Chapter 2
Synchrotron Light Facilities and Applications in Life Sciences

V. M. Tsakanov

Abstract The synchrotron radiation emitted by high-energy ultrarelativistic electrons is one of the most powerful tools for investigating matter. The radiation has a broad continuum spectrum covering radiation wavelengths from infrared to hard X-ray ranges. The radiation is emitted in a narrow cone providing a high brilliance collimated photon beam with a small divergence and size from a high intensity electron source. The continuous spectrum of synchrotron radiation provides more than five orders of magnitude increase in intensity and more than ten orders of magnitude increase in brilliance than more conventional sources, such as VUV lamps and X-ray tubes. In advanced synchrotron light facilities the radiation is produced in bending magnets, undulators and wigglers, enabling dedicated tunable polarized photon beams. The radiation has a pulsed time structure allowing the execution of time-resolved experiments along with scattering, spectroscopy and imaging experiments. These features of synchrotron light have provided a continuous growth of synchrotron radiation usage in diverse fields of life, materials and environmental sciences during the last decades. In this chapter, a brief introduction is provided to synchrotron light sources, the main features of their associated radiation, experimental techniques and applications in life sciences.

Keywords Synchrotron radiation · Insertion devices · Radiation spectrum · Experimental technique · Beamline instrumentation · Life and environmental sciences

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2.1 Introduction

During most of the twentieth century, intensive studies were made into the substructure of the atom and its core, called the nucleus. This led to discoveries of many new subatomic particles such as neutrons, mesons, leptons, quarks, and neutrinos and to the nature of their properties and interactions, which in those instances were more dominant than the electromagnetic interactions. These discoveries were made possible through advancements in the technology of particle accelerators, which propel electrons and protons to energies many orders of magnitude greater than their values within stable atoms. One of these devices was the electron synchrotron, which was especially important in providing the capability of determining the structure of the atomic nucleus. These devices had one rather distressing feature which was that the circulating electrons would radiate more and more of their energy into electromagnetic radiation as their energies increased, subsequently limiting the energy to which electrons could be raised.

This radiation emitted by electrons confined to circular orbits by magnetic fields is named "synchrotron radiation" following its first experimental observation at 70 MeV energy electron synchrotron of General Electric (Elder et al., 1947), although the feature that accelerated charged particles' radiate energy is a general consequence of electromagnetic theory (Jackson, 1998). The spectrum of the radiation, its intensity, and direction relative to the direction of the electron are all predictable (Wiedemann, 2003; Hoffmann, 2004). For a physical device, such as a synchrotron of several GeV electron energy using 1 Tesla field strength magnets, the spectrum is predominantly in the ultraviolet and soft X-ray range of the electromagnetic spectrum. The power of the emitted radiation increases as the fourth power of the electron energy and the direction of the radiation concentrated in the direction of the radiating electron.

During the period of intense development of high energy circular electron accelerators, in the later part of the twentieth century, it became apparent that the intensity of this synchrotron radiation is much higher than the radiation intensity from more conventional devices, such as X-ray tubes. This feature attracted materials scientists, biologists and others to consider the usage of high energy physics facilities like DESY (Lemke & Labs, 1967) and SPEAR (Doniach et al., 1997) for conducting their studies on a "parasitic" basis whenever these facilities were operative (Winick, 1994). Later this family of electron accelerators was classified as the first generation synchrotron light facilities. A 6 GeV ARUS electron synchrotron in Armenia was among them, where three X-ray beamlines were constructed in early 70's to support the solid state, materials science and radiation biophysics research fields (Williams & Winick, 2015).

By the 1980s, the demand for usage of synchrotron radiation had mushroomed to the point where second generation synchrotron light sources were built as "dedicated" facilities. Thus, a whole new industry was spawned from radiation deemed to be a "waste product" by researchers engaged in the studies into sub-atomic physics.

The advancement from the early “parasitic” mode of operation to today’s “state of the art” dedicated facilities has been a rapid evolution and has culminated in a revolution in many diverse areas of research. They include biology, chemistry, pharmacology, geology, materials and environmental sciences, medicine and many other related fields.

In response to user demands for a higher photon flux and brightness, the new third generation facilities have been developed which incorporate a number of new features, including higher circulating currents of electrons, small electron beam phase space, special devices, such as wigglers or undulators inserted into the magnetic structure of the storage ring, and well instrumented photon beam lines with monochromatic, highly collimated and precise properties (Hoffmann, 2004; Wiedemann, 2003; Willmott, 2011).

The current tendency in synchrotron light source development is aimed to even high brilliance photon beams with electron beam phase space at the level of X-ray diffraction limit. This is achieved by using the sophisticated design of the magnetic lattice with multi-band achromats, longitudinal magnetic field gradient, coupling of the horizontal-vertical particles motion and accelerator technology advancement (Borland et al., 2016; Sargsyan et al., 2016; Wanzengerg et al., 2017). With the exponential growth in the usage of synchrotron radiation, the number built in the past twenty years has increased to over 50 facilities throughout the world.

Along with the synchrotron light facilities, the experimental techniques has greatly advanced, enabling researchers to deeper exploit the matter at the cell, molecular and atomic levels. Finally, a strong user community has been established worldwide to propel the frontier research in life, materials and environmental sciences.

2.2 Synchrotron Light and Sources

In synchrotron light facilities the electrons are accelerated to very high energies of several GeV and stored in a ring for many hours by a magnetic guide field. The electrons in the storage ring experience transverse acceleration due to magnetic field in bending magnets and insertion devices like undulators and wigglers with periodic magnetic fields. Due to acceleration, the electrons emit electromagnetic radiation and for highly relativistic particles, most of the radiation is emitted in a forward direction, concentrated in a very small cone with an opening angle of $1/\gamma$, where γ is the electron energy in units of its rest energy. For electrons $\gamma \approx 1957E$, where E is the electron energy in GeV. Thus for 3 GeV electrons, the radiation opening angle is approximately 0.16 mrad.

The typical schematic design of the third generation light sources is similar to the one of CANDLE synchrotron light facility project in Armenia (Tsakanov et al., 2002). The facility consists of 3 GeV energy electron storage ring, full energy booster synchrotron and 100 MeV linear accelerator (Fig. 2.1). To replenish the energy lost to synchrotron radiation, accelerating cavities are located in the ring at

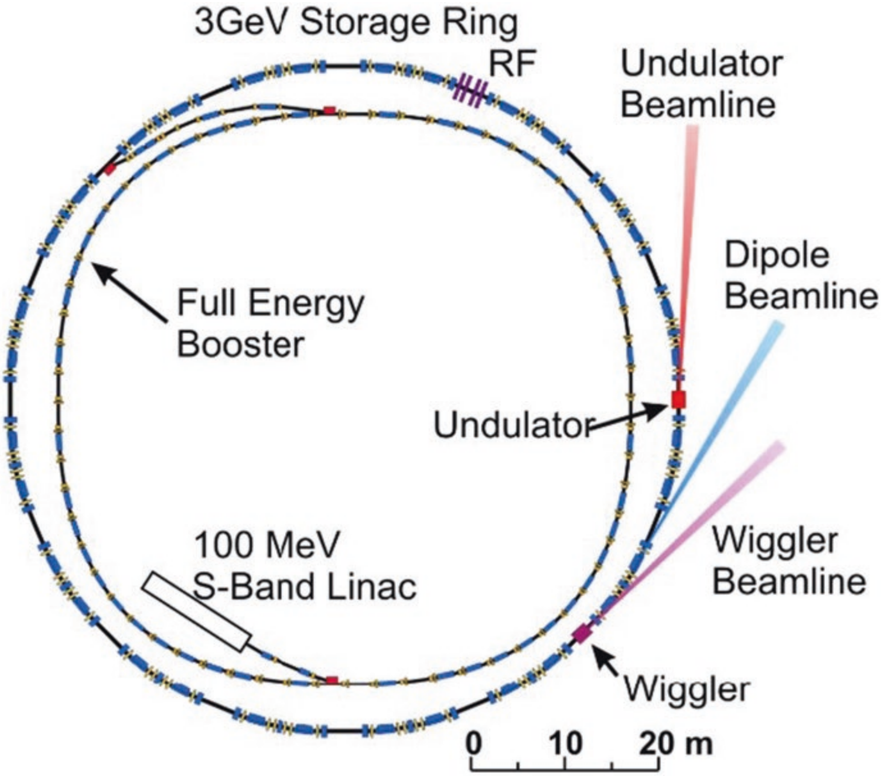

Fig. 2.1 The general layout of CANDLE facility

frequency of about 500 MHz. The electron beam pulse structure consists of 20 psec rms duration individual bunches spaced with 2 nsec time gap.

Important figures of merits for synchrotron radiation are the spectral flux and brightness. The flux is the number of photons emitted into an angular fan per unit time and is the appropriate merit for applications where little beam collimation is required and the sample transverse size is sufficiently large so as to intercept the entire photon beam.

The brightness is the flux per unit phase space and the high brightness is required for experiments that involve samples or optics with very small phase space acceptance or techniques that exploit beam coherence. High brightness of the photon beam is achieved by the electron beam with small transverse size and divergence.

In the CANDLE design, in total 12 straight sections of 4.8 m in length are planned for insertion devices – undulator and wiggler magnets. The photon beams from the dipoles and the conventional insertion devices cover the energy range of 0.01–50 keV with high spectral flux and brightness. Figure 2.2 presents the CANDLE spectral flux and brightness for dipole (1.35 T), undulator (0.3 T) and wiggler (1.3 T, 2 T) sources.

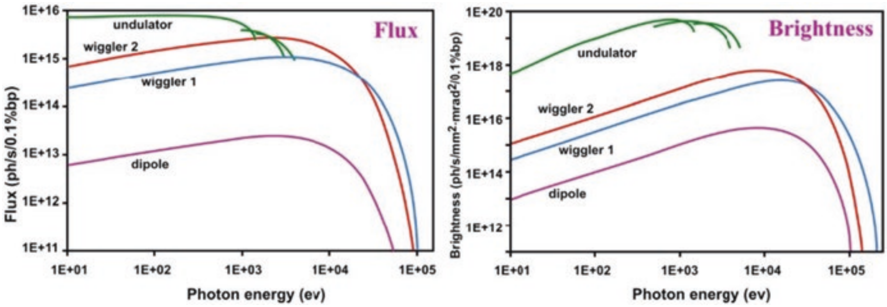

Fig. 2.2 CANDLE photon beam spectral flux (left) and brightness (right) from dipoles, undulator and two types of wigglers

The spectrums of radiation in the bending and wiggler magnets are continuous. Due to the number of magnetic poles and high magnetic field the radiation from wiggler magnets is more intensive and shifted to hard X-ray region.

In undulators, the electrons perform purely sinusoidal oscillations in weak periodic magnetic fields. The radiation cones emitted during each oscillation period overlap and interfere, thus, the intensity of undulator radiation is much higher than for wigglers and bending magnets. The radiation wavelength is given by the undulator period length reduced by a factor due to Lorentz contraction and the Doppler effect. Thus, for the cm's undulator period length the radiation wavelength is in VUV and soft X-Ray regions. The synchrotron radiation is linear polarized in the plane of acceleration. The radiation observed above or below the midplane has an elliptical polarization. The circular polarized radiation can be obtained by using helical undulators, where the electrons move on spiral trajectory. More details about the electron beam physics and synchrotron radiation characteristics can be found elsewhere (Duke, 2000; Hoffmann, 2004; Wiedemann, 1999; Wiedemann, 2003).

2.3 Experimental Techniques

The unique properties of the synchrotron radiation: broad spectrum, high spectral flux and brightness, tunability, polarization and the pulsed structure, make this type of radiation a powerful tool for experimentalists to study the micro-world. The radiation spectrum covering the range of dimensions from atomic level to biological cells makes synchrotron radiation very effective for research in physics, biology, medicine, chemistry, material and environmental sciences by selecting the wavelength required for the particular experiment. Figure 2.3 presents the general schematic layout of a typical synchrotron radiation beamline, that consists of source (dipole, wiggler or undulator magnets), optics that guides the radiation to the sample and detector (Abashian, 2002).

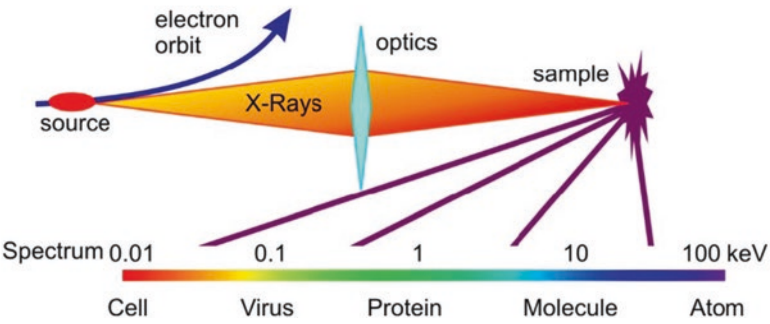

Fig. 2.3 Schematic layout of the of synchrotron radiation beamline

The complexity of the fields under consideration (DNA and ligands, proteins and nucleic acids, chemical dynamics, crystal structure etc) requires a complete description of the sample properties and the state that includes four primary characteristics: namely the energy, momentum, position and dynamics. The corresponding techniques that realize these features using synchrotron radiation are the spectroscopy, scattering, imaging and time-resolved experiments (Mobilio et al., 2014; Willmott, 2011; Winick & Doniach, 1980. The time resolved experiments exploit the pulsed structure of the synchrotron radiation for the sample study in time domain.

Spectroscopy is the technique to determine the emitted or absorbed by sample particle energy under the synchrotron light expose. This technique is used to study the characteristics of chemical bonding and electron motion. The X-ray spectroscopy technique involves: X-ray absorption spectroscopy (XAS), Extended X-ray absorption fine structure (EXAFS), Near-edge X-ray absorption fine structure (NEXAFS), X-ray absorption near-edge structure (XANES), X-ray emission spectroscopy (XES), Resonant inelastic X-ray scattering (RIXS), X-ray magnetic circular dichroism (XMCD), X-ray photoemission spectroscopy (XPS), X-ray fluorescence spectroscopy (XFS).

Scattering observes the diffracted light pattern of a sample as a function of incident and scattered angle, polarization, and wavelength. This technique provides information about the material structure, chemical composition and physical properties. The X-ray scattering technique involves: X-ray diffraction (XRD), X-ray powder diffraction, X-ray standing wave (XSW), multi-wavelength anomalous diffraction (MAD), Small-angle X-ray scattering (SAXS), X-ray Raman scattering, inelastic X-ray scattering (IXS), X-ray emission scattering (XES).

Imaging is a technique to determine sample image with the fine special resolution and is used for visualizing cellular structures in a wide range of biological and medical studies. This technique involves: X-ray diffraction imaging (XDI), diffraction enhanced imaging (DEI), scanning transmission X-ray microscopy (STXM), X-ray tomography and topography, phase contrast imaging, photoelectron emission microscopy (PEEM), computer-aided tomography (CAT), X-Ray lithography.

The beamlines and corresponding instrumentation are an integrated part of the synchrotron light facility design, that define the quality of the machine and efficiency of photon source usage. As an example, the first group of the CANDLE project beamlines implies the General Diffraction and Scattering Beamline from dipole source, X-ray Absorption Spectroscopy Beamline from dipole, Soft X-ray Spectroscopy Beamline from undulator, Imaging and Small Angle X-ray Scattering Beamlines from the wigglers.

General Diffraction and Scattering Beamline. The beamline is based on the dipole source and aimed to produce focused or unfocused tunable hard X-rays (5-30 keV) sequentially serving two experimental stations: 1- for structural study of low or high temperature polycrystalline materials, thin films and multi-layers; 2 - for single crystal structure determination, charge density studies and anomalous dispersion experiments. Figure 2.4 presents the schematic layout of the beamline optical elements (mirrors and double crystal monochromator-DCM).

A 10 keV photon beam profile simulation along the beamline is given in Fig. 2.5. The initial beam (a), the beam reflected by the mirror M1 (b), the focused beam after the DCM (c) and the focused beam at the end station (d) are shown. The simulations are performed by ray tracing code SHADOW (Sanchez del Rio et al., 2011).

XAS Beamline. The XAS beamline will cover a photon energy range up to 35 keV with sufficient intensity in soft X-ray region. The spectrum covers the K edges of elements such as Si, S, P and Cl, which are of high technical interest. Using double crystal monochromator and gold coated reflection mirror, the beamline will be able to operate in hard X-ray region allowing users to measure EXAFS of all elements either at K or L3 edges.

Imaging Beamline. Using the radiation from 3 T permanent wiggler this beamline will provide a high flux "white" or tuneable monochromatic coherent radiation in 6–120 keV photon energy range at about 150 m from the source. The experimental program will include: phase contrast and diffraction-enhanced imaging; hard X-ray microscopy; holographic imaging and tomography; micro-focusing; X-ray topography, diffractometry; micro-fluorescence and high resolution inelastic scattering.

SAXS Beamline. The beamline utilizes a non-destructive method to study the nanoscale structure of any type of material ranging from new composite nanosystems to biological macromolecules. The primary elements of the beamline include

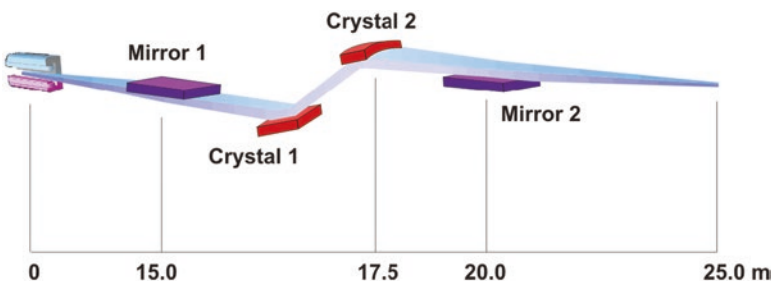

Fig. 2.4 Schematic layout of the diffraction and scattering beamline

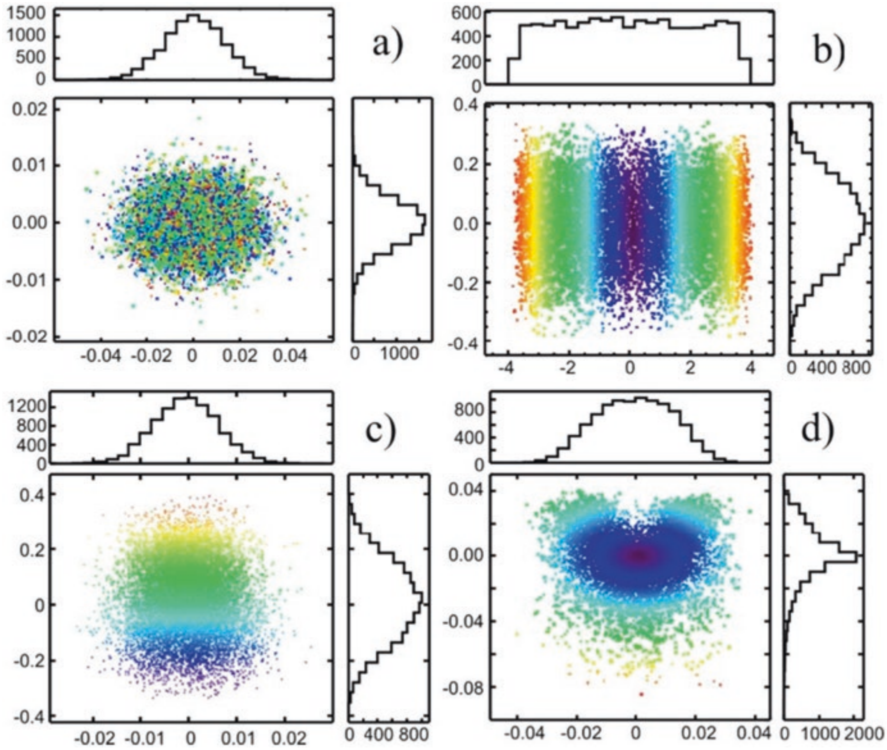

Fig. 2.5 The spatial distribution of photon beam along the general scattering and diffraction beamline

a pin-hole geometry X-ray scattering camera, high resolution and high heat load monochromators.

Soft X-ray Spectroscopy Beamline. The high brightness photon beam from the undulator will support this beamline addressing complex problems in materials, environmental and biological sciences. The beamline implies two types of microscopes: a zone plate based scanning transmission X-ray microscope and a photoelectron emission microscope.

2.4 Applications in Life Sciences

Synchrotron radiation usage in life sciences is one of the most propounded applications in synchrotron light facilities. Application fields include a wide range of diverse branches in biology, medicine, chemistry, ecology, food, pharmacology etc.

Medical imaging and radiation therapy. The use of synchrotron radiation in medical research has become an important application field at synchrotron radiation facilities (Ando & Uyama, 1998; Bravin, 2007; Suortti & Thomlinson, 2003). The high brightness, tunability and coherence distinguish these sources from standard clinical and research instruments. The highlights for medical therapy and diagnosis by synchrotron radiation usage include:

- Angiography
- Bronchography
- Mammography
- Computed Tomography
- Microbeam Radiation Therapy
- Photon Activation Therapy

The high brilliance and tunability of synchrotron X-ray beams can dramatically improve the speed, clarity and safety of diagnostic tools, such as coronary angiography. The coronary angiography is an X-ray procedure in which coronary vessels are made visible through the injection of iodine as a contrast medium. Two monochromatic beams with an energy above and below the K-absorption edge of iodine at 33.17 KeV are used to record two images simultaneously. The difference image of arteries is greatly enhanced allowing usage of much lower iodine concentrations and lower X-ray doses, compared to conventional angiography. With such low iodine level, the contrast agent can safely be introduced through an arm vein. Monochromatic X-rays of sufficient intensity to visualize coronary arteries with an extremely low iodine mass density are only provided by synchrotron radiation.

Macromolecular Crystallograph. A macromolecular crystallography is dedicated to the determination of the 3-dimensional structure of large biological molecules using X-ray diffraction (Drenth, 2006; Helliwell, 2005). The scientific and application research of macromolecular crystallography using synchrotron radiation include a broad fields of life sciences like:

- Enzyme Mechanism
- Supra-molecular structure
- Molecular Recognition
- Nucleic Acids
- Structural Genomics
- Drug design

The synchrotron radiation is an effective instrument to study the structures of DNA, RNA, or large molecular assemblies, such as ribosomes and viruses. After sequencing the human genome, the next scientific challenge is to elucidate the structure and function of the proteins encoded by the genes. Following November 21, 2017 Protein Data Bank (http://www.rcsb.org/pdb), the number of biological macromolecular structures (proteins, DNA, RNA and protein nucleic acid complexes) deposited are 135,600 (Fig. 2.6), from which more than 90% have been deposited using synchrotron radiation.

The knowledge about these structures has profound implications for overall understanding of life processes in general and for the understanding and treatment of disease. The results of high-resolution structure analyses extracted from X-ray diffraction studies of macromolecular crystals provide invaluable information for modeling drug-receptor binding.

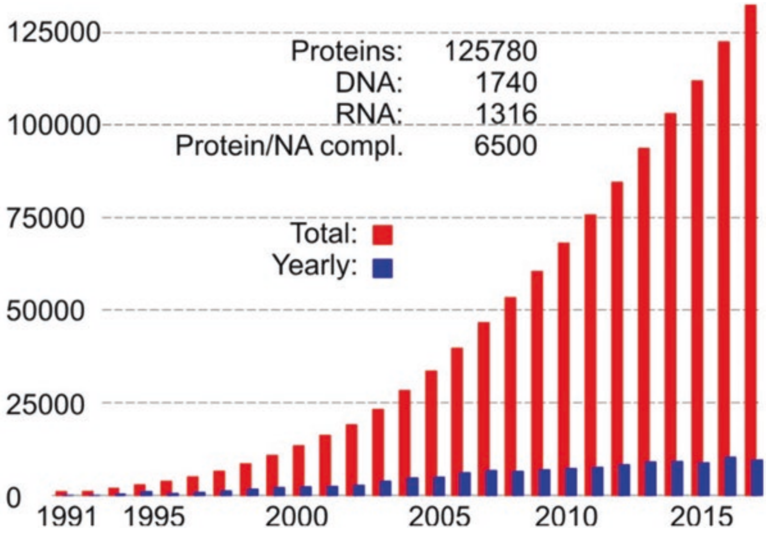

Fig. 2.6 Yearly growth of deposited macromolecular structures. Protein Data Bank, 21 November 2017

Because proteins are large and flexible, protein crystals tend to be small, imperfect, and weakly diffracting compared to crystals of small molecules. The intensity of the synchrotron beam allows data to be collected from the weakly diffracting protein crystals. The well-collimated X-ray beams can be focused to a size comparable to that of the samples used, typically on the order of 10–100 mm. Collimation can also be particularly important for crystals with large cell dimensions where separation of reflections on the detector can be difficult.

Another significant advantage of synchrotron radiation is that it provides the opportunity to select the energy of the X-ray beam. Tunability allows to perform experiments that utilize the small variations in the intensity of diffracted reflections at different energies due to the resonant scattering of a heavy atom. Two popular techniques: SAD (single-wavelength anomalous dispersion) phasing and MAD (multi-wavelength anomalous dispersion) phasing rely on this effect.

Environmental sciences. Many spheres of human activity are result in negative impact on the environment. Among them, it is necessary to mention the chemical industry, which can be a source of highly toxic xenobiotics; civil and weapon nuclear technologies - source of radionuclides; metallurgy - source of heavy metals; transport - products of fuel combustion; agriculture - pesticides and fertilizers. All these compounds enter the human organism through water, air or food. Many of them are already dangerous at very low concentrations. The topics of environmental sciences are numerous:

- Determination of heavy metals, radionuclides, toxic organic compounds;
- Investigation of environmental transport and accumulation places of these contaminants;
- Investigation of their utilization, identification and dead-end products;

- Investigation of contaminants' influence on ecosystems;
- Development of tools for environment monitoring;

These problems are closely interconnected and have a strong connection with biological sciences: biochemistry, biotechnology, microbiology, etc. How and which contaminants are distributed in the environment, how these contaminants interact with soil, plants, way of their migration with ground waters, changes related to this effects are not an exhaustive list of the problems related to environmental science (De Giudici et al., 2015; Hettiarachchi et al., 2017).

The solution of these problems requires an investigation of physical, chemical, biological processes at the level of molecular scale in addition to the macroscopic one. The study should be performed both in native conditions and under the effect of contaminants. Only such comprehensive approach allows to have a complete understanding and description of the fundamental mechanisms, which underlie the processes in the environment. The experimental techniques used in synchrotron radiation application in environmental sciences involve XAS, EXAFS, XANES, XFS, SXTM and X-ray tomography.

2.5 Summary

This chapter presents a brief description of the basics of synchrotron radiation and sources, techniques and instrumentation, as well as a number of applications in the field of life sciences. Synchrotron radiation facilities, experimental methods and applications are rapidly developing areas enabling frontier research across the entire range of basic and applied sciences, and their discussion goes far beyond the scope of this chapter.

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References

Abashian, A., Aghasyan, M., Amatuni, G., Arakelyan, V., Avagyan, V., Avakian, R., Ayvazyan, V., Gagiyan, H., Grigoryan, A., Grigoryan, B., Ivanian, M., Jalalyan, V., Harutiunyan, S., Harutiunian, V., Kirakosyan, A., Khachatryan, V., Laziev, E., Martirosyan, Y., et al. (2002). Design study of CANDLE 3 GeV synchrotron light source, ASLS-CANDLE R-001-02. http://candle.am/design_report

Ando, M., & Uyama C. (Eds) (1998). Medical applications of synchrotron radiation, Springer, 200 p.

Borland M., Hettel, R. O., Leemann, S. C., & Robin, D. (2016). Accelerator physics challenges in the design of multi-bend-achromat-based storage ring, Proc. of NAPAC 2016, Chicago, USA, 278–283.

Bravin, A. (2007). The biomedical programs at the ID17 beamline of the ESRF. In V. Tsakanov & H. Wiedemann (Eds.), *"Brilliant light in life and material sciences", NATO security through science series B; physics and biophysics* (pp. 225–239). Springer.

De Giudici, G., Lattanzi, P., & Medas, D. (2015). Synchrotron radiation and environmental sciences. In S. Mobilio, F. Boscherini, & C. Meneghini (Eds.), *Synchrotron radiation* (pp. 661–676). Springer.

Doniach, S., Hodgson, K., Lindau, I., Pianetta, P., & Winick, H. (1997). Early work with synchrotron radiation at Stanford. *Journal of Synchrotron Radiation, 4*, 380–395.

Drenth, J. (2006). *Principles of protein X-ray crystallography* (332 p). Springer.

Duke, P. J. (2000). *Synchrotron radiation* (251 p). Oxford University Press.

Elder, F. R., Gurewitsch, A. M., Langmuir, R. V., & Pollock, H. C. (1947). Radiation from electrons in a synchrotron. *Physical Review, 71*(11), 829–830.

Helliwell, J. R. (2005). *Macromolecular crystallography with synchrotron radiation* (595 p). Cambridge University Press.

Hettiarachchi, G. M., Donner, E., & Doelsch, E. (2017). Application of synchrotron radiation-based methods for environmental biogeochemistry: Introduction to the special section. *Journal of Environmental Quality, 46*(6), 1139–1145.

Hoffmann, A. (2004). *The physics of synchrotron radiation* (323 p). Cambridge University Press.

Jackson, J. D. (1998). *Classical electrodynamics* (3rd ed., 832 p). Wiley.

Lemke, D., & Labs, D. (1967). The synchrotron radiation of the 6-GeV DESY machine as a fundamental radiometric standard. *Applied Optics, 6*(6), 1043–1048.

Mobilio, S., Boscherini, F., & Meneghini, C. (Eds.). (2014). *Synchrotron radiation: Basics, methods and applications* (799 p). Springer.

Sanchez del Rio, M., Canestrari, N., Jiang, F., & Cerrina, F. (2011). SHADOW3: A new version of the synchrotron X-ray optics modelling package. *Journal of Synchrotron Radiation, 18*, 708–716.

Sargsyan, A., Zanyan, G., Sahakyan, V., & Tsakanov, V. (2016). Sub-nm emittance lattice design for CANDLE storage ring. *Nuclear Instruments and Methods A, 832*, 249–253.

Suortti, P., & Thomlinson, W. (2003). Medical applications of synchrotron radiation. *Physics in Medicine and Biology, 48*(13), R1–R35.

Tsakanov, V., et al. (2002). CANDLE: A new project for 3 GeV intermediate energy light source in the Republic of Armenia. *The Review of Scientific Instruments, 73*(3), 1411–1413.

Wanzenberg, R., et al. (2017). Research activities towards a conversion of PETRA III into a diffraction limited synchrotron light source, Proc. of IPAC 2017, Copenhagen, Denmark, 3077–3080.

Wiedemann, H. (1999). *Particle accelerator physics* (Vol. 1,2). Springer.

Wiedemann, H. (2003). *Synchrotron radiation* (274 p). Springer.

Williams, G. P., & Winick, H. (2015). Introduction to the special issue on pioneers in synchrotron radiation. *Synchrotron Radiation News, 28*(4), 2–3.

Willmott, P. (2011). *An introduction to synchrotron radiation. Techniques and applications* (352 p). Wiley.

Winick, H. (Ed.). (1994). *Synchrotron radiation sources – A primer* (507 p). World Scientific.

Winick, H., & Doniach, S. (Eds.). (1980). *Synchrotron radiation research* (754 p). Plenum Press.