METALLOMICS WITH PROFESSOR JOANNA COLLINGWOOD

TALKING POINTS

KNOWLEDGE
1. What is metallomics?
2. What is a synchrotron?

COMPREHENSION
3. Why does the research team want to understand the role of trace metals in the development of neurodegenerative diseases?
4. Why do we need to look at the brain as a dynamic system?

APPLICATION
5. What research would you want to undertake at Diamond Light Source?
   For example, would you be interested in studying viruses or ancient paintings? Why?

ANALYSIS
6. How is the study of brain tissue, using synchrotron X-ray spectromicroscopy, similar to the study of viruses?
7. How is it different?

SYNTHESIS
8. Imagine the researchers have discovered a link between high concentrations of metals in the brain and neurodegenerative disorders. What questions would researchers need to answer to develop successful treatments?'

EVALUATION
9. Jo and the team are excited to be able to approach difficult questions from a range of perspectives. What are the benefits and challenges of working with a group of people with different expertise?

CREATIVITY
10. Can you come up with a question or problem that needs a range of perspectives to solve it?

ACTIVITIES

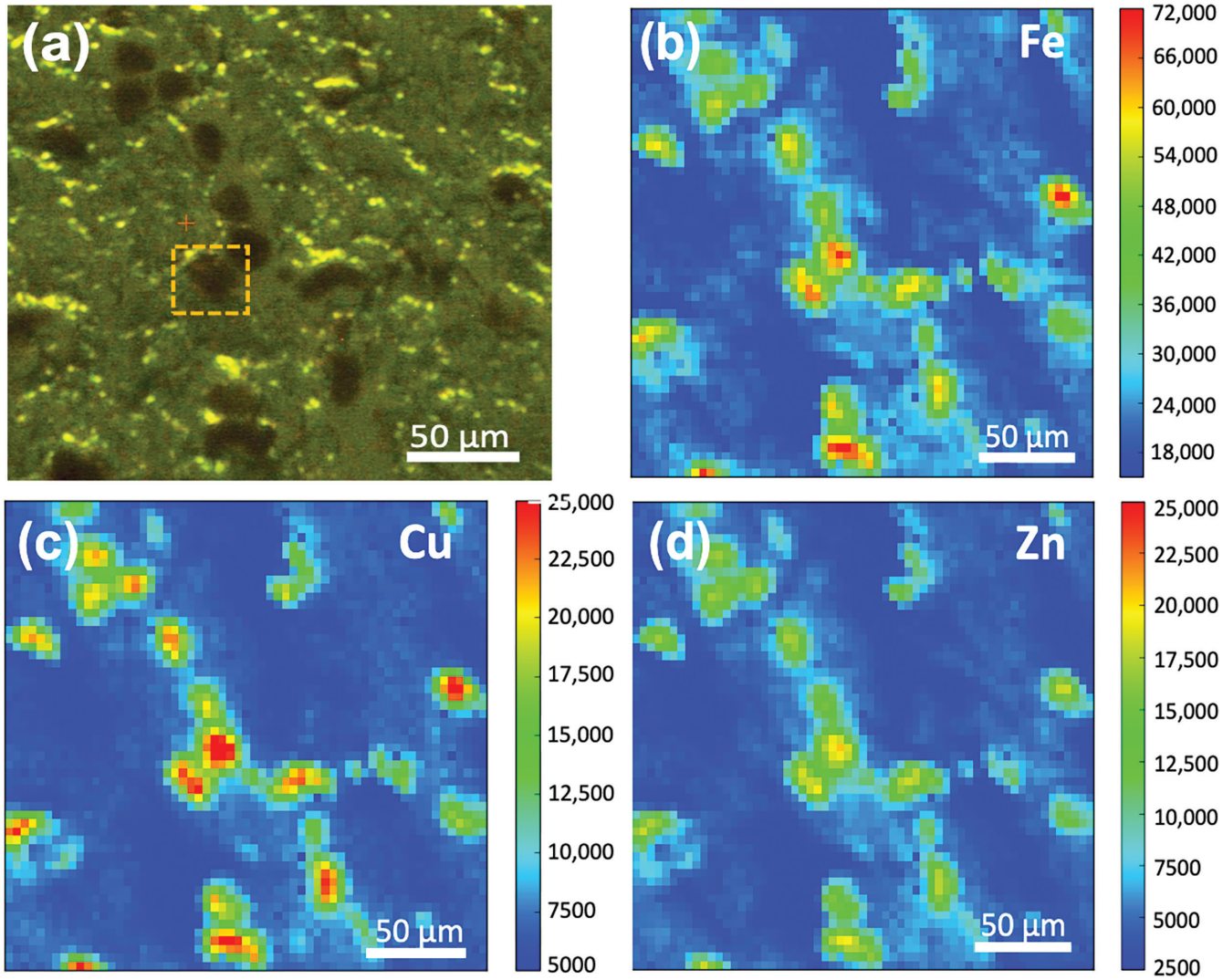
1. STEP IN JO'S SHOES!
The research team is investigating the role trace metals play in the development of Alzheimer's and Parkinson's disease. They are using a state-of-the-art synchrotron technique called X-ray spectromicroscopy to image and analyse the brain in innovative ways. The images on the right were shared in a research paper published by the team to show how this type of X-ray imaging can be used to study samples. It is free for everyone to read, and can be found at **www.mdpi.com/2073-4409/8/10/1231**

- Can you see a tiny red + in image a)? This was the team's marker to show where the X-ray beam was hitting the tissue section when they collected the image.

- Distribution of multiple trace metals in brain tissue can be visualised simultaneously using micro-focus X-ray fluorescence (XRF) mapping. Look closely in the iron (Fe), copper (Cu) and zinc (Zn) images. You can see the individual pixels where the tissue sample, a thin section of human brain tissue on a microscope slide, has been moved through the X-ray beam to measure the amount of fluorescence from each point. This information gets collected in a grid of rows and columns, and the team uses that to make the pictures for each metal element.

- The picture in (a) looks very dark because this is an image the researchers collected on a camera in the synchrotron measurement chamber. It is not the best microscope image in the world, but it is enough for the team to be able to see the area of the tissue they want to image, to check they are in the right place. If you look carefully, you can see that the dark brown regions correspond to the pattern in the metal element maps.

- The dark brown objects in figure (a) contain a pigment called neuromelanin, which, under a microscope, can look like instant coffee granules packed into the cell! We also have melanin



pigment in our skin, which is a slightly different form than the melanin in these special brain cells. Can you estimate how big the cells are using the scale-bar? If you look up the properties of 'dopaminergic neurons' on the internet, are the cell bodies about the right size? Have you identified them correctly?

- The research team was looking in a region of the brain called the 'substantia nigra compacta' – search the internet to find out what job(s) these cells do. They might look a bit like 'brain freckles' in a tissue section viewed under the microscope, but these pigmented neurones are vital for our bodies to work normally; we can't function properly without them. In Parkinson's disease, this type of cell is particularly likely to die. [Extension activity – look up the drug, Levadopa. See what it is, why it is given to people, and why it can help in Parkinson's disease when a lot of these neurones, that make the neurotransmitter dopamine, stop functioning properly.]

- Metals are concentrated in these pigmented neurones, because they bind to the neuromelanin pigment. There are lots of ideas about what neuromelanin is and does, but no one is completely sure, and we don't know if it protects the cells or might actually be a problem as the cells age or if people develop Parkinson's disease. This is one of the things the team want to understand more about, as understanding what is going wrong in the cells is the first step in working out how to treat a disease and keep people healthier.

- What does the blue-to-red scale represent in each image? These numbers tell the researchers how much signal they were getting from the detector, so they are not converted into units of concentration (yet) but you can make comparisons between the images. For example, which element has the highest concentration a) in the pigmented cells, and b) in the tissue surrounding the pigmented cells? You might think there is more Cu than Fe in the cells, but there is not. Can you spot why? (The research team uses the colour 'temperature scale' to help them see the distribution of elements in each map, but notice the difference in the signal intensity values on each scale for each map.)

2. JET ENGINES, ANCIENT PAINTINGS AND VIRUSES

Synchrotrons can be used for a wide range of research projects. Visit the 'Research Areas' webpage at Diamond Light Source: **www.diamond.ac.uk/Science/Research/ResearchArea.html**

- Choose 1-3 disciplines that interest you (i.e. chemistry, Earth science, engineering). Read about the research opportunities available at Diamond Light Source for each of the disciplines you have chosen.

- Now come up with research projects, relevant to your chosen disciplines, that might benefit from these opportunities.

- Think about and answer the following questions:

- How would state-of-the-art synchrotron techniques advance the research?
- What impact might the research project have?
- What expertise would the project need?

MORE RESOURCES

- Take a virtual tour of Diamond Light Source! **www.diamond.ac.uk/Public/VisitUs/Virtual-Visit.html**

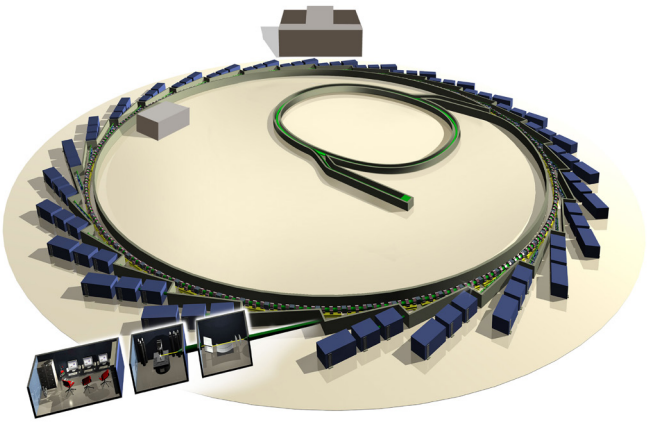
  Diamond Light Source has an interactive map and lots more activities for students and schools: **www.diamond.ac.uk/Public.html**

- You can also visit Diamond Light Source in person: **www.diamond.ac.uk/Public/VisitUs.html**

- If you are interested in the School of Engineering at the University of Warwick, visit: https://warwick.ac.uk/fac/sci/eng/. Its outreach resources include a podcast featuring students interviewing academics and a journal club.

  There is also the pre-university summer school: **warwick.ac.uk/study/summer-with-warwick**

- The International Day of Light is celebrated on 16th May every year. To find out more, including about the annual photo competition organised by the Society for Optics and Photonics, visit: **lightsources.org/international-day-of-light/**



A 3D model of Diamond showing the individual beamlines around the ring - © Diamond Light Source Ltd 2022

Aerial view of Diamond Light Source - © Diamond Light Source Ltd 2022