Dr Robert Neely and Anna Dumitriu: The Chemistry of Biology: An Alchemy of DNA

I was contacted by artist Anna Dumitriu as a result of the work I was doing on the large, collaborative BeyondSeq project (an EU Horizon 2020 project, grant number 634890). As a result of this, Anna and I applied for external funding for her to develop an artistic interpretation of the work we were carrying out for the BeyondSeq project.

Our Artist in Residence project began on the 2nd of January 2017 and was funded for ten months, until the 2nd October 2017. During this time, Anna and I collaborated extensively on the project with the project culminating in an exhibition at the Birmingham Open Media Gallery on the 11th October. Anna made a total of seven visits to Birmingham during the course of the project (6th January, 13th February, !5th March, 22nd-25th May, 19th-23rd June, 17th-21st July and the week of the exhibition on the 11th October).

Project Aim
The aim of our project was to begin to open a dialogue between artists, scientists and the wider community about the rapid advance of genomic and genetic technologies. We have focused our discussions on the potential impact that these technologies have, and are likely to have, on our society.

Background
The focus of Anna's work prior to this project has been on pathogenic organisms and genetic engineering and stimulating the complex dialogue that surrounds these issues. We aimed to weave this together with research from my laboratory in Birmingham, which is developing a novel approach for the visualization of DNA using fluorescence microscopy.

Making DNA barcodes: My laboratory has pioneered the use of the DNA methyltransferase enzymes as molecular tools for fluorescent labelling of DNA, work currently funded through the BeyondSeq project (an EU Horizon 2020 project, grant number 634890). These enzymes target short palindromic DNA sequences, such as 5'-TCGA-3', and using a small molecule that we synthesise, are able to catalyse the transfer of fluorophores to these sequence motifs. By stretching DNA molecules onto a surface, we are able to image individual molecules and see the pattern of fluorophores that have been attached to the DNA by our enzymes. As the fluorescent labelling depends on the DNA sequence, each DNA molecule has a barcode that can be used to identify the organism from which it came.

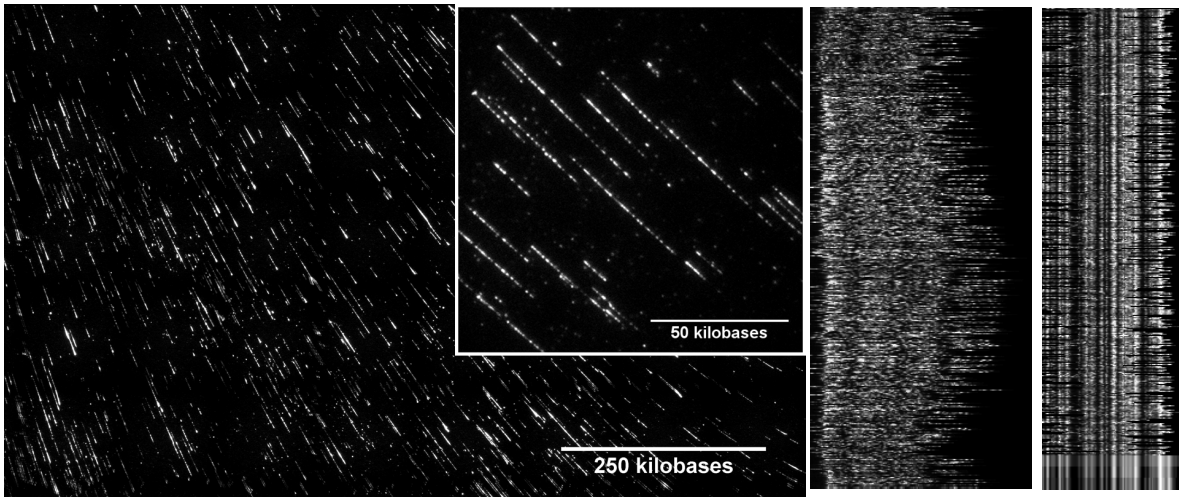

Figure 1. Left to right: Microscope image of deposited DNA barcodes; extracted barcodes; filtered and aligned barcodes (bottom traces show consensus barcode and reference barcode).

Project Implementation
Anna's time in Birmingham was spent largely in my research laboratory, where she has learned to create DNA maps, from the extraction of DNA to the microscopy and subsequent image analysis. The project began with short visits from Anna to Birmingham during which we began to compare language and understanding and

develop initial ideas where our interests aligned (January/February). In March and May, Anna spent several days in my laboratory shadowing researchers working on the BeyondSeq project and preparing some samples for DNA barcoding experiments. We performed the experiments to produce barcodes of Anna's 'make do and mend' strain of E.coli during June and July. During Anna's visits, we spent time debating and shaping our collaboration that I feel certain we will continue into the future.

At the heart of our work has been the central question, posed by Anna "what is DNA?". When confronted with this question, no two members of my lab (currently 10 PhD students and 4 postdoctoral researchers) gave the same response. Given that we have developed a means by which a single DNA molecule can be made visible you would imagine my group to be capable of formulating some consensus to such a simple question. Yet the images we produce are not consistent with the famous double helix that most people imagine DNA to be. In fact, we see threads of DNA that are derived from the meters of the molecule contained within each of our cells. "What DNA is" depends on the scale used to observe the molecule. Indeed, I have still to come up with a reasonable answer to this question because the answer really depends on why you are asking the question.

We felt this fertile philosophical ground upon which to base our collaboration. We have focussed on the development of two significant threads of this debate. The first is the deconstruction of the DNA molecule into its component atoms and the second is the use of our DNA barcodes to show a new side of DNA to the public.

Scientifically, we examined the application of DNA mapping to the visualisation of the genome of a strain of bacteria (*E.coli*) that Anna produced. The genome contains a short edit (~70 base pairs), introduced by Anna, using a cutting-edge CRISPR/Cas9 genome editing method. The insert encodes a short piece of text that reads 'make do and mend'. The concept of finding this edit in the E.coli genome mirrors our aim in the BeyondSeq project to identify the genomic causes of human disease.

Using our DNA barcoding approach, we imaged thousands of individual DNA molecules from Anna's E. coli bacterial genome (4.6 million base pairs in length) and were able to identify a handful with barcodes that indicate they contain the CRISPR/Cas9 edit. This is the first time that this has been achieved and we believe it offers an important new tool for the detection and/or validation of edits of bacterial genomes. This work will be incorporated into a more extensive manuscript on the development of DNA mapping for studying bacterial genomes.

Project Outcomes

Perceived benefit to the PI: Anna's residency at Birmingham has undoubtedly raised my profile as a scientist and has demonstrated to me that the art/science interface is a powerful mechanism for stimulating public debate around the work we do in the lab. This is a valuable aspect of the applied work we do in my lab, which is improved by feedback from potential end-users/stakeholders. Beyond this, Anna is a determined connector of people and my network of potential collaborators has significantly extended through our collaboration.

Perceived benefit to students at Birmingham: My research group are the primary beneficiaries of Anna's time spent in Birmingham. She has actively participated in the research in my laboratory and has stimulated lively discussion and debate within my group. It is these discussions that led to the mapping of the 'make do and mend' E. coli and Anna's persistence that led us to develop software for identifying and displaying specific molecules in our DNA mapping data.

Benefit for the BeyondSeq project: Our work with Anna, mapping her genome-edited bacteria has been included in our recent work to the journal 'Nucleic Acids Research' and forms a critical aspect of the progress towards the goals of the BeyondSeq project.

Impact on the local community: As part of the project, we visited our local science museum, ThinkTank (23rd May 2017), and now plan a piece for one of the cabinets in their 'Medicine Matters' exhibit. We agreed an installation date in the spring of 2018 for the work, which will further explore our 'what is DNA?' question.

The residency culminated in a two-week exhibition of Anna's work in which she used images of DNA barcodes, which she prepared in collaboration with researchers in my laboratory:

http://www.bom.org.uk/event/exhibition-preview-the-chemistry-of-biology-an-alchemy-of-dna/

The exhibition was promoted using social media, by the gallery and through a University of Birmingham press release (details below). Alongside the art installation that Anna created (Figure 2), PhD students and PDRAs from my lab demonstrated DNA extraction, made DNA cocktails for guests and gave practical demonstrations using small pieces of equipment (for visualization of fluorescence and deposition of DNA molecules) from my lab. As part of the preview evening, Anna and I were interviewed by gallery Head of Programme, Louise Latter and took questions on our collaboration from the audience (30-40 people). The exhibition was installed at BOM for a total of two weeks from the 12th to the 26th of October 2017.

Figure 2- Images taken by Anna of the 'Chemsitry of Biology' exhibition at the Birmingham Open Media gallery.

Media:
I have given interviews to Claudia Schnugg who recently included details of our collaboration in a book on the art/science collaboration (https://www.palgrave.com/gp/book/9783030045487) and Rachel Brazil, a freelance science writer who is published a piece about our work in the Royal Society of Chemistry's 'Chemistry World' magazine (https://www.chemistryworld.com/careers/art-imitating-life/3008365.article).

The project has been widely promoted and communicated. I have over 30 tweets (214 retweets) on my Twitter profile that relate to the project.

I co-wrote a press releases for the University for our exhibition:

https://www.birmingham.ac.uk/schools/chemistry/news/2017/birmingham-chemist-bioartist-dna-art-collaboration-bom.aspx

I co-wrote an article with the 'Physical Sciences for Health' centre for doctoral training about the residency:

https://www.birmingham.ac.uk/research/activity/sci-phy/news/Introducing-Artist-in-Residence-Anna-Dumitriu.aspx

And Anna has publicised our collaboration through her personal website:

http://annadumitriu.tumblr.com/post/166011815444/anna-dumitrius-residency-with-dr-rob-neely-at-in

Anna's virtual reality piece showing users the view from inside our microscope won a prize at a Korean Bio-Art competition:

https://bioart.biocon.re.kr/en/virtual-and-reality-virtual-life/

Future plans:
Our immediate focus is on extending our work to develop a piece for our local science museum, ThinkTank. Beyond this, I am keen that my lab continues to collaborate with artists as a mechanism for exploring the impact of the work we do in greater detail. I am in the process of writing applications for funding to follow up on our DNA barcoding work and will include a request for funds to continue to work with Anna as part of the impact/translational aspect of this project.