Meth*. **7**, S56–68. DOI: 10.1038/nmeth.1436
- Kuntal, B.K. and Mande, S.S. (2019) Visual exploration of microbiome data. *J. Biosci.* **44**, 119. DOI: 10.1007/s12038-019-9933-z
- Pavlopoulos, G.A., Malliarakis, D., Papanikolaou, N. et al. (2015) Visualizing genome and systems biology: technologies, tools, implementation techniques and trends, past, present and future. *GigaScience* **4**, 38. DOI: 10.1186/s13742-015-0077-2

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