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## Seeing into Hi-C: How our scientific connectivity revealed the close connections in our DNA to be a work of art

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## ABSTRACT

Scientific data can be beautiful. An example where the data itself have a particularly striking appearance even before any scientific meaning has been ascribed is the so-called “Hi-C” chromatin interaction map with its distinct checker-board patterns which when combined with simulations have revealed the complex structure of the folded genome. Here, we describe an art-science collaboration which arose through combining local and global inter-personal connections, and which illustrates the equivalent short- and long-range contacts within folded genomes.

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## METHODS

Impressed by the esthetic appeal of the Hi-C imagery created by Job Dekker and Leonid Mirny, Caroline Austin and Sarah Harris connected with artist Mary Griffiths with the intention of collaboratively investigating the visual language of these images from the disciplines of science and art (see Inset 1 for further details). Mary Griffiths had previously made works of art commissioned by, and then in collaboration with, physicist Professor Sir Kostya Novoselov at the University of Manchester based upon their shared preoccupation with graphite and his isolation of graphene. These are “From Seathwaite” (2015) a 5-storey high permanent wall drawing in the National Graphene Institute, University of Manchester<sup>1</sup> and “Prospect Planes” (2018) a video drawing made from data derived from a drawing by Mary that Novoselov imprinted onto a flake of graphene.<sup>2</sup>

### **Inset 1: The importance of scientific connectivity.**

The pandemic lockdown in 2020 was a strange time, because while our freedom to travel physically was curtailed, we compensated by opening our minds to new ideas and connections we could make online. The UC Santa Barbara Kavli Institute for Theoretical Physics hosted its scheduled “Biological Physics of Chromosomes” summer program entirely online,<sup>3</sup> and serendipitously both Sarah Harris and Caroline Austin attended Job Dekker’s talk “Building the Compartmentalised Interphase Nucleus” delivered from Massachusetts, USA, over Zoom,<sup>4</sup> where Job showed his stunningly beautiful Hi-C images representing the folded structure of chromatin.<sup>5</sup> In the discussion following the seminar, Caroline described her vision of Job’s team’s Hi-C images as works of art, for example displayed on the wall of the Tate Gallery in St Ives. Inspired by this idea,

Sarah spoke with an old school friend, Helen Waters, who is one of the senior directors of the Cristea Roberts Gallery on Pall Mall in London,<sup>6</sup> to ask if she had knowledge of contemporary artists happy to collaborate with scientists. Sarah made this association between Helen and art-science collaborations because Cristea Roberts display art by Anni Albers, whose drawings and textiles were inspired by knot theory and topology through her collaboration with the mathematician Max Dehn. DNA packing within the nucleus has received considerable attention from the pure mathematics and topology community. Dehn surgery, which describes the mathematics of making cuts in and resealing closed loops, has been used to describe the action of DNA manipulating enzymes critical for maintaining the genome.<sup>7,8</sup> Helen put us in touch with Mary Griffiths, who is based in Manchester. In subsequent online conversations between Mary, Sarah, Caroline (Manchester/Leeds/Newcastle in the UK) and Job and Leonid Mirny (in Massachusetts, USA), we saw drawing functioning as an essential way of communication, both for the biophysicists and the artist.

**Scientific interpretation of Hi-C images:** DNA needs to be highly organized to fit into the nucleus of a cell. The total length of DNA of the human genome within chromatin is around 2m long but only two nanometers wide and is packaged into a nucleus that is only micrometers in diameter. Methods have been developed to infer exactly how the DNA is organized in 3D. One of these methods is Hi-C,<sup>9</sup> it captures the conformation of chromosomes (3C)<sup>10</sup> by cross-linking nearby loci together with formaldehyde and then using next generation sequencing to generate the sequence of the glued together regions. Once aligned to the genome, these sequences give information on the chromosome regions that are neighbors in 3D. This 3D arrangement changes throughout the cell cycle. A representative image from the Hi-C experiments is shown in Fig. 1(a). Such two-dimensional maps represent all pair-wise interaction frequencies of all loci along chromosomes that together reflect the three-dimensional folding of the genome. In these maps, darker colors indicate where chromatin chains come more frequently into close contact.

When viewed at the scale of a complete chromosome, the Hi-C map displays striking plaid patterns. To unravel the detailed structures that give rise to these patterns, computer simulations are essential.<sup>11</sup> Many putative folded configurations of the chromatin chain are generated, and those closest to the experiment results are selected. The striking checkerboard pattern is the result of spatial clustering of loci in at least two types of nuclear neighborhoods: in one type active genes come together, while in the other inactive segments of genome congregate. Affinities among segments are sufficient to drive the formation of such neighborhoods. This checkerboard pattern differs between cell types, because in different cell types different parts of the genome are active and inactive.

When one zooms into the Hi-C contact maps, increasingly large amounts of details emerge. The dark diagonal line in the center shows that regions close together in sequence along the chain are more likely to be close when packed within the nucleus, as would be expected. Besides this dark diagonal, an array of dots, triangles, lines, etc., is observed. In spite of this apparent complexity in features, a single

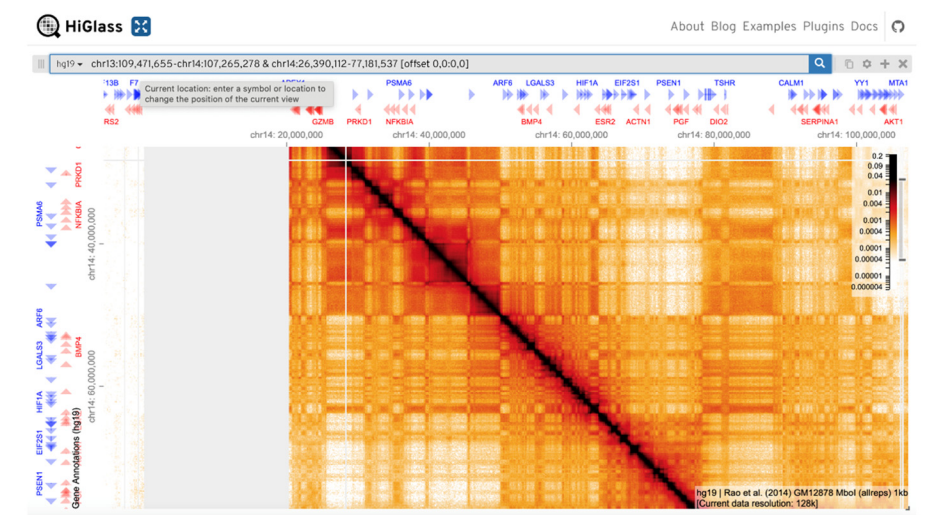
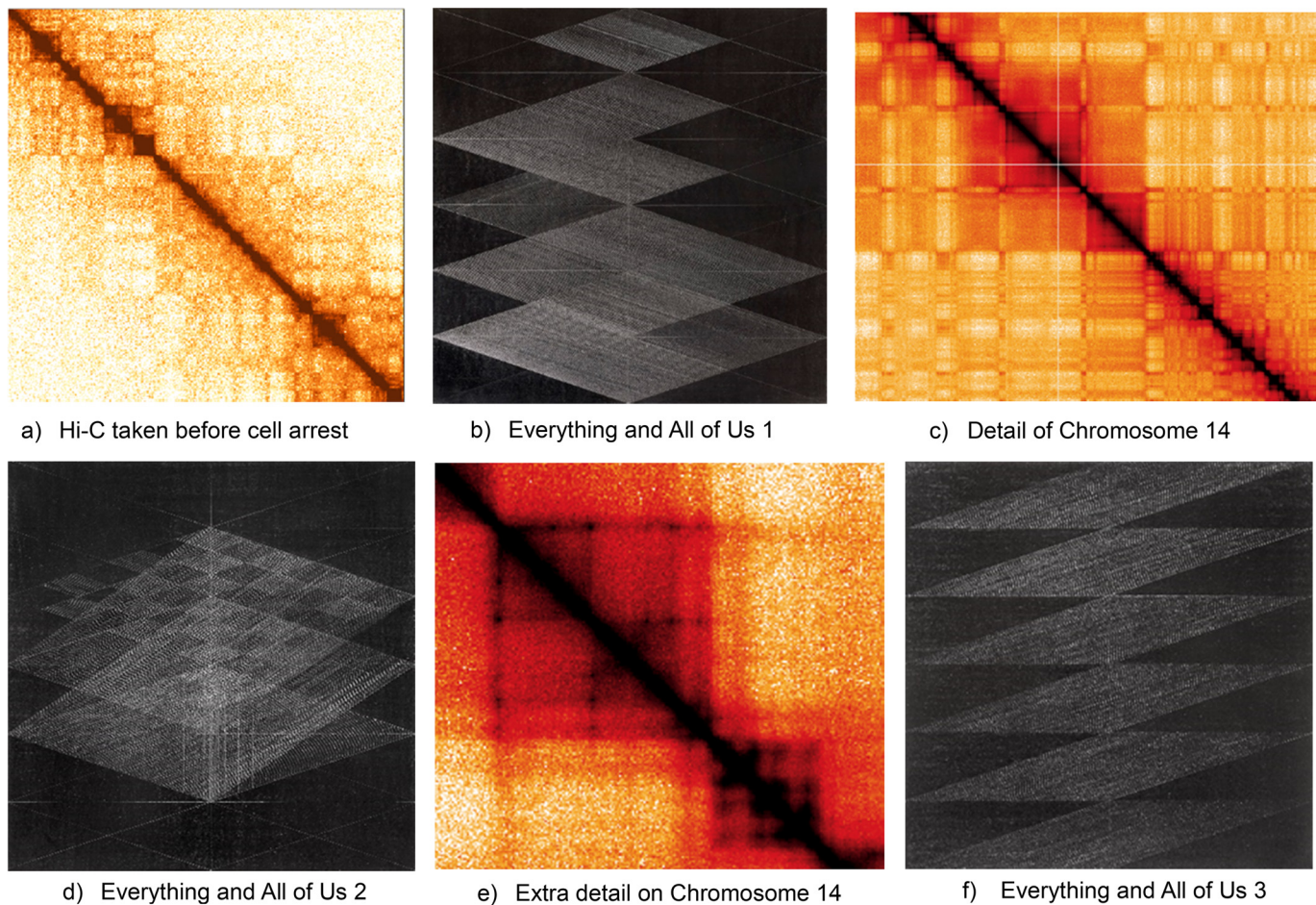
process of dynamic loop formation can explain their formation. For instance, dots represent frequent loops between pairs of specific loci, lines represent dynamic loops anchored in one locus, and triangles emerge as the summation of many different loops. The contacts formed between these loops perform an important biological function because they enable genes and other DNA elements that may be located far apart in sequence on the chromosome to influence each other at key stages within the cell cycle. For a review of the techniques used to construct the 3D shape of chromosomes from experimental data such as Hi-C maps see Refs. 12–14.

The bewildering variety and complex dynamics of chromosome folds arise because of a myriad of processes such as loop extrusion by molecular motors and compartmentalization of the DNA into “active” and “silent” regions where genes are either expressed or remain dormant respectively. To enable understanding, scientists need to construct simplified models that capture only the most essential elements. Similarly, the artistic representations are an abstraction of the experimental data, and are therefore also a model, but expressed in visual rather than physical or mathematical terms.

**Artistic interpretation of Hi-C images:** Griffiths addressed the Hi-C imagery over three months by making numerous drawings from it and developing a finished work of art, “Everything and All of Us 1.” This drawing is made of densely applied graphite on paper. The graphite is burnished to compact it and then polished. A drawing is inscribed into this with an etching needle. This first drawing in the series “Everything and All of Us” looked at one area of chromosome 14 using the Hi-C visualization tool HiGlass.<sup>15</sup> Griffiths drew this area as having three dimensions by creating overlapping levels of geometric imagery. Her method of cross hatching polished graphite to create oscillating densities succeeded in representing the Hi-C areas of chromosome interactions and the relationships between levels. It was noted by the group that these levels were linked, so for the next drawing “Everything and All of Us 2,” Griffiths introduced the new element of angled linking planes. For the final drawing “Everything and All of Us 3,” Griffiths stripped the drawing back to the underlying matrix, notionally returning the drawing to the earliest state of cell-development and also the most minimalist artistic presentation of the structure.<sup>16</sup>

**Impact and learnings from our art-science collaboration:** Two series of works of art were produced as a consequence of this art-science collaboration: the three drawings on paper titled “Everything and All of Us 1, 2 and 3” (2022) and the three hand-made etchings also titled “Everything and All of Us 1, 2 and 3” (2024). All of these works were shown in Griffiths’s exhibitions “Everything and All of Us” at the Stanley and Audrey Burton Gallery, University of Leeds (2024) and “Mary Griffiths: Printmaker in Focus” at Ruthin Craft Centre, Denbighshire, Wales (2025).<sup>17</sup> A drawing and an etching were also shown at the Royal Academy Summer Exhibition, London in 2023 and 2024. The University of Leeds has since acquired the drawings “Everything and All of Us 1, 2 and 3” for their collection of fine art. During the Leeds exhibition, Harris was part of a panel discussion for a general audience about this and other collaborations which also included the linguist Professor Tony Crowley, University of Leeds, who also has an interest in neighborhoods and place, but from a linguistic perspective.<sup>18</sup> The analogy between social connectivity and connectivity within chromatin is explored in Inset 2.





g) Example view of the Hi-C visualisation software tool used to explore the data both scientifically and artistically.

**FIG. 1.** Hi-C maps and their relationship to the Everything and All of Us series. “Everything and All of Us” by Mary Griffiths was exhibited at the Stanley and Aubrey Gallery at the University of Leeds (2024), and at Ruthin Craft Centre (2025).

**Inset 2: Parallels between scientific connectivity and genomic contacts.**

There is an interesting analogy between the looped chromatin structure and the scientific interactions that gave rise to the art-science collaboration. Sarah Harris and Helen Waters were both at the West Somerset School in the small town of Minehead in Somerset, UK, as teenagers. Their relationship is based on close locality and is analogous to strong diagonal seen in all Hi-C maps at neighboring DNA sequences within chromatin. A small chromatin loop between nearby structures would be equivalent to relationships such as Caroline Austin/Sarah Harris who are both UK scientists working in the field of chromatin structure and DNA topology; Leonid Mirny/Job Dekker who are close collaborators working on chromatin structure in the USA and Helen Waters/Mary Griffiths who are both in the field of fine art in the UK. The four UK and US biophysicists are connected over even longer relationship length-scales equivalent to a larger loop still, and the connection associated with the largest loop would be Mary/Job/Leonid, who are distant both in physical location and in discipline. While it would have been highly unlikely for Sarah and Helen to never have met, for Mary to know Job and Leonid required circumstances that would not have been predicted from a knowledge of their CVs alone.

From these outcomes, it can be seen that this art-science collaboration made possible art that communicated the complexities of Hi-C to a nonscientific audience successfully. At least 150 000 attended each of the Royal Academy exhibitions, while the Leeds exhibition brought in an audience of 6600 arts, humanities, and science students and general visitors alike. Of 157 people surveyed, 62% were first-time visitors showing the appetite the public has for art-science projects. A selection of written comments is provided in Inset 3.

The development of those works of art was dependent upon the shared practice within art and science of close-looking for pattern, repetition, and esthetics. The group used drawing to think and to communicate, demonstrating the significance of the drawn line as a means of note-taking and discussing through a visual language.

Our working together connected our otherwise completely separate worlds. We hope that our story may inspire the scientists who are reading this paper to communicate their work to artists, and for our artistic readers to reach out and work with scientists, and that our collaborative efforts to see and express the beauty in scientific data brings enjoyment of both science and art to a wide and general audience.<sup>19</sup> The process of chromosome folding has also inspired musicians; the composer Amir Bitran wrote a musical composition that was performed in Paris and Boston.<sup>20,21</sup> While the value of science is often stated in terms of benefits to economics, industry, or health, here we

**Inset 3: Examples of written comments from visitors to the “Everything and All of Us” exhibition at the Stanley and Audrey Burton Gallery, University of Leeds.**

“The way the light shifts in these dense geometric meshes whilst reflecting the observer says a lot about our relation to science. As someone passionate of the sciences, this exhibition was very engaging. Incredible work Mary Griffiths!”

“Very maths based work! I love the geometry involved and the different lines and material used. Maths person dream decor! I love maths and I love this art work.”

“Made me think of physics, graphs and maths n stuff. Was cool though.”

“Fabulous, this form of art is new to me. I enjoyed looking at each etch from different perspectives and seeing something new. I love the conversation between art, science and society.”

are celebrating the profound joy it brings through new perceptions and understanding.

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**AUTHOR DECLARATIONS****Conflict of Interest**

The authors have no conflicts to disclose.

**Author Contributions**

**Mary Griffiths:** Conceptualization (equal); Methodology (lead); Writing – original draft (equal). **Caroline Austin:** Conceptualization (equal); Methodology (supporting); Writing – original draft (supporting). **Job Dekker:** Conceptualization (equal); Methodology (equal); Writing – original draft (equal). **Leonid Mirny:** Conceptualization (equal); Methodology (equal); Writing – original draft (equal). **Sarah Harris:** Conceptualization (equal); Methodology (supporting); Writing – original draft (equal).

**DATA AVAILABILITY**

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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