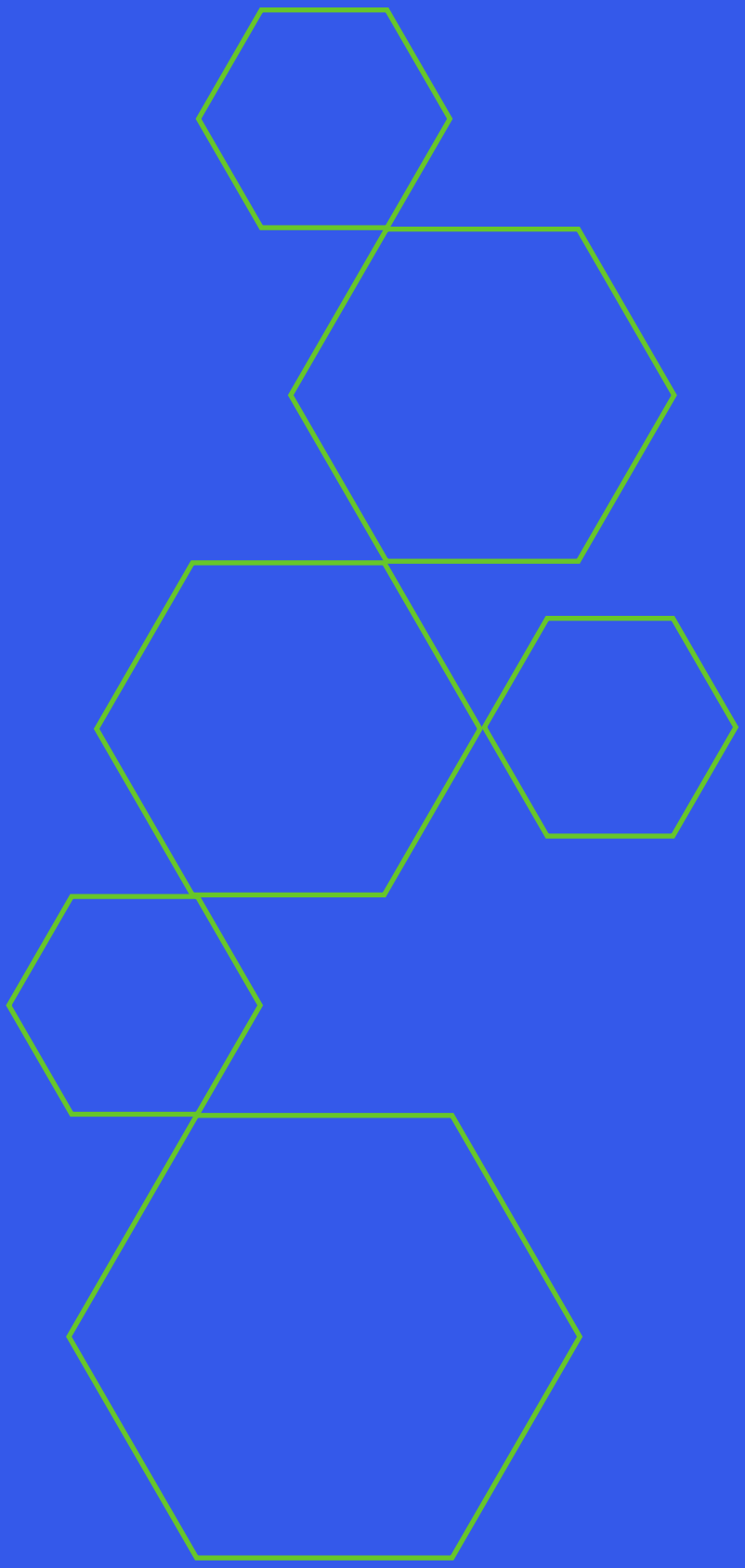


AI for science

An emerging agenda

Machine Learning for Science:
Bridging Data-Driven and Mechanistic Modelling

Summary

Today's scientific challenges are characterised by complexity. Interconnected natural, technological, and human systems are influenced by forces acting across time- and spatial-scales, resulting in complex interactions and emergent behaviours. Understanding these phenomena – and leveraging scientific advances to deliver innovative solutions to improve society's health, wealth, and wellbeing – requires new ways of analysing complex systems.

Artificial intelligence (AI) offers a set of tools to help make sense of this complexity. In an environment where more data is available from more sources than ever before – and at scales from the atomic to the astronomical – the analytical tools provided by recent advances in AI could play an important role in unlocking a new wave of research and innovation. The term AI today describes a collection of tools and methods, which replicate aspects of intelligence in computer systems. Many recent advances in the field stem from progress in machine learning, an approach to AI in which computer systems learn how to perform a task, based on data.

Signals of the potential for AI in science can already be seen in many domains. AI has been deployed in climate science to investigate how Earth's systems are responding to climate change; in agricultural science to monitor animal health; in development studies, to support communities to manage local resources more effectively; in astrophysics to understand the properties of black holes, dark matter, and exoplanets; and in developmental biology to map pathways of cellular development from genes to organs. These successes illustrate the wider advances that AI could enable in science. In so doing, these applications also offer insights into the science of AI, suggesting pathways to understand the nature of intelligence and the learning strategies that can deliver intelligent behaviour in computer systems.

Further progress will require a new generation of AI models. AI for science calls for modelling approaches that can: facilitate sophisticated simulations of natural, physical, or social systems, enabling researchers to use data to interrogate the forces that shape such systems; untangle complicated cause-effect relationships by combining the ability to learn from data with structured knowledge of the world; and work adaptively with domain experts, assisting them in the lab and connecting data-derived insights to pre-existing domain knowledge. Creating these models will disrupt traditional divides between disciplines and between data-driven and mechanistic modelling.

The roadmap presented here suggests how these different communities can collaborate to deliver a new wave of progress in AI and its application for scientific discovery. By coalescing around shared challenges for AI in science, the research community can accelerate technical progress. By creating user-friendly toolkits, and implementing best practices in software and data engineering, researchers can support wider adoption of effective AI methods. By investing in people working at the interface of AI and science – through skills-building, convening, and support for interdisciplinary collaborations – research institutions can encourage talented researchers to develop and adopt new AI for science methods. By contributing to a community of research and practice, individual researchers and institutions can help share insights and expand the pool of researchers working at the interface of AI and science. Together, these actions can drive a paradigm shift in science, enabling progress in AI and unlocking a new wave of AI-enabled innovations.

The transformative potential of AI stems from its widespread applicability across disciplines, and will only be achieved through integration across research domains. AI for science is a rendezvous point. It brings together expertise from AI and application domains; combines modelling knowledge with engineering know-how; and relies on collaboration across disciplines and between humans and machines. Alongside technical advances, the next wave of progress in the field will come from building a community of machine learning researchers, domain experts, citizen scientists, and engineers working together to design and deploy effective AI tools.

Contents

Introduction: bridging data driven and mechanistic modelling

The 21st century has been characterised as the century of complexity.[1] Shifting social, economic, environmental, and technological forces have created increasingly interconnected communites, affected by 'wicked' problems in domains such as health, climate, and economics.[2] This complexity is reflected in today's scientific agenda: whether in natural, physical, medical, environmental, or social sciences, researchers are often interested in the dynamics of complex systems and the phenomena that emerge from them. Science has always proceeded through the collection of data.Through their experiments and observations, researchers collect data about the world, use this data to develop models or theories of how the world works, make predictions from those models, then test those predictions, leading to further refinements to the model and the underpinning theory. Digitisation of daily activities – in the lab, and elsewhere – means that researchers today have access to more data from a greater range of sources than ever before. In parallel, more sophisticated tools to collect data have opened new scales of scientific inquiry, from detailed patterns of gene expression to light signals from other galaxies. Data proliferation is both a signal of the complexity of today's environment, and an opportunity to make sense of such complexity.

Advances in artificial intelligence (AI) have produced new analytical tools to make sense of these data sources. The term 'AI' today describes a collection of methods and approaches to create computer systems that can perform tasks that would typically be associated with 'intelligent' behaviour in living sytems.[3] In this document, the term AI is used broadly, to refer to algorithmic decision-making systems that combine data, mathematical models, and compute power to make predictions about the world.

AI is already unlocking progress across research disciplines:

- In Earth sciences, it is helping researchers investigate how different parts of the Earth's biosphere interact, and are affected by climate change.[4]
- In climate science, it supports modelling efforts to reconstruct historical climate patterns, enabling more accurate predictions of future climate variability.[5]
- In agricultural science, it is helping farmers access faster diagnoses of animal diseases, enabling more effective responses.[6]
- In astrophysics, it is advancing understandings of the nature of dark matter and its role in the Universe.[7]
- In developmental biology, it is generating insights into the genetic processes that shape how cells develop and differentiate into specialist roles.[8]

1 This quote is attributed to Stephen Hawking, in an interview with the San Jose Mercury News in January 2000.

2 Rittel, H., and Webber, M.M. (1973) Dilemmas in a general theory of planning. Policy Sciences 4, 155–69. (Reprinted in N. Cross, ed. Developments in design methodology, pp. 135–44. Chichester: J. Wiley & Sons, 1984).

3 While not the only branch of the field, machine learning is the approach to AI that has delivered many of the recent advances in AI. Machine learning is an approach to AI in which models process data, learning from that data to identify patterns or make predictions. In this document, the terms machine learning and AI are used interchangeably.

4 These examples are inspired by talks given at the Dagstuhl seminar; these are provided later in the document. This example is inspired by a talk by Markus Reichstein.

5 This example is inspired by Ieva Kazlauskaitė's talk.

6 This example is inspired by Dina Machuve's talk.

7 This example is inspired by Siddharth Mishra-Sharma's talk.

8 This example is inspired by Maren Büttner's talk.

- In environmental science, it allows researchers to analyse the features of natural environments more accurately, aiding land and resource managers.[9]

- In neuroscience, it can help model how different neural circuits fire to deliver different behaviours in animals.[10]

The diversity of these successes illustrates the transformative potential of AI for research across the natural, physical, social, medical, and computer sciences, arts, humanities, and engineering. By enabling researchers to extract insights from a greater volume of data, drawn from a wider variety of sources, and operating across multiple dimensions and scales, AI could unlock new understandings of the world. In so doing, AI could influence the conduct of science itself. AI-enabled analytical tools mean researchers can now generate sophisticated simulations of natural or physical systems, creating 'digital siblings' of real-world systems that can be used for experimentation and analysis. Machine learning models that combine the ability to learn adaptively from data with the ability to make structured predictions reflecting the laws of nature can help researchers untangle the web of cause-effect relationships that drive the dynamics of complex systems. AI-assisted laboratory processes could increase the efficiency of experiments, and support researchers to develop and test new hypotheses.

Achieving this potential will require advances in the science of AI, the design of AI systems that serve scientific goals, and the engineering of such systems to operate safely and effectively in practice. These advances in turn rely on interdisciplinary collaborations that connect domain expertise to the development of machine learning models, and feed the insights generated by such models back into the domain of study. As interest in the potential of AI to drive a new wave of research grows, the challenge for the field is to identify technical and operational strategies to realise this potential. In the process, new questions arise about the future of 'AI for science'; whether this will emerge as a distinct field, characterised by its own research agenda and priorities, or whether its benefits can be best achieved through separate, domain-focused sub-fields, which seek to integrate AI into business-as-usual across research disciplines.

In response, this document proposes a roadmap for 'AI for science'. Synthesising insights from recent attempts to deploy AI for scientific discovery, it proposes a research agenda that can help develop more powerful AI tools and the areas for action that can provide an enabling environment for their deployment. It starts by exploring core research themes – in simulation, causality, and encoding domain knowledge – then draws from these ideas to propose a research agenda and action plan to support further progress. The ideas presented are inspired by discussions at 'Machine Learning for Science: Bridging Mechanistic and Data-Driven Modelling Approaches', a Dagstuhl seminar convened in September 2022 (see Annex 1).

Abstracts from the talks given at the seminar are shown throughout this document. These talks and the discussions they provoked should be credited for the ideas that have shaped it. Thank you to the speakers and participants for their thoughtful contributions to both the seminar and the development of this work.

9 This example is inspired by Christian Igel's talk.

10 This example is inspired by Jakob Macke's talk.

Snapshots of AI in science

Across domains, AI is being deployed to advance the frontiers of science. The snapshots below introduce some current areas of research in AI for science, and explore the issues raised by these research projects. Across these snapshots, some common themes emerge:

- How can researchers most effectively combine observations, data-driven models, and physical models to enhance understanding of complex systems? To answer this question, methods are needed to integrate different types of model, operating across different levels of granularity, while managing the impact ofthe uncertainties that emerge when a machine learning model is integrated in a wider system. New approaches to simulation and emulation can support progress in tackling these challenges, alongside new strategies for examining the robustness or performance of machine learning models.

- How do the outputs from an AI system align with what researchers already know about the world, and how can such systems help uncover causal relationships in data? Advances in causal machine learning are needed to connect the laws and principles already established in many areas of research with data-driven methods.

- How can AI be integrated into the scientific process safely and robustly? Effective integration will rely on the ability to encode domain knowledge in AI systems, the design of interfaces that facilitate interaction between humans and AI, and the development of mechanisms for sharing knowledge and know-how about how to use AI in practice.

In Earth sciences

The Earth is a complex system,[11] comprised of terrestrial, marine, and atmospheric biospheres that interact with each other and are shaped by biological, chemical, and physical processes that exchange energy across scales from the molecular to the planetary. It is also a unique system: researchers have yet to discover other planets that replicate its dynamics. Studies of the Earth system therefore rely on observations and physical models, which describe the dynamics of energy exchange from first principles and use those principles to build models of the Earth's sub-systems. As climate change perturbs this complex system, it is increasingly important to have accurate models that can be used to analyse how the Earth will respond to increasing carbon dioxide levels. The challenge for Earth system science is to build more complex models that represent the web of relationships between biospheres under changing conditions, without generating overwhelming uncertainties and while generating actionable insights that can be used by individuals, organisations, and policymakers to understand the localised impact of changing environmental conditions.[12]

For example, how much carbon dioxide is absorbed by different biospheres can be affected by diverse factors including volume and type of vegetation cover, water and drought stress in different areas, and local temperature, which have implications for how

11 This example is inspired by Markus Reichstein's talk, the abstract for which is provided later in this document.

12 Summers, T., Mackie, E., Ueno, R., Simpson, C., Hosking, J.S., Suciu, T., Coburn, A., et al. (2022) Localised impacts and economic implications from high temperature disruption days under climate change. Climate Resilience and Sustainability https://doi.org/10.1002/cli2.35

carbon dioxide contributes to climate change. Researchers have access to data that describes local uptake of carbon dioxide by some ecosystems, such as tropical rainforest, European beech forest, or Mediterranean savanna, for example, but lack sufficient observational coverage to scale from these local observations to accurate global representations of carbon exchange. One response to this challenge is to leverage data-driven models to knit together the different mechanistic models that describe (for example) carbon, water, and energy cycles in different biospheres.

By starting with observational data and combining this with physics-informed modelling, researchers can leverage machine learning to create simulations that can generate new understandings of how complex systems function. Taking this approach, the FLUXNET project combines observed data on carbon emissions from different sources to generate a data-driven picture of global carbon dynamics. By combining data across scales to establish a statistical model of global carbon dynamics, this project can generate simulations of how the Earth breathes.[13] The ability to integrate across scales and combine models of different Earth sub-systems can also contribute to wider efforts to build a 'digital twin' of the Earth, with the aim of better understanding the implications of climate change across biospheres and communities.

As the Earth's climate changes,[14] researchers anticipate that local environmental conditions will change and extreme weather events will increase. Understanding the impact of these changes is important for those seeking to develop appropriate responses, for example developing environmental management plans or planning human activities.

How a landscape responds to changing environmental conditions will vary depending on the local climate, characteristics of the terrain (vegetation type, for example), and-human activities in the area. Under changing climate conditions, as extrapolation beyond known limits becomes necessary, the assumptions or abstractions that form the basis of a model can be rendered invalid. Relying solely on either mechanistic descriptions of the system – the impact of temperature on plant growth, for example[15] – or statistical models could result in inaccuracies. Machine learning can help respond to this challenge, through the creation of hybrid models that combine an understanding of the physical laws with model parameters learned from data. Researchers often already have access to known physical parameters for a system (for example, the equations that govern how water evaporates to air). These parameters can be fed into a machine learning model that will learn other patterns. Known equations specify the chemical and physical processes; machine learning can then help elucidate the other biological forces at play. Integrating this physical structure in the model helps make it both more interpretable to the domain scientists and more reliable in its predictions. The resulting model can accurately forecast the impact of climate change on the features of local landscapes,

13 Beer, C., Reichstein, M., Tomelleri, E., Ciais, P., Jung, M., Carvalhais, N., Rodenbeck, C., Arain, M.A., Baldocchi, D., Bonan, G.B., Bondeau, A., Cescatti, A., Lasslop, G., Lindroth, A., Lomas, M., Luyssaert, S., Margolis, H., Oleson, K.W., Roupsard, O., Veenendaal, E., Viovy, N., Williams, C., Woodward, F.I., Papale, D. (2010) Terrestrial gross carbon dioxide uptake: global distribution and covariation with climate, Science, 329 (5993) (2010), pp. 834–838, https://doi.org/10.1126/science.1184984

14 This example is inspired by Markus Reichstein's talk, the abstract for which is provided later in this document.

15 Under conditions of extreme temperature, patterns of stomatal opening and closing in plants changes. See, for example: Marchin, R.M., Backes, D., Ossola, A., Leishman, M.R., Tjoelker, M.G., & Ellsworth, D.S. (2022). Extreme heat increases stomatal conductance and drought-induced mortality risk in vulnerable plant species. Global Change Biology, 28, 1133–1146. https://doi.org/10.1111/gcb.15976

operating within the bounds set by the laws of physics.[16]

Ice loss[17] has been the greatest contributor to sea-level rise in recent decades.[18] Large volumes of fresh water are stored as ice: NASA estimates that if all the world's glaciers and ice sheets melted, sea levels globally would rise by over 60 metres, flooding all coastal cities.[19] Researchers can estimate the contribution that melting ice makes to sea level rise through mechanistic models that describe the underlying physical processes (that turn ice to water) and through observational data about the velocity of ice sheet movement. Machine learning could offer a toolkit to make these models more accurate, connecting ice sheet models to ocean and atmospheric models, and integrating different data types in hybrid mechanistic-data models.

Efforts to build such models, however, illustrate the complexity of designing tools to meet domain needs. Projects in this space have considered emulating the ice sheet system – or its individual components – to see if models could be run faster; though successful methodologically, it has not been clear that such efforts address a clear research need. Another approach is to use machine learning to streamline simulations, for instance by identifying the most effective level of granularity for different models (is a spatial breakdown of 5km or 10km more interesting?). An important lesson from such collaborations is the specificity of domain needs: machine learning is a tool for research, but just because researchers have a hammer, does not mean every research problem is a nail. Effectively deploying machine learning for research requires both suitable AI toolkits and an understanding of which toolkits are best deployed for which challenges.

16 Requena-Mesa, C., Reichstein, M., Mahecha, M., Kraft, B., Denzler, J. (2019). Predicting Landscapes from Environmental Conditions Using Generative Networks. In: Fink, G., Frintrop, S., Jiang, X. (eds) Pattern Recognition. DAGM GCPR 2019. Lecture Notes in Computer Science, vol 11824. Springer, Cham. https://doi.org/10.48550/arXiv.1909.10296

17 This example is inspired by Ieva Kazlauskaitė's talk, the abstract for which is provided later in this document.

18 IPCC (2019) IPCC Special Report on the Ocean and Cryosphere in a Changing Climate [Pörtner, H.-O., Roberts, D.C., Masson-Delmotte, V., Zhai, P., Tignor, M., Poloczanska, E., Mintenbeck, K., Alegría, A., Nicolai, M. Okem, A. Petzold, J. Rama, B. Weyer N.M. (eds.)]. Cambridge University Press, Cambridge, UK and New York, NY, USA, pp. 3–35. https://doi.org/10.1017/9781009157964.001, www.ipcc.ch/srocc

19 NASA, Understanding sea level, available from: https://sealevel.nasa.gov/understanding-sea-level/global-sea-level/ice-melt

In environmental and agricultural sciences

Poultry farming[20] is a vital source of income and food for many communities in Tanzania. 4.6 million households in the country raise approximately 36 million chickens, but despite the importance of this activity, poultry farming suffers from relatively low productivity due to the prevalence of disease. Efforts to tackle poultry diseases such as Salmonella, Newcastle disease, and Coccidiosis are held back by the accessibility of diagnostic processes and lack of data. Diagnosis currently requires lab analysis of droppings, which can take 3–4 days. Once disease is confirmed, farmers often lose their entire farm's flock.

Farm-level tests and diagnostics could increase the effectiveness of disease surveillance and treatment, giving farmers rapid access to information about the diseases affecting their flock and action plans about how to manage outbreaks. With mobile phones ubiquitous across the country – there are almost 49 million mobile phone subscriptions in Tanzania – there are opportunities for new uses of local data to detect disease outbreaks.

By collecting images of droppings from farms, researchers have been creating a dataset to train a machine learning system that can identify the symptoms of these diseases. Fecal images are taken on farms, annotated with diagnostic information from agricultural disease experts and the results of lab tests, then used to train an image recognition system to automate the diagnosis process.[21] System robustness and accuracy is vital, given the significant implications of a positive diagnosis, and careful design is necessary to incentivise farmers to make use of the app.

Collaboration with experts from different domains is central to developing this system. Input from farmers is needed to collect data and test the system in practice; from veterinary pathologists to help annotate the data and ensure the system's accuracy; and from technologists to develop an AI system that is effective in deployment as an app on mobile phones. These collaborations also open opportunities for new forms of citizen science, as farmers and local communities are engaged in efforts to develop and maintain an open toolkit for disease diagnosis, providing a gateway for communities to take ownership of machine learning as a tool to serve their needs.

Trees and forests[22] play a crucial role in maintaining healthy ecosystems. Despite this, an estimated ten million hectares of forest are lost globally each year due to reforestation, with only around half of this balanced by tree-planting efforts.[23] Africa experienced an annual rate of forest loss of approximately 3.9 million hectares per year from 2010–2020. This loss has implications for biodiversity and people, with trees a vital contributor to ecosystem services such as carbon storage, food provision, and shelter. In this shifting landscape, understanding the number and distribution of trees is important for the development of forestry management plans and for understanding the carbon storage implications of changes to land use.

To estimate the number and biomass of trees in the West African Sahara and Sahel, researchers have used satellite imagery of 90,000 trees from 400 sampling sites to create a labelled dataset for use in machine learning. Using an image segmentation tool to identify the location of trees, an automated system was able to count the number of trees, with domain experts guiding the system to distinguish trees

20 This example is inspired by Dina Machuve's talk, the abstract for which is provided later in this document.

21 Machuve D, Nwankwo E, Mduma N, Mbelwa J. (2022) Poultry diseases diagnostics models using deep learning. Front Artif Intell. 5, 733345. https://doi.org/10.3389/frai.2022.733345. Erratum in: Front Artif Intell. 2022 Sep 01; 5:1016695. PMID: 35978651; PMCID: PMC9376463.

22 This example is inspired by Christian Igel's talk, the abstract for which is provided later in this document.

23 Ritchie, H. and Roser, M. (2021) – "Forests and Deforestation". Published online at OurWorldInData.org, https://ourworldindata.org/forests-and-deforestation

from surrounding vegetation. This tree count can then be used to estimate the biomass of trees in the area, and predict the amount of carbon they store; the prediction is generated using allometric calculations, which translate the properties of the tree to its carbon storage potential. In this approach, machine learning measures the properties of the ecosystem from satellite images, then these properties are used to feed mechanistic models that describe the ecosystem's physical functions.[24] This opens the possibility of new tools to estimate tree cover, leveraging these insights for more effective environmental management. However, in the process, care is needed to manage the type and nature of the uncertainties created by different modelling approaches. Different allometric models, for example, can be more or less suited to different types of tree cover,[25] meaning that the method for estimating biomass from satellite imagery can be subject to biases when applied across a large area. A small error in the calculation of the biomass from one tree can have a cumulatively large effect when that method is scaled to country-level. The type and nature of such uncertainties need to be considered when a machine learning model is used within a wider system.

Vector borne diseases[26] account for more than 17% of diseases in people and over 700,000 deaths annually.[27] Changes to the climate and patterns of land use, amongst other factors, are bringing human populations into contact with new vectors of disease. In Africa, for example, populations of mosquitoes carrying malaria that might previously have been found mainly in rural areas are spreading into cities.

Tools to characterise building features from satellite imagery have already been developed and made available for use.[28] Leveraging these to analyse multi-scale data – from household to city-level – researchers are investigating how the built environment influences people's risk of contracting mosquito-borne disease. For example, it has been found that the prevalence of mosquitos in an area is related to the type of roofing used in construction; metal roofing tends to be associated with lower mosquito prevalence, potentially due to the high temperatures they attract during the day.[29] These insights can be deployed by policymakers in the development of appropriate policy responses.[30]

Decisions made on the basis of insights generated by machine learning models will be influenced by the assumptions made in those models. In the context of housing, for example, the decision about which type of housing to identify as 'at risk' or which building materials to flag as 'problematic' may have significant consequences for individuals or communities. When those decisions are assimilated within a model or analysis before a downstream 'policy decision', the implications for those communities of different courses

24 Brandt, M., Tucker, C.J., Kariryaa, A. et al. (2020) An unexpectedly large count of trees in the West African Sahara and Sahel. Nature 587, 78–82. https://doi.org/10.1038/s41586-020-2824-5

25 Hiernaux, P. and Issoufou, B.H., Igel, C., Kariryaa, A., Kourouma, M., Chave, J., Mougin, E. and Savadogo, P. (2023) Allometric Equations to Estimate the Dry Mass of Sahel Woody Plants from Very-High Resolution Satellite Imagery. Forest Ecology and Management, 529, https://doi.org/10.1016/j.foreco.2022.120653

26 This example is inspired by Christian Igel's talk, the abstract for which is provided later in this document.

27 Hernandez-Triana, L. and Bell, S. (2022) Taking the sting out of vector borne diseases, APHA Science Blog, available at: https://aphascience.blog.gov.uk/2022/07/06/vector-borne-diseases

28 For example: Quinn, J. (2021) Mapping Africa's Buildings with Satellite Imagery, Google Research Blog, available at: https://ai.googleblog.com/2021/07/mapping-africas-buildings-with/html

29 Lindsay, S.W., Jawara, M., Mwesigwa, J., Achan, J., Bayoh, N., Bradley, J., Kandeh, B., Kirby, M.J., Knudsen, J., Macdonald, M., Pinder, M., Tusting, L.S., Weiss, D.J., Wilson, A.L. and D'Alessandro, U. (2019) Reduced mosquito survival in metal-roof houses may contribute to a decline in malaria transmission in sub-Saharan Africa. Scientific Reports 9, 7770, https://doi.org/10.1038/s41598–019–43816–0

30 Royal Danish Academy (2022) New research to combat malaria mosquitoes in African metropolises, available at: https://royaldanishacademy.com/news/ny-forskning-skal-bekaempe-malariamyg-i-afrikanske-storbyer

of action may be obscured, creating a risk of marginalising or disadvantaging individuals or groups. The assumptions are built into the model, and how visible those assumptions are made to different user groups, can have significant social and scientific consequences.

In physical sciences

Understanding the nature of dark matter[31] is one of the biggest unsolved challenges of particle physics today. The matter that researchers can measure using cosmological observations makes up about 5% of the Universe.[32] While not directly observable, evidence for the existence of dark matter can be found in a variety of phenomena not otherwise accounted for by currently known laws of physics: stars rotate around galaxies faster than might be expected; the pattern of fluctuations in primordial microwave observations indicate that there were sources of gravitation in the early Universe beyond ordinary matter; light bends around galaxy clusters due to gravitational effects from dark matter.

Despite knowing that dark matter exists and that it plays an important role in how the Universe formed, its particle composition or properties remain unclear. Investigating these properties is the focus of large-scale experimental studies, for example in particle colliders.[33] A variety of data could contain information about the properties of dark matter, from studies of cosmic rays, cosmic microwave radiation, properties of stars, gravitational lensing studies, and more. These datasets are complex: they are typically high-dimensional, represent complex relationships between the micro-physics and macro-phenomena in a system, and may contain artefacts or noise from the instruments used to collect them. To make use of this data, researchers need to account for this complexity and tether their models to assumptions about physical processes.

The challenge for machine learning in astro-particle physics research is to extract insights about the particle composition of dark matter from the macroscopic patterns that can be observed in the Universe. For example, gravitational lensing is a phenomenon in which the pathway of light traveling through the Universe is deflected due to the influence of gravity from an intervening mass, distorting how this background light is observed.[34] Gravitational lensing effects arising from dark matter clumps ("substructure") could hold information about the structure of dark matter at a microscopic level. To infer the presence of substructure of these lensing systems, researchers need models that describe the effect of dark matter, ordinary matter, and the wider environment while simultaneously modelling the form of the background light, which can be a morphologically-complex galaxy. By letting a machine learning model, like a neural network, describe the complex background light source, it is possible to make predictions about how the light might appear after being lensed with and also without the impact of dark matter clumps. By performing

31 This example is inspired by Siddharth Mishra Sharma's talk, as well as insights from Gilles Louppe's talk, the abstracts for which are provided later in this document.

32 NASA, Dark Energy, Dark Matter, available at: https://science.nasa.gov/astrophysics/focus-areas/what-is-dark-energy

33 For example: Aad, G., Abat, E., Abdallah, J., Abdelalim, A.A., Abdesselam, A., Abdinov, O., Abi, B.A., Abolins, M., Abramowicz, H., Acerbi, E., Acharya, B.S., Achenbach, R., Ackers, M., Adams, D.L., Adamyan, F., Addy, T.N., Aderholz, M., Adorisio, C., Adragna, P., … Zychacek, V. (2008). The ATLAS Experiment at the CERN Large Hadron Collider. Journal of Instrumentation, 3(S08003). https://doi.org/10.1088/1748-0221/3/08/S08003

34 Mishra-Sharma, S. and Yang, G. (2022) Strong Lensing Source Reconstruction Using Continuous Neural Fields, arXiv:2206.14820 [astro-ph.CO], https://doi.org/10.48550/arXiv.2206.14820

many simulations considering various possibilities, researchers can compare these with observations from telescopes and understand which dark matter theories are compatible with the data.

Rapid progress in this field is generating a variety of models and approaches. In its next wave of development, further research is needed to test how trustworthy these methods are, by assessing their performance in generating physically plausible results and robust constraints on the properties of dark matter and other forms of new physics.[35]

How particles move[36] across their environment is a shared area of interest for many domains. In chemistry, for example, researchers are often interested in how molecules diffuse, and where they end up distributed, based on the physical forces that shape their movement over time.

The analogy of particle movement can also be applied as an abstraction of larger scale physical processes, such as in agent-based models for crowd simulation.[37] In these systems the initial system state is represented in an initial probability distribution, the scientific objective can then also be represented as a target distribution. The dynamics underpinning this diffusion are formalised mathematically in the Schrödinger bridge problem. This long-standing problem is concerned with finding the most likely paths along which particles move from their starting distribution to their distribution at a defined point in time, based on experimentally-observed start and end positions. In general, finding analytic solutions to the Schrödinger bridge problem is intractable, but machine learning tools are providing new approaches for finding approximate numerical solutions that can be deployed across domains.[38]

35 Dvorkin, C., Mishra-Sharma, S., Nord, B., Villar, V.A., Avestruz, C., Bechtol, K., Ćiprijanović, A., Connolly, A.J., Garrison, L.H., Narayan, G. and Villaescusa-Navarro, F. (2022) Machine learning and cosmology, arXiv:2203.08056 [hep-ph], https://doi.org/10.48550/arXiv.2203.08056

36 This example is inspired by Francisco Vargas's talk, the abstract for which is provided later in this document.

37 Examples of agent-based models for crowd simulation include: Makinoshima, F., Oishi, Y. (2022) Crowd flow forecasting via agent-based simulations with sequential latent parameter estimation from aggregate observation. Sci Rep 12, 11168. https://doi.org/10.1038/s41598–022–14646–4 and Malleson, N., Minors, K., Kieu, L., Ward, J.A., West, A. and Heppenstall, A (2020) Simulating Crowds in Real Time with Agent-Based Modelling and a Particle Filter, Journal of Artificial Societies and Social Simulation 23 (3) 3 http://jasss.soc.surrey.ac.uk/23/3/3.html, https://doi.org/10.18564/jasss.4266

38 Vargas, F., Thodoroff, P., Lawrence, N.D. and Lamacraft, A. (2021) Solving Schrödinger Bridges via Maximum Likelihood, arXiv:2106.02081 [stat.ML], https://doi.org/10.48550/arXiv.2106.02081

In biological sciences

The development and differentiation of cells into tissues and organs[39] is a complicated process, shaped by hormonal and genetic influences on cell growth.[40] Advances in genomics have allowed researchers to characterise the genetic material of different organisms; more recent progress in single-cell genomics extends this ability to the single-cell level, unlocking detailed analysis of how genetic activity determines cellular function.

Single-cell RNA studies examine how ribonucleic acids (RNA) shape cellular properties and development pathways. The RNA profiles created by genetic sequencing techniques allow researchers to identify which genes are active in a cell. The question for the field today is how to move from these single-cell analyses to an atlas of cell development that shows how cells specialise and form tissues or organs.

By combining statistical and machine learning techniques, researchers can reconstruct the gene dynamics – which genes are activated at which time – that influence cell development.[41] Cells in the small intestine, for example, undergo a pattern of differentiation that takes them from their base state to highly specialised units, able to variously secrete mucus, absorb nutrients, or respond to hormones. By studying what genes are expressed in a cell at an early stage, researchers can predict how the cell will specialise and identify which genetic changes are associated with that specialisation, opening opportunities to treat intestinal diseases.[42]

Building these models relies on effective data management. Lab processes can inject artefacts into datasets, for example batch effects arising from how cells were grown or harvested for study, which need to be removed from data before analysis. Effective data correction maintains biologically-relevant information, while removing noise from the data. A variety of tools exist for this correction, including regression models, dimensionality reduction, graph methods, and deep learning. For domain researchers to be able to identify the tools that are useful for them, benchmarking studies are vital in identifying the most effective data integration method for their purpose.[43] However, there remain open questions about how best to benchmark the performance of a system when there are complex pipelines of analysis involved. Understanding the end-to-end nature of an analytical pipeline can be difficult, and new approaches to assessing performance may be needed.

To understand how the brain works,[44] neuroscientists develop mathematical models that describe the activity of individual neurons, and how these connect across brain networks. Models on the mechanistic level take the form of differential equations. These models are based on data from experiments that examine how neurons respond to different signals or perturbations. To build a computational model from this data, it is first necessary to find which

39 This example is inspired by Maren Büttner's talk, the abstract for which is provided later in this document.

40 Krishnamurthy, K.V., Bahadur, B., John Adams, S., Venkatasubramanian, P. (2015). Development and Organization of Cell Types and Tissues. In: Bahadur, B., Venkat Rajam, M., Sahijram, L., Krishnamurthy, K. (eds) Plant Biology and Biotechnology. Springer, New Delhi. https://doi.org/10.1007/978–81–322–2286–6_3

41 Haghverdi, L., Büttner, M., Wolf, F. et al. (2016) Diffusion pseudotime robustly reconstructs lineage branching. Nat Methods 13, pp. 845–848. https://doi.org/10.1038/nmeth.3971

42 Böttcher A, Büttner M, Tritschler S, Sterr M, Aliluev A, Oppenländer L, Burtscher I, Sass S, Irmler M, Beckers J, Ziegenhain C, Enard W, Schamberger AC, Verhamme FM, Eickelberg O, Theis FJ, Lickert H. Non-canonical Wnt/PCP signalling regulates intestinal stem cell lineage priming towards enteroendocrine and Paneth cell fates. Nat Cell Biol. 2021 Jan; 23(1):23–31. doi: 10.1038/s41556–020–00617–2. Epub 2021 Jan 4. Erratum in: Nat Cell Biol. 2021 May;23(5):566–576. PMID: 33398177. https://doi.org/10.1038/s41556–020–00617–2

43 Luecken, M.D., Büttner, M., Chaichoompu, K. et al. Benchmarking atlas-level data integration in single-cell genomics. Nat Methods 19, 41–50 (2022). https://doi.org/10.1038/s41592–021–01336–8

44 This example is inspired by Jakob Macke's talk, the abstract for which is provided later in this document.

factors influence how a neuron acts, creating a set of parameters that determine how the model works. This process of finding parameters is often labour-intensive, relying on trial-and-error, which limits researchers' ability to scale models across complex neural networks. Machine learning can help streamline that model definition process, by predicting which models are more likely to be compatible with data. Byautomatically identifying model parameters, researchers can rapidly develop simulations of complex structures, such as brains or nervous systems in different animals.[45]

45 Gonçalves, P., Lueckmann, J.M., Deistler, M., Nonnenmacher, M., Öcal, K., Bassetto, G., Chintaluri, C., Podlaski, W.F., Haddad, S.A., Vogels, T.P., Greenberg, D., and Macke, J.H. (2020) Training deep neural density estimators to identify mechanistic models of neural dynamics eLife 9:e56261 https://doi.org/10.7554/eLife.56261

Box 1: Talks given during this workshop session

Markus Reichstein: Machine-learning-model-data-integration for a better understanding of the Earth System

The Earth is a complex dynamic networked system. Machine learning, i.e. derivation of computational models from data, has already made important contributions to predict and understand components of the Earth system, specifically in climate, remote sensing and environmental sciences. For instance, classifications of land cover types, prediction of land-atmosphere and ocean-atmosphere exchange, or detection of extreme events have greatly benefited from these approaches. Such data-driven information has already changed how Earth system models are evaluated and further developed. However, many studies have not yet sufficiently addressed and exploited dynamic aspects of systems, such as memory effects for prediction and effects of spatial context, e.g. for classification and change detection. In particular new developments in deep learning offer great potential to overcome these limitations. Yet, a key challenge and opportunity is to integrate (physical-biological) system modelling approaches with machine learning into hybrid modelling approaches, which combines physical consistency and machine learning versatility. A couple of examples are given with focus on the terrestrial biosphere, where the combination of system-based and machine-learning-based modelling helps our understanding of aspects of the Earth system.

Dina Machuve: Poultry Diseases Models using Deep Learning

Coccidiosis, Salmonella, and Newcastle are the common poultry diseases that curtail poultry production if they are not detected early. In Tanzania, these diseases are not detected early due to limited access to agricultural support services by poultry farmers. Deep learning techniques have the potential for early diagnosis of these poultry diseases. In this study, a deep Convolutional Neural Network (CNN) model was developed to diagnose poultry diseases by classifying healthy and unhealthy fecal images. Unhealthy fecal images may be symptomatic of Coccidiosis, Salmonella, and Newcastle diseases. We collected 1,255 laboratory-labeled fecal images and fecal samples used in Polymerase Chain Reaction diagnostics to annotate the laboratory-labeled fecal images. We took 6,812 poultry fecal photos using an Open Data Kit. Agricultural support experts annotated the farm-labeled fecal images. Then we used a baseline CNN model, VGG16, InceptionV3, MobileNetV2, and Xception models. We trained models using farm and laboratory-labeled fecal images and then fine-tuned them. The test set used farm-labeled images. The test accuracies results without fine-tuning were 83.06% for the baseline CNN, 85.85% for VGG16, 94.79% for InceptionV3, 87.46% for MobileNetV2, and 88.27% for Xception. Finetuning while freezing the batch normalization layer improved model accuracies, resulting in 95.01% for VGG16, 95.45% for InceptionV3,98.02% and 98.24% for Xception, for MobileNetV2, with F1 scores for all classifiers above 75% in all four classes. Given the lighter weight of the trained MobileNetV2 and its better ability to generalize, we recommend deploying this model for the early detection of poultry diseases at the farm level. There are open questions about the deployment of the model at the farm level and potential areas for further research.

Siddharth Mishra-Sharma: Simulation-based approaches to astrophysics dark matter searches

We are at the dawn of a data-rich era in astrophysics and cosmology, with the capacity to extract useful scientific insights often limited by our ability to efficiently model complex processes that give rise to the data rather than the volume and nature of observations itself. I will describe recent progress in applying mechanistic forward

modeling techniques to a range of astrophysical observations with the goal of searching for signatures of new physics, in particular the nature of dark matter. These leverage developments in machine learning-aided inference, e.g. using simulation-based inference as well as differentiable probabilistic programming, while encoding domain knowledge, in order to maximize the scientific output of current as well as future experiments.

Maren Büttner: Single-cell transcriptomics

Cells are the fundamental units of life. Understanding cellular processes is a basis for improving human health, disease diagnosis and monitoring. The advent of single-cell transcriptomics (scRNA-seq) allows characterizing the gene expression patterns of entire organs and organisms at single cell resolution. The human genome encodes more than 30.000 genes, and high-throughput scRNA-seq methods create samples with tens of thousands of cell measurements. The analysis of such data requires a variety of methods from the machine learning field, e.g. dimensionality reduction techniques from PCA to variational autoencoders, graph-based clustering, classification of cell types, trajectory inference and causal inference of gene regulation to understand cell fate decision making. To date, scRNA-seq is a widely applied research technique, which has the potential for standard application in the clinics. My presentation focusses on current approaches for large-scale scRNA-seq data, current open questions, and implications for human health.

Christian Igel: Estimating ecosystem properties: Combining machine learning and mechanistic models

Progress in remote sensing technology and machine learning algorithms enables scaling up the monitoring of ecosystems. This leads to new knowledge about their status and dynamics, which will be helpful in land degradation assessment (e.g., deforestation), in mitigating poverty (e.g., food security, agroforestry, wood products), and in managing climate change (e.g., carbon sequestration). We apply deep learning for the mapping of individual trees and forests. Tree crowns are segmented in satellite imagery using fully convolutional neural networks. This provides detailed measurements of the canopy area and of the distribution of trees within and outside forests. Allometric equations are applied to estimate the biomasses (and thereby the stored carbon) of the individual trees. We use iterative gradient-based optimization of the allometric models and suggest techniques such as jackknife+ for quantifying the uncertainty of the model predictions. Tree biomass can also be directly inferred from LiDAR (laser imaging, detection, and ranging) measurements using 3D point cloud neural networks. This leads to highly accurate results without requiring a digital elevation model. In a new project, we consider risk assessment of vector-borne diseases based on deep learning and remote sensing. Malaria risk is related to the housing conditions, for example, the type of roofing material, which can be determined from satellite images.

Ieva Kazlauskaite: Partial differential equations and Variational Bayes

Inverse problems involving partial differential equations (PDEs) are widely used in science and engineering. Although such problems are generally ill-posed, different regularisation approaches have been developed to ameliorate this problem. Among them is the Bayesian formulation, where a prior probability measure is placed on the quantity of interest. The resulting posterior probability measure is usually analytically intractable. The Markov Chain Monte Carlo (MCMC) method has been the go-to method for sampling from those posterior measures. MCMC is computationally infeasible

for large-scale problems that arise in engineering practice. Lately, Variational Bayes (VB) has been recognised as a more computationally tractable method for Bayesian inference, approximating a Bayesian posterior distribution with a simpler trial distribution by solving an optimisation problem. The talk covered some recent experiences of applying Bayesian inference, generative models and probabilistic programming languages in the context of learning material properties in civil engineering and in ice sheet and ice core modelling. The main shortcomings of PPLs and differentiable problems were highlighted.

Francisco Vargas: The Schrödinger bridge problem

Recent works in diffusion-based models have been achieving competitive results across generative modelling and inference, in this presentation we propose to explore a unifying framework based on Schrodinger bridges to explore/explain diffusion-based methodology.

The Schrödinger bridge problem (SBP) finds the most likely stochastic evolution between two probability distributions given a prior (reference) stochastic evolution. Recently SBP based methodology has made its way into generative modelling, sampling, and inference. In this talk we propose the exploration of a unifying framework for the aforementioned works based on the renowned IPF/Sinkhorn algorithm. The motivation behind this is to cast a unifying lens via the Schrodinger perspective relating inference, sampling and transport, in a way that we can leverage many of the useful techniques and heuristics from each field to benefit each other.

Building effective simulations

Moving upstream

Science proceeds through hypothesis, observation and analysis. For hundreds of years, researchers have advanced the frontiers of knowledge by collecting data, compressing those observations into a model, then computing that model to create representations of how the world works, generating new insights about natural and physical phenomena and theories about the systems from which those phenomena emerge in the process.[46] These mathematical models rely on numerical methods: algorithms that help solve mathematical problems where no analytical solution is available. Today, data collection and the basic computational tasks involved in its analysis – linear algebra, optimisation, simulation, and so on – remain consistent features of the scientific process. Progress in machine learning, however, has changed the modelling landscape. 'AI for science' offers a data-centric approach to modelling and simulating the world. Operating alongside the traditional mathematical models that are central to many disciplines, machine learning provides data-centric analytical methods that can be integrated across the scientific pipeline, for example enabling sophisticated simulations of real world systems. These simulations can be used to inform model development, test hypotheses and shape areas of research focus, or unlock insights from complex data.

Nurturing a diversity of approaches

Simulations are a well-established tool for scientific discovery. Their fundamental task is to allow data sampling from a model where the differences between simulation and the real world are reduced as far as feasible, to enable experimentation or testing of the impact of different perturbations, while allowing some measure of simplification of the system. Effective simulators allow researchers to move from theory to an understanding of what data should look like.

Domains such as particle physics, protein folding, climate science, and others, have developed complex simulations that use known theories and parameters of interest to make predictions about the system of study. AI for science can be brought in to speed up some of these through surrogate models. Machine learning can complement 'traditional' approaches to scientific simulation, adding components that model the most uncertain elements of a system to strongly mechanistic models that might otherwise be too restrictive in their assumptions.

Much early excitement surrounding AI for science was rooted in the reverse process, asking: instead of starting with theory, could researchers instead start with the large amounts of data available in many areas of research and, from that data, build an understanding of what an underpinning theory might be? Given a set of observations, is it possible to find parameters for a model that result in simulations that reflect the measured data? Such simulation-based inference (SBI) offers the opportunity to generate novel insights across scientific disciplines.

To enable such analysis, machine learning methods are needed that can extract insights from high-dimensional, multi-modal data, in ways that are labour- and compute-efficient.[47] The field of probabilistic numerics offers a way to flexibly combine infor-

46 Blei, D.M. (2014) Build, Compute, Critique, Repeat: Data Analysis with Latent Variable Models, Annual Review of Statistics and Its Application, Vol. 1:203–232, https://doi.org/10.1146/annurev-statistics-022513-115657

47 Cranmer, K., Brehmer, J., Louppe, G. (2019) The frontier of simulation-based inference, arXiv:1911.01429[stat.ML], https://doi.org/10.1073/pnas.1912789117

mation from mechanistic models with insights from data, solving numerical problems through statistical approaches.[48] Operationalising these methods to create effective data-driven simulations requires balancing different model characteristics. The model's parameters must be specified to a sufficient level of granularity to describe the real-world system, while operating at a level of abstraction that is amenable to analysis and computation; almost all models are 'wrong' or falsifiable because of this, but some level of abstraction is necessary to make them useful for analysis. The simulation must also be designed to be robust, and able to generate inferences that align with real-world observations.

Truth, truthiness, and interfacing with the real world

The excitement underpinning AI for science stems from the aspiration to unearth new understandings of the world, leveraging data to advance the frontiers of knowledge. While subject to their own limitations, the scientific community has developed checks and balances to scrutinise new knowledge and maintain the rigour of scientific inquiry. Recent years have seen a variety of challenges or benchmarks emerge in the machine learning community that have come to represent the field's expected standards of performance from algorithms on defined tasks. However, these standards do not necessarily align with the expectations of domain researchers.[49] As data-centric simulations are integrated into scientific process, machine learning researchers must consider their responsibility in maintaining the integrity of the domains into which they are deployed, raising the question: what guardrails are needed to ensure researchers can be confident in the outputs from machine learning-enabled simulations?

A variety of diagnostic tests can help. Core to many of these diagnostics is analysis of whether a model is computationally faithful. In short: the inferences generated by a simulation should reflect those from observations.[50] One approach to checking this alignment is to consider the consistency of distributions from inferred and observed datasets. If the model is a good fit, the data it generates should broadly match the data observed through experimentation.

Underpinning these diagnostics is a fundamental question about how to manage uncertainty, in a context where different failure modes have different implications. Put simply: when a model fails, is it worse to be over-confident in its results, or over-conservative? In the scientific context, over-confidence seems more likely to result in negative outcomes, whether through giving misleading interpretations or results or driving lines of inquiry in unproductive directions. Machine learning methods can be designed for conservatism, reducing the risk of false positives.

Implementing a schedule of model building, computing, critiquing, and repeating can refine this process. One lesson from experiences of building machine learning-enabled simulations is that there can be a disconnect between how machine learning approaches inference and model building, and how the same task is approached by domain scientists. From a domain perspective, model building seems naturally an iterative process: collect data, fit a model, find errors or areas for improvement, update the model, and so on. This iterative process is guided by expert intuition and knowledge; deep understanding of the system under study and how it responds to perturbation. Machine learning research has developed practices for prior elicitation – using domain knowledge to shape the structure of probabilistic models – but the nuances of this domain intuition are often not easily captured a priori, instead emerging when models fail as an informal sense of what 'feels' like it should be true. This qualitative input is vital in building effective simulations. It requires close collaboration, which in turn requires an investment of time and energy from domain communities, generated through mutual trust, incentives, and long-term relationship-building.

48 Hennig, P., Osborne, M.A. and Kersting, H. (2022). Probabilistic Numerics – Computation as Machine Learning. Cambridge University Press.

49 Hermans, J., Delaunoy, A., Rozet, F., Wehenkel, A. and Louppe, G. (2021), A Trust Crisis In Simulation-Based Inference? Your Posterior Approximations Can Be Unfaithful, arXiv:2110.06581 [stat.ML], https://doi.org/10.48550/arXiv.2110.06581

50 Ibid.

Connecting simulation to practice

Computational tools are central to the effective deployment of machine learning-enabled simulation. The function and form of such tools must align with the requirements of the community deploying them. Designing computational systems to match user needs – and work effectively in practice – requires both effective software engineering and close collaboration with domain groups that can articulate the requirements and expectations of those working in the field. To remain effective over the longer-term, such systems must leverage effective software engineering practices, including embedding version control and building interfaces that work with other models and systems. Those practices, and the software systems that emerge from them, must be designed for the needs of those using the system, drawing from existing best practices in software engineering, but adapting those practices to reflect the needs of the domain for deployment.

Constructing computational tools requires a mix of technical insight and craft skill – of knowledge and know how. Tools produced by the machine learning community differ in their usefulness on different problems: some work well for certain tasks, but not for others. Without access to such craft skills, those outside the 'AI for science' community can find it challenging to determine which tools to use for which purposes, reducing the generalisability of existing methods and approaches. This challenge becomes particularly visible when practitioners are tightly integrated into the analysis pipeline, such as in applications in developmental biology, in the developing world, and in data-centric engineering. Widening access to the field will require user guides that characterise which simulations are effective for which tasks or purposes, supported by case studies or user stories that help demystify how machine learning can work in practice.

Directions

Machine learning typically requires an explicit representation of a likelihood, but these are often difficult to compute. Further advances in SBI are necessary to allow researchers to identify model parameters from data.

- Techniques such as likelihood-free inference can enhance existing Bayesian methods for inferring posterior estimations.[51]
- Building surrogate models,[52] using Bayesian approaches for simulation planning to optimise information gain,[53] or deploying emulations[54] can also enhance the efficiency of simulations.
- Probabilistic numerics offers a route to develop statistically-optimal algorithms that are amenable to comprehensive uncertainty quantification, leveraging Gaussian Process-based Ordinary Differential Equation (ODE) solvers to pursue simulation as an inference problem.[55]

51 Alsing, J., Charnock, T., Feeney, S. and Wandelt, B. (2019) Fast likelihood-free cosmology with neural density estimators and active learning, arXiv:1903.00007 [astro-ph.CO] https://doi.org/10.48550/arXiv.1903.00007

52 See above, and Lavin, A., Zenil, H., Paige, B., Krakauer, D., Gottschlich, J., Mattson, T., Anandkumer, A., Choudry, S., Rocki, K., Baydin, A.G., Prunkl, C., Paige, B., Isayev, O., Peterson, E., McMahon, P.L., Macke, J., Cranmer, K., Zhang, J., Wainwright, H., Hanuka, A., Veloso, M., Assefra, S., Zheng, S., and Pfeffer, A. (2021) Simulation Intelligence: Towards a New Generation of Scientific Methods, arXiv:2112.03235 [cs.AI], https://doi.org/10.48550/arXiv.2112.03235

53 See, for example, Cranmer, K., Heinrich, L., Head, T. and Louppe, G. Active sciencing, at: https://github.com/cranmer/active_sciencing

54 Boelts, J., Lueckmann, J.M., Gao, R., and Macke, J.H. (2022) Flexible and efficient simulation-based inference for models of decision-making eLife 11:e77220 https://doi.org/10.7554/eLife.77220

55 Kersting, H. (2021) Uncertainty-aware numerical solutions of ODE's by Bayesian Filtering, available at: https://hanskersting.github.io/publication/phd-thesis

Operationalising these approaches will also require new toolkits to support implementation of probabilistic numerical methods.[56] Computational faithfulness – alignment of inferred parameters with scientific knowledge – can be achieved through:

- Diagnostic checks in the self-consistency of the Bayesian joint distribution, which measure the scientific quality of the regions computed by Bayesian SBI methods.[57] Checking for self-consistency gives a sense whether the model is 'good enough' (i.e whether the inference engine gives a good sense of the posterior).
- Enforcing conservative neural ratio estimation through binary classifier specification, producing more conservative posterior approximations.[58]
- Hybrid modelling, which combines machine learning components learned from data with the mechanistic components specified by existing domain knowledge.[59]
- Further study of the impact of model misspecification could also help generate new robustness diagnostic checks.[60]

'Digital twins' have recently received much attention as a tool to exploit sophisticated simulations. In Earth sciences, for example, ambitious efforts to develop a digital twin of the Earth propose to allow more accurate forecasting, visualisation, or scenario testing of the impact of climate change and efforts to mitigate it.[61] The challenge is to integrate different models or components of a system – for example, connecting atmospheric models, with land models, with models of human behaviour – in a way that represents the complete Earth system. That requires consideration of the different levels of granularity with which these different models operate: economic models of human behaviour, for example, operate with different assumptions and levels of enquiry in comparison to physical models of ocean circulation. The full range of granularities becomes apparent when considering that specific applications, such as disease monitoring on poultry farms, sit within the wider ecosystem of the natural and built environment. A digital twin needs to make choices about what levels of granularity it is operating at, from the scale of the poultry farm to the planet. The questions that emerge from such ambitions is: what level of granularity is helpful or necessary to deliver effective results? And what interfaces between diverse models might be possible?

56 See, for example, the previous Dagstuhl meeting on this topic: https://www.probabilistic-numerics.org/meetings/2021_Dagstuhl/ Dagstuhl and Schmidt, J., Kramer, N. and Hennig, P. (2021) A Probabilistic State Space Model for Joint Inference from Differential Equations and Data, arXiv:2103.10153 [stat.ML], https://doi.org/10.48550/arXiv.2103.10153

57 Hermans, J., Delaunoy, A., Rozet, F., Wehenkel, A. and Louppe, G. (2021), A Trust Crisis In Simulation-Based Inference? Your Posterior Approximations Can Be Unfaithful, arXiv:2110.06581 [stat.ML], https://doi.org/10.48550/arXiv.2110.06581 and Mishra-Sharma, S. (2021) Inferring dark matter substructure with astrometric lensing beyond the power spectrum, arXiv:2110.01620 [astro-ph.CO], https://doi.org/10.48550/arXiv.2110.01620

58 Delaunoy, A., Hermans, J., Rozet, F., Wehenkel, A. and Louppe, G. (2022) Towards Reliable Simulation-Based Inference with Balanced Neural Ratio Estimation, arXiv:2208.13624 [stat.ML], https://doi.org/10.48550/arXiv.2208.13624

59 Wehenkel, A., Behrmann, J., Hsu, H., Sapiro, G., Louppe, G., and Jacobsen, J.H. (2022) Robust Hybrid Learning With Expert Augmentation, arXiv:2202.03881 [cs.LG], https://doi.org/10.48550/arXiv.2202.03881

60 Cannon, P., Ward, D. and Schmon, S.M. (2022) Investigating the Impact of Model Misspecification in Neural Simulation-based Inference, arXiv:2209.01845 [stat.ML], https://doi.org/10.48550/arXiv.2209.01845

61 For example: European Commission (2022) Destination Earth – new digital twin of the Earth will help tackle climate change and protect nature, available at: https://ec.europa.eu/commission/presscorner/detail/en/IP_22_1977

Box 2: Talks given during this workshop session

Philipp Hennig: Information from data and compute in scientific inference

Simulations are central to scientific inference. Simulators are typically treated as black boxes, with the inference loop wrapped around them. This approach is convenient for the programming scientists, but can be highly inefficient. Probabilistic numerical methods represent computational and empirical data in the same language, which allows for inference from mechanistic knowledge and empirical data in one combined step. I will argue that scientific computing needs to embrace such new computational paradigms to truly leverage ML in science, which also requires rethinking scientific codebases.

Hans Kersting: ODE filters and smoothers: probabilistic numerics for mechanistic modelling

Probabilistic numerics (PN) unifies statistical and numerical approximations by formulating them in the same language of statistical (Bayesian) inference. For ODEs, a well-established probabilistic numerical method is ODE filters and smoothers which can help to deal more aptly with uncertainty in mechanistic modeling. In the first half of this talk, we will first introduce PN and then present ODE filters/smoothers as a specific instance of PN. In the second half, we will discuss how ODE filters/smoothers can improve mechanistic modeling in the natural sciences and present a recent application of inferring the parameters of a real-world dynamical system.

Jakob Macke: Four short stories on simulation-based inference

Many fields of science make extensive use of simulations expressing mechanistic forward models, requiring the use of simulation-based inference methods. I will share experiences and lessons learned from four applications: describing the dynamics and energy consumptions of neural networks in the stomatogastric ganglion; inferring parameters of gravitational wave models; optimising single-molecule localisation microscopy, and building computational models of the fly visual system. I will try to convey some thoughts on the challenges and shortcomings of current approaches.

Gilles Louppe: Towards reliable simulation-based inference and beyond

Modern approaches for simulation-based inference build upon deep learning surrogates to enable approximate Bayesian inference with computer simulators. In practice, the estimated posteriors' computational faithfulness is, however, rarely guaranteed. For example, Hermans et al., 2021 have shown that current simulation-based inference algorithms can produce posteriors that are overconfident, hence risking false inferences. In this talk, we will review the main inference algorithms and present Balanced Neural Ratio Estimation (BNRE), a variation of the NRE algorithm designed to produce posterior approximations that tend to be more conservative, hence improving their reliability.

Tom Dietterich: Modeling the data collection process: My journey

In this talk, I will describe three examples of my attempts to integrate subject-matter knowledge with machine learning. The first example involves predicting grasshopper infestations. I will sketch the methodology in which we first modeled the life cycle of the grasshoppers to capture the factors that affect their population. Unfortunately, most variables of interest were not measured, so we used the model to guide the construction of proxy variables. Ultimately, this project did not succeed, but it is hard to determine whether this is due to modeling problems or to the chaotic nature of the biological phenomenon.

Connecting data to causality

Causality in science and data

Most scientific endeavours have a causal element: researchers want to characterise how a system works, why it works that way, and what happens when it is perturbed. How researchers identify cause-and-effect relationships varies across domains. For some disciplines, the process of hypothesis design – data collection – model development provides the core structure for interrogating how a system works. In others, where experimentation is more difficult, researchers may rely on natural experiments and observations to compare the response of a system under different conditions. Those studying the Earth system, for example, have little scope to replicate planetary conditions, so instead rely on observational data and modelling to identify the impact of different interventions. These different approaches, however, share a modelling approach in which researchers provide variables to create structural, causal models.

In contrast, machine learning proceeds by learning representations or rules from data, based on statistical information, rather than structured rules about how a system works (such as physical laws). Causal inference – the ability to identify cause-and-effect relationships in data – has been a core aim of AI research, in service of both wider ambitions to replicate intelligence in machines and efforts to create AI systems that are robust in deployment. However, in many respects efforts to integrate causal inference into AI systems have yet to deliver.[62]

An apocryphal story in AI tells of efforts by US researchers during the 1980s to train a computer system that could distinguish between images of tanks from the US and USSR. The resulting system delivered high accuracy on its training data, but failed repeatedly in practice. The system was subsequently found to be classifying images based on their resolution and background features – is the image grainy? Does it contain snow? – rather than the tanks themselves. It found patterns in the data that were co-incident, rather than causal. That same error has real-world implications for the AI systems deployed today. In medical sciences, AI systems trained to detect collapsed lungs from medical images have been proven inaccurate, after the model was found to have learned to detect the tube inserted into the lung to enable a patient to breath as a response to its collapse, rather than the physical features of the lung itself.[63] In medical sciences, deployment of such systems could put patient care at risk. In social sciences, these AI design and data bias failures can combine to marginalise vulnerable populations.[64]

Conversely, an understanding of the structures within data can improve the accuracy of machine learning analyses. In exoplanet discovery, for example, machine learning is used as a tool to detect variations in light signals from large-scale astronomical datasets. The movement of exoplanets around stars results in periodic changes to the light signals from those stars, as the planet obscures them in its transit. Machine learning can detect those signals and predict where exoplanets might be located, but the data is often noisy. Noticing that the structure of this noise was consistent across a number of stars, which were too distant from each other to be interacting, researchers concluded that instrumentation

62 Schölkopf, B., Locatello, F., Bauer, S., Ke, N.R., Kalchbrenner, N., Goyal, A., and Bengio, Y. (2021) Towards Causal Representation Learning, arXiv:2102.11107 [cs.LG], https://doi.org/10.48550/arXiv.2102.11107

63 Rueckel, J., Trappmann, L., Schachtner, B., Wesp, P., Hoppe, B.F., Fink, N., Ricke, J., Dinkel, J., Ingrisch, M., and Sabel, B.O. (2020) Impact of Confounding Thoracic Tubes and Pleural Dehiscence Extent on Artificial Intelligence Pneumothorax Detection in Chest Radiographs. Invest Radiol. 2020 Dec;55(12):792–798. https://doi.org/10.1097/RLI.0000000000000707 . PMID: 32694453. https://pubmed.ncbi.nlm.nih.gov/32694453

64 Emspak, J. (2016) How a machine learns prejudice, Scientific American Blogs, available at: www.scientificamerican.com/article/how-a-machine-learns-prejudice/

effects were distorting the data, and developed a method to model those effects and remove them from exoplanet predictions. The result was an efficient method for exoplanet identification that subsequently contributed to the discovery of the first potentially habitable planet.[65]

Causal models as a route to advancing the science of AI and AI for science

Many of these errors in misdiagnosing cause-effect relationships arise from a core assumption in many machine learning methods: that data follows an independent and identical distribution (IID). In practice, almost all data from real-world, or complex, systems will violate this assumption, given the interconnectedness of different variables. The task of causality in machine learning is to create models that can manage this violation, distinguishing between patterns in data that simply co-occur and patterns that are causal. The resulting AI systems would be able to solve a task in many different environments, based on an understanding of the fundamental causal mechanisms in a system.[66] They would be more robust in deployment, being less likely to make incorrect predictions as the environment in which they operate changes, and could be more efficient to train and deploy. They would also represent a step towards replicating human- or animal-like intelligence, being able to solve a task in many different environments.

In these regards, causal machine learning offers a route to balancing the widespread utility of statistical modelling with the strengths of physical models. Causality allows models to operate at a level of abstraction beyond strongly mechanistic approaches, such as those based on differential equations, moving along a continuum from mechanistic to data-driven modelling. They provide researchers with the ability to make accurate predictions under conditions of dataset shift (enable out of distribution generalisation); can provide insights into the physical processes that drive the behaviour of a system; unlock progress towards AI systems that 'think' in the sense of acting in an imagined space; while also leveraging insights that can be learned from data, but not otherwise detected.[67] They also offer opportunities to explore counterfactuals in complex systems, asking what the impact of different interventions could have been, opening a door to the development of simulation-based decision-making tools.[68]

Achieving this potential requires technical developments in a number of directions, but can also yield more effective AI systems. Such systems would:

- Be able to operate on out of distribution data, performing the task for which they are trained in environments with varying conditions.
- Be able to learn how to perform a task based on relatively few examples of that task in different conditions, or be able to rapidly adapt what they have learned for application in new environments through transfer, one-shot, or lifelong learning approaches.
- Support users to analyse the impact of different interventions on a system, providing explanations or ways of attributing credit to different actions.
- Respond to different ways of transmitting information between individuals and groups, enabling effective communication with their users or other forms of cultural learning.

65 Schölkopf, B. (2019) Causality for Machine Learning, arXiv:1911.10500 [cs.LG], https://doi.org/10.1145/3501714.3501755

66 Peters, J., Janzing, D. and Schölkopf, B. (2017) Elements of causal inference: foundations and learning algorithms, MIT Press, Cambridge, MA, ISBN 9780262037310.

67 For reference, see the table on page 11 of reference 69.

68 Such tools may have particular relevance in policy. For example: Mastakouri, A.A. and Schölkopf, B. (2020) Causal analysis of Covid-19 spread in Germany, arXiv:2007.11896 [stat.AP], https://doi.org/10.48550/arXiv.2007.11896.

From methods to application

Achieving the level of technical sophistication required for causal modelling requires careful model design, based on close collaboration between machine learning and domain scientist. The process of specifying what to represent in a causal machine learning system involves a series of 'micro-decisions' about how to construct the model, negotiated by integrating machine learning and domain expertise. In this regard, causal machine learning can be a positive catalyst for deeper interdisciplinary collaboration; model construction can be a convening point for sharing understandings between domains. However, the level of detail required can also be in tension with efforts to promote widespread adoption of AI methods across research. The availability of easy-to-use, off-the-shelf AI tools has been an enabler for adoption in many domains. The hand-crafted approach inherent to current causal methods renders them less accessible to non-expert users. Part of the challenge for the field is to make such methods more broadly accessible through open-source toolkits or effective software engineering practices.

This tension between specification and learning also highlights the importance of nurturing a diversity of methods across the spectrum from data-driven to mechanistic modelling. The domain (or, how much prior knowledge is available and what knowledge should be included), research question of interest, and other practical factors (including, for example, compute budget), will shape where along this spectrum researchers wish to target their modelling efforts.

While pursuing practical applications, advances in causal inference could help answer broader questions about the nature of intelligence and the role of causal representations in human understanding of how the worlds work. Much of human understanding of the world arises from observing cause and effect; seeing what reaction follows an intervention – that an object falls when dropped, for example – in a way that generalises across circumstances and does not require detailed understanding of mathematical or physical laws. Integrating this ability into machine learning would help create systems that could be deployed on a variety of tasks. The process of building causal machine learning forces researchers to interrogate the nature of causal representations – What are they? How are they constructed from the interaction between intelligent agents and the world? By what mechanism can such agents connect low-level observations to high-level causal variables? – which may in turn support wider advances in the science of AI.

Directions

Causality in machine learning is a long-standing and complex challenge. In the context of scientific discovery, learning strategy, model design, and encoding domain knowledge all play a role in helping identify cause-effect relationships.

Different learning strategies can improve the 'generalisability' of machine learning, increasing its performance on previously unseen tasks, based on learning underlying structure of a task or environment in ways that can contribute to broader understandings of causality. Such learning strategies include:

- Transfer learning, taking learning from one task or domain and applying it in another.
- Multi-task learning, enabling a system to solve multiple tasks in multiple environments.
- Adversarial learning, to reduce the vulnerability of models to performance degradation on out-of-distribution data.
- Causal representation learning, defining variables that are related by causal models.[69]

69 Schölkopf, B. (2019) Causality for Machine Learning, arXiv:1911.10500 [cs.LG], https://doi.org/10.1145/3501714.3501755

- Reinforcement learning strategies that reward agents for identifying policies based on invariances over different conditions.

Across these new learning approaches, attempts to establish causal mechanisms are also prompting progress in machine learning theory, through statistical formulations of core principles.[70]

Combining different methods can also enhance the functionality of an AI system. For example:

- Neural ODEs have been shown to identify causal structures in time series data.[71]
- Describing causal effects as objective functions in constrained optimisation problems can deliver a form of stochastic causal programming.[72]
- Technical interventions[73] can constrain or optimise a model towards causal outcomes. As with simulation design, diagnostic checks can also help identify cause-effect relationships by examining model outputs against 'reality criteria',[74] which compare outputs to real-world results.

There are also a variety of approaches to representing existing scientific knowledge in machine learning models, notably by specifying the assumptions made about the world through symmetries, invariances, and physical laws (see Figure 1).

70 Guo, S., Tóth, V., Schölkopf, B. and Huszár, F. (2022) Causal de Finetti: On the Identification of Invariant Causal Structure in Exchangeable Data, arXiv:2203.15756 [stat.ML], https://doi.org/10.48550/arXiv.2203.15756

71 Aliee, H., Theis, F. J. and Kilbertus, N. (2021) Beyond Predictions in Neural ODEs: Identification and Interventions, arXiv:2106.12430 [cs.LG], https://doi.org/10.48550/arXiv.2106.12430

72 Padh, K., Zeitler, J., Watson, D., Kusner, M., Silva, R., and Kilbertus, N. (2022) Stochastic Causal Programming for Bounding Treatment Effects, arXiv:2202.10806 [stat.ML], https://doi.org/10.48550/arXiv.2202.10806

73 Jakobsen, M. E., and Peters, J. (2020) Distributional robustness of K-class estimators and the PULSE, arXiv:2005.03353 [econ.EM], https://doi.org/10.48550/arXiv.2005.03353

74 Including syntactic, semantic, and pragmatic elements: Stadler, M. & Kruse, P. (1990) Über Wirklichkeitskrite – rien. In: Riegas, V. & Vetter, C. (eds.) Zur Biologie der Kognition. Frankfurt a. M.: Suhrkamp

Box 3: Talks given during this workshop session

Bernhard Schölkopf: Causality, causal digital twins, and their applications

1. Desiderata for causal machine learning: work with (and benefit from) non-IID data, multi-task/multi-environment, sample-efficient, OOD, generalisation from observation of marginals, interventional.
2. Modelling taxonomy: differential equations, causal models, statistical models.
3. How to get from one level to the next.
4. How to transfer between statistical models that share the same underlying causal model.
5. The assumption of independent causal mechanisms (ICM) (for example, invariance/autonomy) and sparse mechanism design.
6. How to derive the arrow of time from ICM and algorithmic information theory.
7. Statistical formulation of ICM: causal de Finetti.
8. Application to exoplanet discovery and Covid-19 vaccine scenarios.
9. Causal representations as (a) causal digital twins and (b) AI models.

Jonas Peters: Invariance: From Causality to Distribution Generalization

Assume that we observe data from a response Y and a set of covariates X under different experimental conditions (or environments). Rather than focusing on the model that is most predictive, it has been suggested to take into account the invariance of a model. This can help us to infer causal structure (Which covariates are causes of Y?) and find models that generalize better (How well does the model perform on an unseen environment?). We show a few applications of these general principles and discuss first steps towards understanding the corresponding theoretical guarantees and limits.

Niki Kilbertus: Can we discover dynamical laws from observation?

I will start with a brief introduction to identifiability of ODE systems from a unique continuous or discrete observed solution trajectory. Then, I will provide an overview of modern approaches to inferring dynamical laws (in the form of ODEs) from observational data with a particular focus on interpretability and symbolic methods. Finally, I will describe our recent attempts and results at inferring scalar ODEs in symbolic form from a single irregularly sampled, noisy solution trajectory.

Soledad Villar: Invariances and equivariances in machine learning

In this talk, we give an overview of the progress in the last few years by several research groups in designing machine learning methods that repeat physical laws. Some of these frameworks make use of irreducible representations, some make use of high-order tensor objects, and some apply symmetry enforcing constraints. Our work shows that it is simple to parameterise universally approximating functions that are equivariant under actions of the Euclidean, Lorentz, and Poincare group at any dimensionality. The key observation is that O(d)-equivariant (and related group-equivariant) functions can be universally expressed in terms of a lightweight collection of dimensionless scalars (scalar products and scalar contractions of the scalar, vector, and tensor inputs). We complement our theory with numerical examples that show that the scalar-based method

is simple and efficient, and mention ongoing work on cosmology simulations.

Bubacarr Bah: Divide-and-Conquer Equation Learning with R2 and Bayesian Model Evidence

Deep learning is a powerful method for tasks like predictions and classification, but lacks interpretability and analytic access. Instead of fitting up to millions of parameters, an intriguing alternative for a wide range of problems would be to learn the governing equations from data. Resulting models would be concise, parameters can be interpreted, the model can adjust to shifts in data, and analytic analysis allows for extra insights. Common challenges are model complexity identification, stable feature selection, expressivity, computational feasibility, and scarce data. In our work, the mentioned challenges are addressed by combining existing methods in a novel way. We choose multiple regression as a framework and argue how a surprisingly large space of model equations can be captured. For feature selection, we exploit the computationally cheap coefficient of determination (R^2) to loop through millions of models, and by using a divide-and-conquer strategy, we are able to rule out remaining models in the equation class. Final model selection is achieved by exact values of the Bayesian model evidence with empirical priors, which is known to identify suitable model complexity without relying on mass data. Random polynomials, and a couple of chaotic systems are used as examples.

Encoding domain knowledge

Where's my [science] jetpack?

Humans have a long history of imagining futures where human progress is accelerated by intelligent machines. Embedded in these visions for the future are aspirations that AI can be a faithful servant, easing daily activities or enhancing human activities.[75] As with many emerging technologies, the reality of AI today looks different to these Sci-Fi futures.[76] Practical experiences of deploying AI highlights a range of potential failure modes, often rooted in insufficient contextual awareness, misspecification of user needs, or misunderstanding of environmental dynamics.[77]

Today's science builds on thousands of years of attempts to understand the world, which can be leveraged to design AI that serves scientific goals. The result should be a collaborative endeavour between humans and machines. Researchers need the analytical power of AI to make sense of the world, while AI needs input from human understandings of the domain in which it is deployed to function effectively; both need well-designed human-machine interfaces to make this collaboration work. In this context, effective integration of domain knowledge into AI systems is vital, and three (broad) strategies have emerged to facilitate this encoding: algorithmic design; AI integration in the lab; and effective communication and collaboration.

Encoding domain knowledge through model design

Traditional modelling approaches make use of well-defined rules or equations that explain the dynamics of the system under study. The laws of physics, for example, describe how energy moves through a system, based on conservation principles. These laws are complemented by mathematical symmetries that arise from our abstract representations of physical objects and describe what features of an object remain consistent, despite changes or transformations in a system.[78] There may also be known invariances in a system: factors that do not change under any perturbations or that change in a defined way.[79] Building on this existing knowledge, and connecting to efforts to generate causal understandings of the world through machine learning, an area of growing interest has been the design of machine learning models that respect these rules or symmetries.The principle underpinning this design strategy is that it is possible to move across a continuum from statistical (data-driven) models to strongly mechanistic models, creating hybrid systems whose outputs should be constrained by what is physically feasible, while also leveraging insights from data (Figure 1).

75 The Royal Society (2018) AI narratives: portrayals and perceptions of artificial intelligence and why they matter, available at: https://royalsociety.org/topics-policy/projects/ai-narratives

76 The title of this section is inspired by: www.fantasticfiction.com/w/daniel-h-wilson/where-s-my-jetpack.htm

77 Paleyes, A., Urma, R.G. and Lawrence, N.D. (2022) Challenges in Deploying Machine Learning: A Survey of Case Studies, ACM Computing Surveys, https://doi.org/10.1145/3533378

78 Villar, S., Hogg, D.W., Storey-Fisher, K., Yao, W. and Blum-Smith, B. (2021) Scalars are universal: Equivariant machine learning, structured like classical physics, arXiv:2106.06610 [cs.LG], https://doi.org/10.48550/arXiv.2106.06610 and Villar, S., Yao, W., Hogg, D.W., Blum-Smith, B. and Dumitrascu, B. (2022) Dimensionless machine learning: Imposing exact units equivariance, arXiv:2204.00887 [stat.ML], https://doi.org/10.48550/arXiv.2204.00887

79 Ling, J., Jones, R. E., and Templeton, J.A. (2016) Machine learning strategies for systems with invariance properties. United States. https://doi.org/10.1016/j.jcp.2016.05.003

Figure 1: A spectrum of modelling approaches

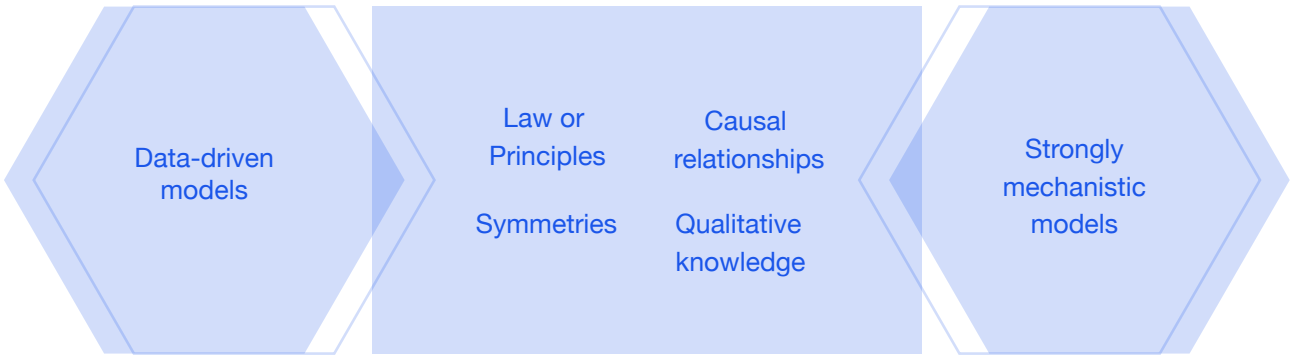


Figure 1: Models along a spectrum from classical i.i.d models to strongly mechanistic differential equation models introduce aspects of causality and symmetries to create a continuum between mechanistic and data-driven worlds. Statistical or data-driven models are weakly mechanistic (i.e. they include smoothness assumptions or similar).

At one end of that continuum, mechanistic models would obey known laws or principles in a strongly deterministic way; at the other, statistical models encode fewer assumptions and rely more on data. The addition of invariances and symmetries, alongside other forms of domain knowledge, allows bridging between these two model classes (Figure 2). Models that describe how much heat is absorbed by the oceans under conditions of climate change, for example, should obey the laws of thermodynamics and energy conservation. By encoding the domain knowledge that has yielded these fundamental laws, such as the conservation of momentum or energy, researchers can ensure the outputs of a machine learning model will have a physically allowable expression. This encoding can come from integrating equations, symmetries, or invariances into model design. These encodings constrain the operation of a machine learning system to align with the known dynamics of physical systems. The resulting models might be expected to produce more accurate results, with smaller generalisation errors, and with better out-of-distribution generalisation.

Figure 2: Approaches to integrating domain insights

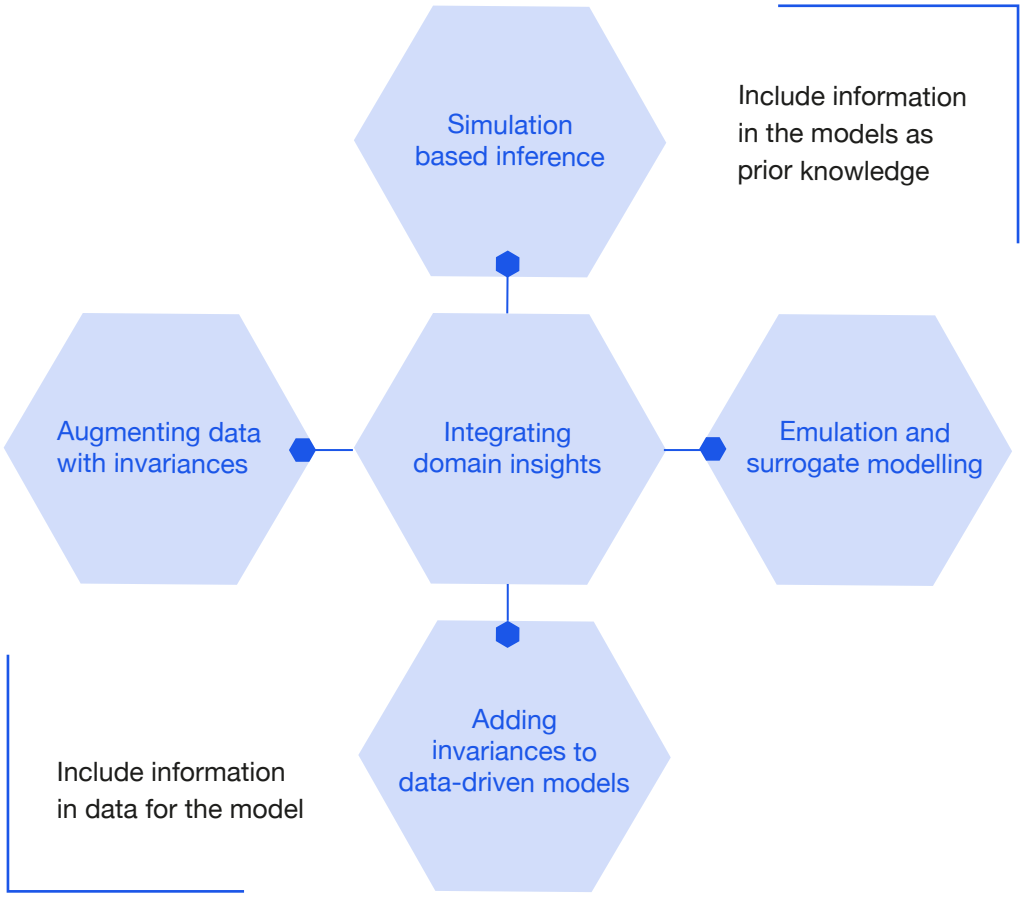


Figure 2: Strategies for integrating domain insights: including information in data and including information as prior knowledge.

Scientific centaurs

Complementing modelling strategies to encode scientific knowledge are deployment strategies to use AI in the lab. The lab has long provided a physical hub for collaboration and knowledge-generation, its function and form having remained broadly consistent across centuries of scientific progress. Today, the digitisation of experimental equipment and laboratory processes offers opportunities to integrate AI in experimental design and create new virtual labs.

By combining data from measurement devices, simulations of laboratory processes, and computational models of research or user objectives, these virtual labs provide a digital sibling of in-person research activities that can be used to optimise such activities. In drug discovery, for example, virtual labs could accelerate the testing and analysis processes that identify candidate drugs from potential drug targets. Instead of relying on physical testing of such starting molecules, multiple rounds of virtual testing can rapidly simulate the processes of drug design, manufacture, testing, and analysis to assess which starting molecules are more (or less) likely to be viable candidate drugs.[80] As a result, AI can help accelerate the research process.

Advances in machine learning methods to enable effective simulations, causal modelling,

80 Klami, A., Damoulas, T., Engkvist, O., Rinke, P., Kaski, S. (2022): Virtual Laboratories: Transforming research with AI. TechRxiv. Preprint. https://doi.org/10.36227/techrxiv.20412540.v1

and encoding pre-existing domain insights – while packaging such methods into usable toolkits – are all necessary foundations for such digital siblings. Moving from virtual laboratory to 'AI assistants' requires further advances in AI system design to create AI agents that can elicit guidance or input from their domain experts. Such agents would not only provide useful intuitions for scientific modelling, but would serve as 'scientific sidekicks', actively helping researchers to drive their research. This new type of AI assistant would combine the ability to model the research problem of interest with the ability to model the goals and preferences of their expert users, even when the user themselves might not be able to clearly articulate those goals. As a starting point, these systems would need to support forms of user interaction that can extract user knowledge, leveraging this to identify appropriate courses of action. To operate in contexts where user goals might be uncertain and user behaviour might change in response to the outputs of the AI system, these AI sidekicks will need insights from cognitive science, studies of team decision-making, and new learning strategies based on limited examples. The sophisticated user modelling so-created would unlock new forms of human-AI collaboration; scientific centaurs that combine both human and machine intelligence.[81]

Enabling communication across domains

Underpinning these efforts to integrate pre-existing knowledge into the design and deployment of AI systems is a feedback loop between domain and machine learning research, in which each elicits from and feeds into the other. This loop requires the ability to exchange knowledge and insights across disciplines through interdisciplinary collaboration and communication.

Matching model to user need requires shared understandings of the research question at hand, the constraints – whether from data, compute, funding, or time and energy available – that affect different collaborators, and the user needs of the domain environment. While AI researchers might be tempted to develop complex models, showcasing assorted theoretical and methodological advances in the field, from a domain perspective, a relatively 'simple' model may seem preferable. Collaborators need to be able to mutually explore what is possible, while also considering what is useful.

To complete the loop, outputs from machine learning models need to feed back into the application domain: insights from AI need to be accessible in ways that allow the transfer of learning from model to user. This implies some level of explainability. It is not sufficient for an AI system to produce highly accurate results; those results must also be interpretable by a domain researcher. As the complexity of AI systems increases, however, understanding why these systems have produced a particular result becomes increasingly challenging. While not an issue for all machine learning methods, this complexity often results in difficulties explaining the functioning of AI systems.

In response, AI researchers have developed a variety of different methods to interrogate how AI systems work, or why a particular output has been produced. Again, to understand which of these methods is desirable in the context of a scientific application, researchers must collaborate closely with domain experts. In the context of pharmaceutical experiments where the aim is to measure how many target cells are killed off at different dosages of a drug (or drug combination), for example, researchers might be seeking to 'sense-check' how different drug dosages affect the model, before investigating specific drugs more rigorously. In astronomical studies, researchers are often working with high-dimensional datasets with many confounding correlations. For example, gravitational waves are ripples in space-time catalysed by the movement of massive bodies in space, such as planets or stars.[82] These invisible phenomena are studied at observatories across the world,[83] based on models to describe

81 Celikok, M.M., Oliehoek, F.A., Kaski, S. (2022) Best-Response Bayesian Reinforcement Learning with Bayes-Adaptive POMDPs for Centaurs, arXiv:2204.01160 [cs.AI], https://doi.org/10.48550/arXiv.2204.01160

82 NASA, What is a gravitational wave? Available at: https://spaceplace.nasa.gov/gravitational-waves/en

83 See, for example, the LIGO project. Information available at: www.ligo.caltech.edu

wave signals and the 'noise' generated by instruments that measure them.[84] Measurements of gravitational waves can be used to infer the properties of black holes that create them, such as their location, mass, and spin, using simulation-based inference to characterise the source of a wave, given the data that detects it. To make such methods more efficient than existing analytical tools, researchers need to take into account the structure that sits underneath it: for example, gravitational wave detectors are located across the globe, and their location affects the angle at which they detect waves hitting the Earth. This structure can be exploited through data sampling strategies to help make machine learning more efficient.[85] An alternative, however, is to use deterministic models that already reflect relevant physical laws.[86] Across these approaches, software packages play an important role in enabling communication and dissemination of methods for wider use.[87]

84 Dax, M., Green, S.R., Gair, J., Macke, J.H., Buonanno, A. and Schölkopf, B. (2021) Phys. Rev. Lett. 127, 241103, Real-Time Gravitational Wave Science with Neural Posterior Estimation, https://link.aps.org/doi/10.1103/PhysRevLett.127.241103

85 Ibid.

86 Bodin, E., Dai, Z., Campbell, N.D.F. and Ek, C.H. (2020), Black-box density function estimation using recursive partitioning, arXiv:2010.13632 [stat.ML], https://doi.org/10.48550/arXiv.2010.13632

87 See, for example: https://lscsoft.docs.ligo.org/bilby

Directions

New modelling approaches and mathematical innovations offer exciting opportunities to integrate domain knowledge, symmetries and invariances into AI systems.[88] Integration can be achieved in different ways:

- Data augmentation can help exploit invariances and symmetries, resulting in improved model performance, by including in the data domain knowledge for a model to ingest.
- Symmetries can be embedded in the design of deep learning systems, for example by using the same convolutional filters in different locations of an image, CNNs can leverage translation and rotation symmetries.
- Latent force models allow representations of known symmetries alongside probabilistic factors, enabling integration of mechanistic models with unknown forces.[89]
- Architectural features can restrict model focus to outputs that satisfy symmetries, for example using weight sharing, irreducible representations, or invoking symmetries as constraints.[90]
- Loss functions can be deployed to penalise predictions that fail to satisfy physical constraints or symmetries.

In the process, emerging mathematical questions include: how can AI learn invariances from data? And is it possible to quantify the performance gain achieved through this?

Research to develop AI assistants in the lab raises interesting questions about learning strategies and human-machine collaboration. These AI agents would need to be able to learn how to assist another agent, in a multi-agent decision-making scenario, where goals might be unclear, uncertain, or changeable. To tackle this challenge:

- Decision-making with delayed reward or zero-shot learning can help agents solve tasks when there is little or nothing known about the reward function, and no previous behaviour to learn from.
- Interactive knowledge elicitation,[91] combining prior knowledge from cognitive science with learning from data,[92] and generative user models[93] can support more effective interactions between user and machine.

88 Villar, S., Yao, W., Hogg, D.W., Blum-Smith, B. and Dumitrascu, B. (2022) Dimensionless machine learning: Imposing exact units equivariance, arXiv:2204.00887 [stat.ML], https://doi.org/10.48550/arXiv.2204.00887

89 Ward, W.O.C., Ryder, T., Prangle, D. and Álvarez, M.A. (2019) Black-Box Inference for Non-Linear Latent Force Models, arXiv:1906.09199 [stat.ML], https://doi.org/10.48550/arXiv.1906.09199

90 See, for example: Kondor, R. and Trivedi, S. (2018), On the Generalization of Equivariance and Convolution in Neural Networks to the Action of Compact Groups, arXiv:1802.03690 [stat.ML], https://doi.org/10.48550/arXiv.1802.03690; Maron, H., Ben-Hamu, H., and Shamir, N. and Lipman, Y. (2019) Invariant and Equivariant Graph Networks, arXiv:1812.09902 [cs.LG], https://doi.org/10.48550/arXiv.1812.09902; Dym, N. and Maron, H. (2020) On the Universality of Rotation Equivariant Point Cloud Networks, arXiv:2010.02449 [cs.LG], https://doi.org/10.48550/arXiv.2010.02449

91 Sundin, I., Peltola, T., Micallef, L., Afrabandpey, H., Soare, M., Majumder, M.M., Daee, P., He, C., Serim, B., Havulinna, A., Heckman, C., Jacucci, G., Marttinen, P., Kaski, S. (2018) Improving genomics-based predictions for precision medicine through active elicitation of expert knowledge, Bioinformatics, Volume 34, Issue 13, 1 July 2018, Pages i395–i403, https://doi.org/10.1093/bioinformatics/bty257

92 Kangasrääsiö, A., Jokinen, J.P.P., Oulasvirta, A., Howes, A. and Kaski, S. (2019), Parameter Inference for Computational Cognitive Models with Approximate Bayesian Computation. Cogn Sci, 43: e12738. https://doi.org/10.1111/cogs.12738

93 De Peuter, S., Oulasvirta, A. and Kaski, S. (2021) Toward AI Assistants That Let Designers Design, arXiv:2107.13074 [cs.HC], https://doi.org/10.48550/arXiv.2107.13074

Across these areas, care is needed in the design of the points of interaction between human and AI system. A core question here is: how can AI researchers extract domain knowledge from relevant experts and integrate it into a machine learning model? Insights from human-machine interaction studies and collaborative decision-making systems are necessary to create effective interfaces between human and machine, based on factors such as:

- What forms of visualisation are helpful for human users?
- What types of interpretability or explainability are needed for a user to achieve their desired interactions?
- What might be the unintended consequences of human-machine interaction, such as over-confidence in results or over-reliance on the AI system?
- What 'theory of mind' is needed to anticipate how human users might be likely to respond to an AI system? A challenge in these interactions is that much of the relevant knowledge held by the domain expert might be qualitative: an intuition of how a system works, developed over a long period of study, rather than quantifiable insights.

Box 4: Talks given during this workshop session

Sami Kaski: Virtual laboratories for science, assisted by collaborative AI

I introduced two ideas: virtual laboratories for science, aiming to introduce an interface between algorithms and domain science that enables AI-driven scale advantages, and AI-based 'sidekick' assistants, able to help other agents research their goals, even when they are not able to yet specify the goal explicitly, or it is evolving. Such assistants would ultimately be able to help human domain experts run experiments in the virtual laboratories. I invited researchers to join the virtual laboratory movement, both domain scientists in hosting a virtual laboratory in their field and methods researchers in contributing new methods to virtual laboratories, simply by providing compatible interfaces in their code. For developing the assistants, I introduced the basic problem of agents that are able to help other agents reach their goals, also in zero-short settings, formulated the problem, and introduced solutions in the simplified setting of prior knowledge elicitation, and in AI-assisted decision and design tasks.

David Hogg: Making data analysis more like classical physics

The laws of physics are very structured: They involve coordinate-free forms, they are equivariant to a panoply of group actions, and they can be written entirely in terms of dimensionless, invariant quantities. We find that many existing machine-learning methods can be very straightforwardly modified to obey the rules that physical law must obey; physics structure can be implemented without big engineering efforts. We also find that these modifications often lead to improvements in generalization, including out-of-sample generalization, in natural–science contexts. We have some intuitions about why.

The second example is work by Dan Sheldon on analysis of doppler radar to extract

bird biomass and motion. The radar measures the radial velocity modulo a constant (i.e., the velocity wraps around to zero). Previous work had attempted to "unwrap" the data using heuristics. Dan instead incorporated the modulus operation into the likelihood function and then developing an algorithm for maximizing this somewhat nasty likelihood. The result has revolutionized radar analysis and has been deployed in the BirdCast product from the Cornell Lab of Ornithology.

The third example is the species occupancy model introduced by MacKenzie et al. (2002). When human observers conduct wildlife surveys, they may fail to detect a species even though the species is present. The occupancy model combines this detection probability with a habitat model. However, the expressiveness of the two models (detection and habitat) must be carefully controlled. Rebecca Hutchinson and I learned this when we tried to replace the linear logistic regression models with boosted trees.

In all cases, downstream use of the estimates that come from such data collection models mustbe aware of the measurement uncertainties. How can we correctly quantify those uncertainties and incorporate them in the downstream analysis? Maybe there are lessons ecologists can learn from physicists?

Mauricio Alvarez: Latent force models

A latent force model is a Gaussian process with a covariance function inspired by a differential operator. Such a covariance function is obtained by performing convolution integrals between Green's functions associated with the differential operators, and covariance functions associated with latent functions. Latent force models have been used in several different fields for grey box modelling and Bayesian inversion. In this talk, I will introduce latent force models and several recent works in my group where we have extended this framework to non-linear problems.

Carl Henrik Ek: Translating mechanistic understandings to stochastic models

Statistical learning holds the promise of being the glue that allows us to improve knowledge parametrised explicitly by a mechanistic model with implicit knowledge through empirical evidence. Statistical inference provides a narrative of how to integrate these two sources of information leading to an explanation of the empirical evidence in "light" of the explicit knowledge. While the two sources of knowledge are exchangeable in terms of predictive performance they are not if our focus is that of statistical learning as a tool for science where we want to derive new knowledge.

In this talk we will focus on challenges associated with translating our mechanistic understanding into stochastic models such that they can be integrated with data. In particular, we will focus on the challenges of translating composite knowledge. We will show how these structures and the computational intractabilities they lead to make knowledge discovery challenging.

The perceived "success" of machine learning comes from application where we have large volumes of data such that only simple and generic models are needed in order to regularise the problem. This means that much of the progress that have been made with predictive models are challenging to translate into useful mechanisms for scientific applications. In this talk we will focus on challenges associated with translating our mechanistic understanding into stochastic models such that they can be integrated with data. In specific we will focus on the challenges of translating composite knowledge. We will show how these structures and the computational intractabilities they lead to makes knowledge discovery challenging. We will discuss properties that we desire from such structures and highlight the large gap that exists with current inference mechanism.

A research agenda in AI for science

'AI for science' sits at a nexus of disciplines, methods, and communities. Both AI and 'science' (broadly defined) share a core interest in learning from data. From this interest emerge different research directions: for AI, questions about the nature of intelligence and how to understand the learning process in humans and machines; for science, the outputs of this learning process are the focus, with the aim of adding new knowledge about natural, physical, and social systems. A distinctive feature of the emerging 'AI for science' agenda is the ability to move between these worlds, using AI to drive progress in science and taking inspiration from science to inspire progress in AI. The result is a continuum of modelling approaches along a spectrum from strongly mechanistic to statistical models, which allow researchers to introduce or operate at different levels of abstraction.

The AI for science community therefore combines the ambitions of AI research with domain-specific goals to advance the frontiers of research and goals in an individual discipline, with an engineering focus on designing systems that work in deployment. From these interfaces emerges a research agenda that – if successful – promises to accelerate progress across disciplines. Inspired by discussions at the Dagstuhl workshop, a list of research questions arising from this agenda is given in Annex 2. These span three themes:

Building AI systems for science: Attempts to deploy AI in the context of scientific discovery have exposed a collection of gaps in current machine learning and AI capabilities. Further work is needed to develop the technical capabilities that will allow AI tobe used more effectively in research and innovation; developing those capabilities also offers opportunities to contribute to wider attempts to deliver sophisticated AI systems. Areas for progress include:

- Advancing methods, software and toolkits for high-quality simulation and emulation, which integrate effective uncertainty quantification and leverage advances in machine learning robustness to ensure the operate safely and effectively.
- Detecting scientifically meaningful structure in data, through advances in causal machine learning.
- Encoding domain knowledge in AI systems through integration of scientific laws, principles, symmetries, or invariances in machine learning models, and through virtual, autonomous systems to make research more effective.

Combining human and machine intelligence: Successful deployment of AI in science requires effective interactions between human, domain and machine intelligence across all stages of the deployment pathway. AI systems can be made more effective by integrating pre-existing knowledge about the system of study, but mechanisms are needed to extract and encode that knowledge. Interfaces are also required in the reverse direction. Translating the outputs of AI analysis to increased human capability requires an understanding of what insights are relevant, how they are best communicated, and the cultural environment that shapes the conduct of science. Areas for progress include:

- Designing interfaces between humans and machines or AI agents that can extract, formalise, and assimilate knowledge that domain researchers have acquired, including tacit knowledge, and that communicate new knowledge back to the user as actionable insights.
- Building mechanisms for explainability that allow researchers to interrogate why and how an AI system delivered a particular result, with the explanations provided being tailored to user need.
- Accelerating the pace of knowledge creation and use, through systems that mine the existing research knowledge base or that automate repetitive or time-consuming elements of the research process.

Influencing practice and adoption: By learning from recent experiences of deploying AI for science, the field has an opportunity to promote wider uptake and progress in both scientific domains and in AI research. This requires capturing both the knowledge that the community has already generated, about how to design AI systems, and the know-how about how to overcome practical challenges that accompanies it, while taking action to grow the community of researchers excited about the potential of AI in science. Areas for progress include:

- Supporting new applications, through challenge-led research programmes that promote interdisciplinary collaborations and support co-design of AI systems to help tackle scientific challenges.
- Developing toolkits and user guides that allow researchers to understand which AI tools are suitable for which purposes, and how to deploy those tools in practice.
- Sharing skills and know-how, through community outreach that disseminates knowledge and know-how in how to use AI.

Together, these areas for action highlight the importance of interfaces – between researchers and between modelling approaches – in shaping the development of AI for science (Figure 3).

Figure 3: Interfaces between different modelling communities

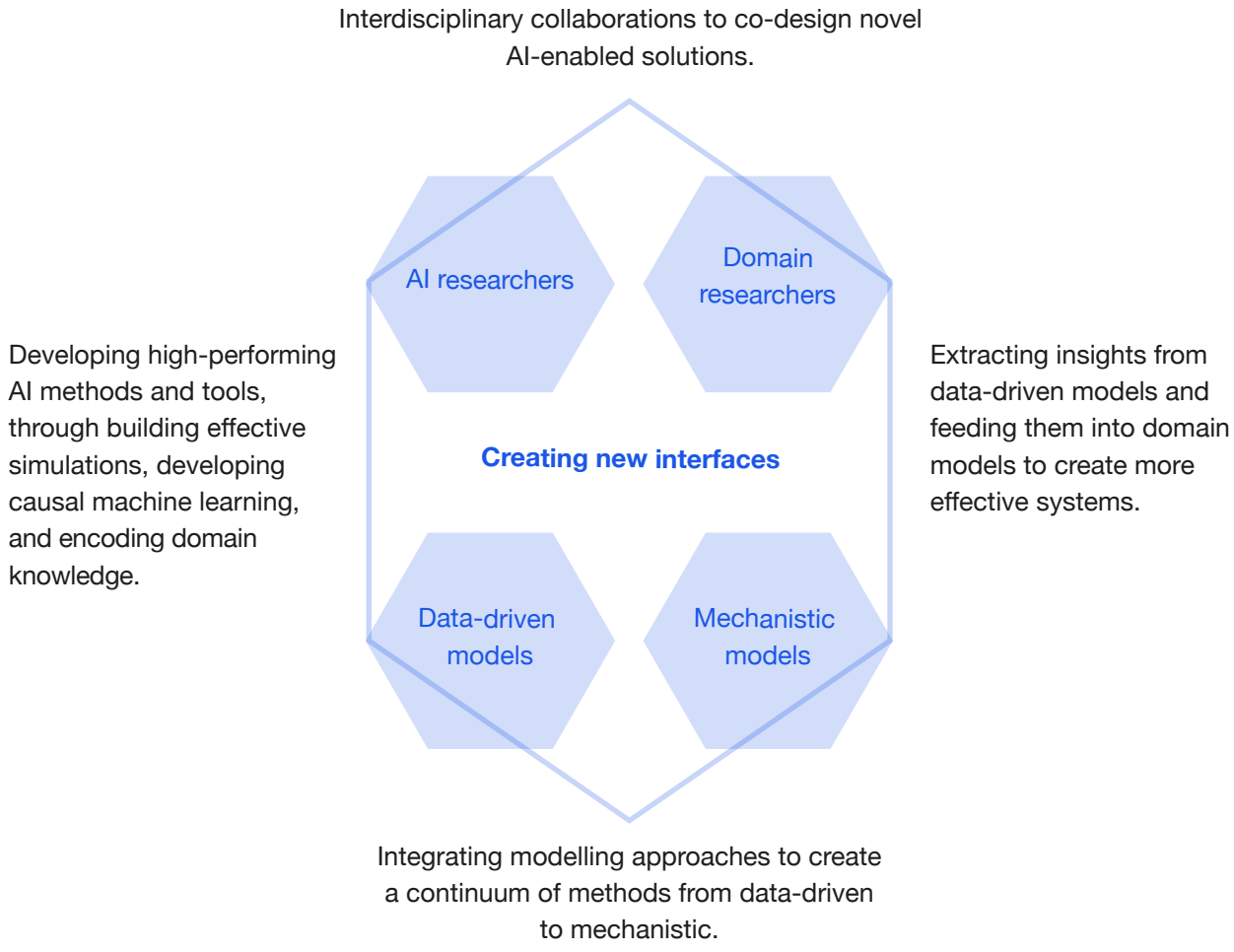


Figure 3: Interfaces between machine learning and domain researchers, and between data-driven and mechanistic models.

Accelerating progress in AI for science

Building on the impressive advances that machine learning has already supported in many domains, widespread adoption of AI for research has the potential to catalyse a new wave of innovations that in turn could drive greater health, wealth, and wellbeing. The question facing researchers, funders, and policymakers today is how to harness that potential. The challenge is to build capability across the research landscape, connect areas of expertise to areas of need, and to accelerate the transfer of successful ideas between domains.

The experiences of deploying AI for science described in this document, and the research agenda that results from these experiences, suggest a roadmap for action. That roadmap charts a pathway to create an enabling environment for AI in science, by advancing research that delivers AI methods to support scientific discovery, building tools and resources to make AI accessible, championing interdisciplinary research and the people pursuing it, and nurturing a community at the interface of these different domains. Progress across these areas can unlock scientific and methodological advances in AI for science, while also helping answer an emerging question about whether there exists a core discipline of 'AI for science'. The shared themes and interests that emerge from research projects at the interface of AI and scientific domains suggest that there is potential or 'AI for science' to surface as a distinct speciality in computer science. In parallel, domain specific efforts to drive the adoption of AI as an enabler of innovation are also needed to deliver the benefits of AI for scientific discovery.

Advance new methods and applications

Efforts to deploy AI in the context of research have highlighted cross-cutting challenges where further progress in AI methods and theory is needed to create tools that can be used more reliably and effectively in the scientific context. Effective simulations are needed to study the dynamics of complex systems; causal methods to understand why those dynamics emerge; and integration of domain knowledge to relate those understandings to the wider world. While elements of these research challenges are shared with other fields – topics such as robustness, explainability, and human-machine interaction also come to the fore in fields such as AI ethics, for example – they share an intersection in the use of AI for science, in the context of efforts to bridge mechanistic and data-driven modelling.

Alongside these 'AI' challenges are a collection of 'science' challenges, where researchers, policymakers and publics have aspirations for AI to deliver real-world benefits.[94] Such challenges offer the opportunity to accelerate progress in AI, while facilitating interdisciplinary exchanges, and opening the field to input from citizen science or other public engagement initiatives. In developing these research missions, care is needed to define cross-cutting questions or challenges that broaden scientific imaginations, rather than restricting them. The process of converting a complicated scientific problem into something tractable with AI necessarily involves some narrowing of focus; to be successful, mission-led innovation efforts must achieve this focus without losing meaning, or creating benchmarks that misrepresent the complexity of the real-world challenge.

Defining shared challenges could help rally the AI for science community and drive progress in both methods and applications of AI in science. There are already examples of how such challenges can build coalitions of researchers across domains from which the field can draw inspiration. These include the

94 See, for example: the EU's Innovation Missions https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/eu-missions-horizon-europe_en and UN SDG's https://sdgs.un.org/goals

GREAT08 project, which developed image analysis techniques to study gravitational lensing;[95] the Open Problems in Single Cell Biology challenge, which convened the machine learning community to make progress in Multimodal Single-Cell Data Integration;[96] and the SENSORIUM challenge, focused on advancing understandings of how the brain processes visual inputs.[97] In pursuing this agenda, researchers can leverage well-established protocols in open-sourcing materials and sharing documentation to help ensure research advances are rapidly and effectively disseminated across disciplines. The result should be more effective methods, and an agile research environment where researchers can flex methods across disciplines.

Invest in tools and toolkits

Complementing these efforts to build and share knowledge, well-designed software tools can help make accessible the craft skills (or know-how) that make AI for science projects successful. Modelling is a core component of all AI for science projects. In some aspects, the task for the field can be thought of as charting a path between the statistician, whose effectiveness comes from proximity to the domain but whose methods struggle to scale, and the mathematician, whose tools are adopted across domains but with some loss of meaning as the distance between method-generator and adopter increases.

The energy already invested in building effective machine learning models can be leveraged for wider progress across domains through investment in toolkits that support the generalisation of effective approaches. Wide-spectrum modelling tools could offer 'off the shelf' solutions to common AI for science research questions. The challenge for such toolkits is to create an effective interface between tool and user. Connecting with the field of human-computer interaction could generate design insights or protocols to help create more effective human-AI interfaces.

Best practices in software engineering can help, through documentation that supports users to successfully deploy modelling tools. User guides – or taxonomies of which models are best suited for which purposes and under what circumstances – can also help make accessible to non-expect users the accumulated know-how that machine learning researchers have gained through years of model development and deployment.

A related engineering challenge is that of data management and pipeline-building. To interrogate how a model works, why a result was achieved, or whether an AI system is working effectively, researchers often benefit from being able to track which data contributed to which output. The data management best practices that allow such tracking need to be embedded across AI for science projects. Data management frameworks – such as the FAIR data principles – have already been developed with the intention of making data more available, and useful, for research. Further investment is now needed in efforts to implement those principles in practice.

Investment in these foundational tools and resources can help build understanding of which AI methods can be used and for what purposes, lowering the barriers to adopting AI methods across disciplines.

95 Bridle, S., Balan, S.T., Bethge, M., Gentile, M., Harmeling, S., Heymans, C., Hirsch, M., Hosseini, R., Jarvis, M., Kirk, D., Kitching, T., Kuijken, K., Lewis, A., Paulin-Henriksson, S., Schölkopf, B., Velander, M., Voigt, L., Witherick, D., Amara, A., Bernstein, G., Courbin, F., Gill, M., Heavens, A., Mandelbaum, R., Massey, R., Moghaddam, B., Rassat, A., Réfrégier, A., Rhodes, J., Schrabback, T., Shawe-Taylor, J., Shmakova, M., van Waerbeke, L., Wittman, D. (2010) Results of the GREAT08 Challenge: an image analysis competition for cosmological lensing, Monthly Notices of the Royal Astronomical Society, Volume 405, Issue 3, July 2010, Pages 2044–2061, https://doi.org/10.1111/j.1365-2966.2010.16598.x

96 For further information, see: https://openproblems.bio/neurips_2021

97 For further information, see: https://sensorium2022.net/home

Build capability across disciplines

Central to progress in both research and toolkit engineering is the availability of talented researchers with a passion for advancing science through AI. People matter at all stages of the AI development and deployment pipeline. Successful projects rely on researchers who are motivated to work at the interface of different domains; collaborators who can explain and communicate core concepts in their work across disciplinary boundaries; engineers who can translate the needs of different users into AI toolkits; and convenors that can inspire wider engagement with the AI for science agenda.

Building these capabilities requires multiple points of engagement. Domain researchers need access to learning and development activities that allow them to understand and use foundational methods in machine learning, whether as formal training or through the availability of tutorials or user guides. AI researchers need access to the scientific knowledge that should shape the methods they develop, the skills to translate their advanced knowledge to materials that can be shared for wider use, and the capacity to dedicate time and resource to learning about domain needs.[98] Both need skills in communication, organisation, and convening to operate across disciplines. Without such capability-building, disciplines risk remaining siloed; domains developing unrealistic expectations about what AI can deliver in practice, and AI losing touch with the scientific questions that are most meaningful to domains.

Institutional incentives shape how individuals engage (or not) with such interdisciplinary exchanges. Interdisciplinary research often takes longer and lacks the outlets for recognition available to those working in single domains, affecting both the motivation of and opportunities for career progression that are open to those working at the interface of different disciplines. Much of the engineering work required to make data and AI accessible beyond a specific project and useful to a wider community is also traditionally unrecognised by academic incentive structures. Aligning individual and institutional incentives in support of interdisciplinarity is a long-standing challenge in research, and one that becomes more critical to address in the context of developments in AI. In this context, there may be new opportunities to recognise and reward successes in AI for science, whether through new fellowships, prizes, or ways of promoting the work done by those at this interface.

Grow communities of research and practice

The areas for action described above feed into and from each other. Progress in research and application can be leveraged to inspire a generation of researchers to pursue interdisciplinary projects; effective toolkits can make such progress more likely; skills-building initiatives can prime researchers to be able to use these toolkits; and so on, to create an environment where researchers and research advances transition smoothly across disciplines, leading to a rising AI tide that lifts all disciplines. Communities of research and practice are the backdrop for creating such positive feedback loops.

A collection of AI for science initiatives are already building links across the research landscape. The Machine Learning for Science Cluster of Excellence at the University of Tübingen is leveraging the strength of its local ecosystem in AI to drive wider progress in research and innovation;[99] the Accelerate Programme for Scientific Discovery at the University of Cambridge is building bridges across disciplines, building a community passionate about opportunities in AI for science;[100] the University of Copenhagen's SCIENCE AI Centre provides a focal point for AI research and education in its Faculty for

98 A comparison here can be drawn with the development of statistics as an enabling discipline for many domains: statisticians have devoted time to understanding domain practices and integrating their work within those practices, often dedicating significant resource to understand the nature of the datasets with which they are working, before introducing modelling ideas.

99 Programme website available at: https://uni-tuebingen.de/en/research/core-research/cluster-of-excellence-machine-learning/home

100 Programme website available at: https://acceleratescience.github.io

Science;[101] New York University's Center for Data Science hosts interdisciplinary faculty pursuing innovative research and education;[102] the University of Wisconsin-Madison's American Family Insurance Data Science Institute is developing strategic partnerships to accelerate the use of data science in research;[103] new investments by Schmidt Futures across a network of research institutions are supporting new postdoctoral fellowships at the interface of AI and sciences.[104] Together, these initiatives demonstrate the appetite for progress in AI for science.

There is an opportunity today to leverage these emerging interests into a wider movement. Existing initiatives can drive capability-building, by making training and user guides open, reaching out to engage domain researchers in skills-building activities, and fostering best practice in software and data engineering across disciplines. The links they establish across research domains can form the basis of new communication channels, whether through discussion forums, research symposia, or newsletters to share developments at the interface of AI and science. These communications can be deployed to raise the profile of people and projects at this interface, celebrating successes, sharing lessons, and demonstrating the value of interdisciplinary work. Together, they can help develop an infrastructure for AI in science.

That infrastructure may also benefit from new institutional interventions to address long-standing challenges in interdisciplinary AI. New journals could provide an outlet to publish and recognise high-quality AI for science research, bringing in contributions from multiple disciplines and helping translate lessons across areas of work. Membership organisations could help foster a sense of belonging and community for researchers working at the interface of AI, science, and engineering, developing career pathways and incentives. Efforts to convene across disciplines can also catalyse new connections and collaborations.

Emerging from these efforts is a paradigm shift in how to drive progress in science. Historically, a small number of foundational texts have been the catalyst that changed how researchers studied the world; Newton's Principia; Darwin's Origin of Species; and so on. For much of its modern history, scientific knowledge has been transmitted through textbooks; canonical descriptions of the current state of knowledge. Today, the transformative potential of AI is driven by its pervasiveness; its impact in science will be achieved through integration across disciplines. This integration requires widespread mobilisation, convening machine learning researchers, domain experts, citizen scientists, and affected communities to shape how AI technologies are developed and create an amenable environment for their deployment. It takes a community.

AI and science: building the interface

Advances in AI have disrupted traditional ways of thinking about modelling in science. Where researchers might previously have conceptualised models as mechanistic – reflecting known forces in the world – or data-driven, the 'AI for science' methods that are emerging today reject this separation. They are both, combining insights from mechanistic and data-driven methods, integrating methods to create something new. What follows from these developments is a spectrum of modelling approaches, which researchers can deploy flexibly in response to the research question of interest.

Today, the field of AI for science is characterised by intersections. Between AI and scientific domains; between science and engineering; between knowledge and know-how; between human and machine. It operates across disciplinary boundaries, across scales from the atomic to the universal, and across both the mission to understand intelligence and the quest to deploy human intelligence to understand the world. Emerging from these missions is a continuum of models and methods that allow researchers to work across domains, extracting the knowledge that humans have acquired, and levels of inquiry,

101 Programme website available at: https://ai.ku.dk

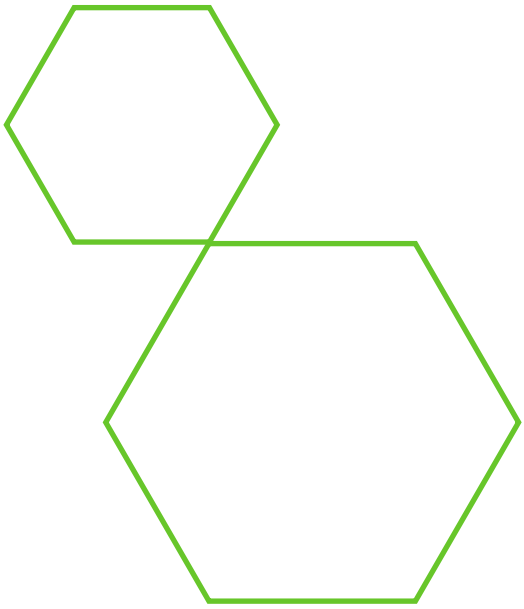
102 Programme website available at: https://cds.nyu.edu

103 Programme website available at: https://datascience.wisc.edu/institute

104 Schmidt Futures (2022) Schmidt Futures Launches $148M Global Initiative to Accelerate AI Use in Postdoctoral Research, available at: https://www.schmidtfutures.com/schmidt-futures-launches-148m-global-initiative-to-accelerate-ai-use-in-postdoctoral-research

enhancing that knowledge and returning it in actional form.

As both a domain itself and an enabler of other disciplines, the power of AI in science lies in its ability to convene diverse perspectives in ways that accelerates progress across research areas. AI for science is a rendezvous point. Its next wave of development will come from taking strength from its diversity, and bringing more people into its community.



Annex 1: Participants at Machine Learning for Science: Bridging Data-driven and Mechanistic Modelling (Dagstuhl Seminar 22382, 18–23 September 2022)

Organisers: Philipp Berens, Kyle Cranmer, Neil Lawrence, Jessica Montgomery, Ulrike von Luxburg.

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Annex 2: Research questions arising from the ‘AI for science research agenda’ discussion during the Dagstuhl workshop

Building AI systems for science

- How can AI systems accurately generalise from finite observations? How can they detect causality or structure from finite observations?
- What is the computational cost of complexity, and what methods can help manage this?
- What forms of system calibration and uncertainty quantification are useful in the context of scientific discovery? Are theoretical guarantees necessary?
- What new forms of explainability or interpretability could facilitate the deployment of AI in science?
- How could AI support generalisation from a small number of observations? What methods could enable few – or one-shot learning?
- How can AI researchers build meaningful models from data to accurately represent causal mechanisms in the system of study? How can researchers identify the most effective model for their system of study?
- What does it mean to understand a model? How can researchers combine explainability with complexity?
- How can AI methods be made robust and easy to use in deployment by domain scientists?
- How can advances in simulation methods be applied in domains where the system at hand is less easily described by equations?
- What advances are needed to expand the use of simulations in science? How can AI help simulate laboratory experiments or environments, helping make more efficient different elements of the scientific process? How might this be expanding in the long-term, for example to planning experimental design or helping identify where data is missing?
- How can ‘digital siblings’ be used to explore the impact of different interventions on complex systems?

Combining human and machine intelligence

- How can AI researchers best extract, formalise and assimilate the knowledge that domain researchers have acquired? What forms of knowledge representation can formalise scientific understandings of the world, translating these to objective functions for AI systems? What forms of human-AI engagement can make use of the ‘qualitative’ knowledge – or intuitions about a system – that domain researchers have accumulated?
- How can AI capture the qualitative understanding that researchers have of their domain to more accurately or effectively characterise a system?
- How can AI be effectively deployed to mine the existing research knowledge base – for example, papers, databases, and so on – to extract new insights?
- Where can automation support research progress? Which elements of the scientific process could be automated, and where is human input vital?
- What forms of collaboration are needed to effectively specify helpful outputs from an AI system?

- How can insights from AI analysis be returned to researchers in an actionable way? What mix of AI design, engineering, social interaction, and education can make effective interfaces between domain researchers and AI systems?
- How can the outputs of AI systems be made interpretable for scientific users?
- How can AI researchers better understand and design for the forms of interpretability that resonate with domain researchers?
- What processes of collaboration or co-design can help describe what scientists 'need to know from an AI system?
- What best practices or methods can be deployed to effectively communicate uncertainty from AI systems to human users?

Influencing practice and adoption

- What are the craft skills in AI for science? What 'know how' is necessary to make AI work effectively in practice?
- What skills-building or forms of outreach can help take AI tools out of the AI community and into 'the lab'?
- How has machine learning been used most effectively for research and innovation? What best practices, or lessons, do existing efforts in AI for science offer?
- Which AI tools are suitable for which purposes, disciplines, or experimental designs? Is it possible to create a taxonomy for science?
- Are there generalisable methods or conclusions that can be taken from domain-specific efforts to deploy AI for science?

AI for science: an emerging agenda
Working paper
February 2023

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