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Review of Canadian Light Source facilities for biological applications

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ABSTRACT

The newly-created Biological and Life Sciences Department at the Canadian Light Source (CLS) encompasses four sets of beamlines devoted to biological studies ranging in scope from the atomic scale to cells, tissues and whole organisms. The Canadian Macromolecular Crystallography Facility (CMCF) consists of two beamlines devoted primarily to crystallographic studies of proteins and other macromolecules. The Mid-Infrared Spectromicroscopy (Mid-IR) beamline focusses on using infrared energy to obtain biochemical, structural and dynamical information about biological systems. The Bio-Medical Imaging and Therapy (BMIT) facility consists of two beamlines devoted to advanced imaging and X-ray therapy techniques. The Biological X-ray Absorption Spectroscopy (BioXAS) facility is being commissioned and houses three beamlines devoted to X-ray absorption spectroscopy and multi-mode X-ray fluorescence imaging. Together, these beamlines provide CLS Users with a powerful array of techniques to study today's most pressing biological questions. We describe these beamlines along with their current powerful features and envisioned future capabilities.

1. Introduction

The Canadian Light Source Inc. (CLS) is a mid-size 3rd generation 2.9 GeV synchrotron located on the campus of the University of Saskatchewan in Saskatoon (www.lightsource.ca). Last year, the CLS celebrated its 10th anniversary of operations. Currently there are 15 beamlines operating at the facility, with an additional two being commissioned and five under construction (Fig. 1). The Biological and Life Sciences Department at the CLS was created one year ago to facilitate support and research in the biological and health related fields. It is composed of the following facilities: Canadian Macromolecular Crystallography Facility (CMCF), Mid Infrared Spectromicroscopy (Mid-IR), Biomedical Imaging and Therapy (BMIT) and, recently built, Biological X-ray Absorption Spectroscopy (BioXAS) which is currently being commissioned. The department is well equipped to study biological objects ranging from atomic resolution (CMCF and BioXAS) to cells and tissues (BioXAS and Mid-IR) through to larger samples such as organs, live animals and plants (BioXAS and BMIT) (Fig. 2). A current summary of Biological and Life Sciences Department publication activity is presented in Fig. 3. Since 2006, researchers acquired data at the Biological and Life Sciences beamlines to produce a total of 542 peer-reviewed articles, 59 doctoral theses, 50 masters theses, as well as several patents.

2. Facilities

2.1. CMCF

The Canadian Macromolecular Crystallography Facility (CMCF) is composed of two beamlines (08ID-1 and 08B1-1), and serves more than 65 Canadian and some international labs [1–3]. Specifications of the CMCF beamlines are shown in Table 1. The main techniques available at the CMCF are as follows; high resolution macromolecular X-ray crystallography, Multi/Single wavelength Anomalous Dispersion (MAD/SAD), small molecule crystallography and EXAFS on crystals (cmcf.lightsource.ca). Since its inception 10 years ago, 400 peer reviewed papers were published with data collected at the CMCF and more than 750 structures deposited in the Protein Data Bank (PDB) [4]. Local users collect data directly at the beamlines whereas the majority of other users collect data remotely or use mail-in service, where staff members collect data.

Drug development is an important area of Canadian research and we outline here an example of a successful path from a high-resolution crystal structure to a therapeutic antibody. About 2 in 5 Canadians will develop cancer in their lifetime, and about

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0168-583X/

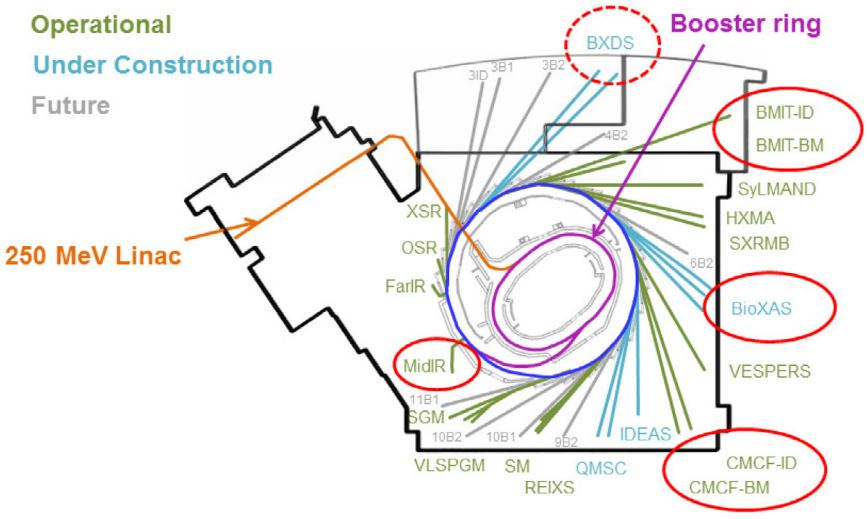

Fig. 1. CLS layout with the biological and life sciences beamline names highlighted in red circles. The dashed circle indicates the Brockhouse beamlines that may potentially host the BioSAXS endstation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

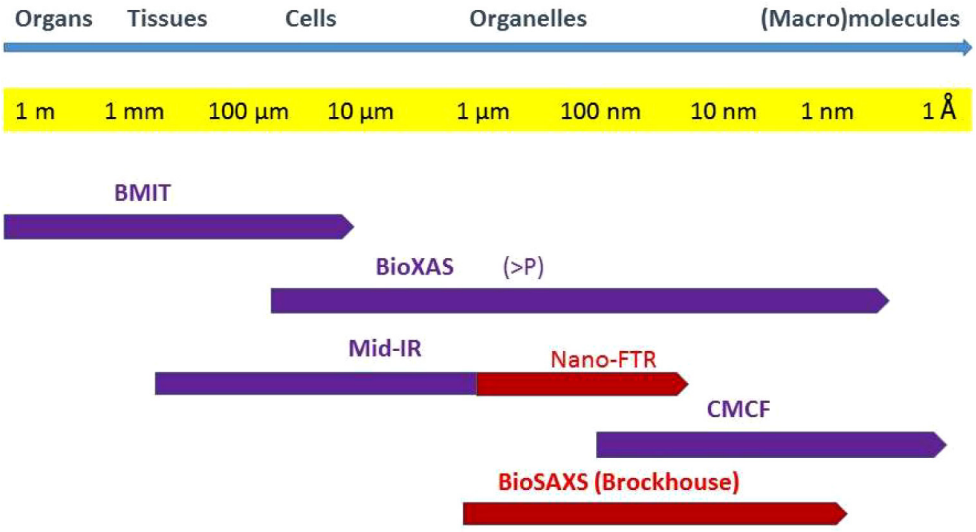

Fig. 2. Complementarity of the biological and life sciences beamlines. The red color indicates potential future developments; infrared imaging beyond the diffraction limit (Nano-FTR) and BioSAXS endstation at the Brockhouse facility. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

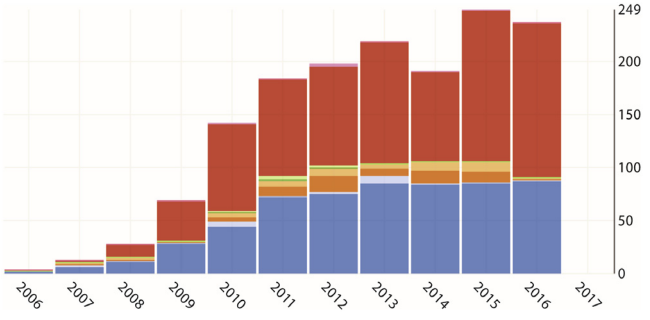

Fig. 3. CLS biological and life sciences department activity summary. Number of publications containing data from associated beamlines by year, including: peer-reviewed articles (blue), conference proceedings (light blue), doctoral theses (orange), masters theses (light orange), magazine articles (green), book/chapter sections (light green), PDB depositions (red) and patents (pink). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

1 in 4 Canadians will die of cancer. In 2015, it is estimated that 196,900 Canadians developed cancer, and 78,000 died of cancer. More than half of new cancer cases (51%) are lung cancers. Netrin-1 is a protein involved in neuronal navigation, immune cell migration and cell survival. Its interaction with receptor (UNC5) is responsible for cell proliferation; therefore, finding a molecule that would interrupt this interaction would trigger tumor cell death. Using the high-resolution capabilities of the CMCF beamlines at the CLS, a Canadian-European collaboration was able to identify the part of Netrin-1's structure that actually performs this function [5]. Using this information the researchers were able to design an antibody to target that area of Netrin-1, and showed it triggers death of cancer cells under laboratory conditions. The antibody, now named NP137, is currently in clinical trials.

Some bacterial families express the conserved outer-membrane zinc transporter zinc-uptake component D (ZnuD) to overcome nutritional restrictions imposed by the host organism during infection. A research group from the University of Toronto

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