Chapter 6.14

LASE: *Logiciel d'Analyse des Spectres Expérimentaux*

Emmanuel Curis*

Laboratoire de Biomathématiques, EA 7537 BioSTM, Faculté de Pharmacie de Paris, Université Paris Descartes, Paris, France. *Correspondence e-mail: emmanuel.curis@parisdescartes.fr

LASE (http://xlase.online.fr) is XAS analysis software that pays special attention to the handling of statistical and systematic errors. Once estimated, statistical errors are propagated across all analysis steps and can be used in the fitting process, both as an (optional) weighting scheme and to obtain the distribution of the fit parameters. The influence of systematic errors is investigated through experiment simulation, adding one or several sources of such errors. *LASE* also provides a graphical interface to build and visualize the structural model used in *FEFF*6 simulations and in the fitting process, and tools to deal with XAS cartography experiments.

1. Overview of *LASE*

LASE, which stands for *Logiciel d'Analyse des Spectres Expérimentaux* (Experimental Spectra Analysis Software in English), was initially written to provide XAS users in the French bioinorganic chemistry and biology communities with user-friendly yet powerful software to analyse XAS data. It is available, as C source code, for computers based on Unix/X Windows and requires an OpenGL library (such as the MESA GL library) and the GNU scientific library in order to be fully functional. Links to the official websites to obtain these packages are given on the *LASE* website; however, the native packages provided with major Linux distributions should work.

The main functionalities related to XAS analysis will be summarized before a more detailed presentation of some of the unique features of *LASE*. *LASE* offers several generic possibilities that will not be described here. It can be downloaded at http://xlase.online.fr.

Use of *LASE* is based on the 'graph' concept: a graph is a set of (x, y) couples, with x being a real value and y being either a real value (for most applications) or a complex value (for Fourier transforms), associated with additional information (name, legends, units *etc.*) and a *type* that determines the data-analysis options available. *LASE* can handle as many graphs, of any size, as needed for an analysis, as long as sufficient memory is available. The user sees the graphical representation of the (x, y) couples; operations on graphs give new graphs.

1.1. Experimental data

Experimental data files can be imported as one or several graphs. A generic import function from delimited text files exists. For some beamlines (mainly at ESRF and SOLEIL), special import functions allow single-step preprocessing of the data, such as detector averages for multi-detector fluorescence experiments. Functions for other beamlines can be added by

editing the C source code, which is freely available and modifiable.

1.2. Data reduction

LASE offers tools to graphically extract the EXAFS oscillations from raw data from transmission or fluorescence detection, normalize them and filter them using forward and backward Fourier transformation. Background removal (matrix contribution, μ_m, and isolated atom absorption, μ_0) is based on the four-step algorithm described in Kuzmin (1995), as used in the *EDA* package (Kuzmin, 2024), with additional functional forms for μ_m and real-time visual checking of the consequences of removal on the Fourier transform. Briefly, μ_m is modelled by a Victoreen model, a straight line or a low-order polynomial, whereas μ_0 is modelled by a polynomial in E-space and then corrected by a polynomial in k-space followed by a spline in k-space. Normalization can be performed using either the experimentally obtained μ_0 or theoretical cross-sections: *LASE* is provided with tabulated values for Victoreen (MacGillavry *et al.*, 1985), McMaster *et al.* (1970) and Ebel *et al.* (2003) models to compute them, but any $[E, \mu_0(E)]$ graph can be used. Although automatic removal of low-frequency peaks in R-space (Newville *et al.*, 1993) is not implemented, real-time visual inspection of the Fourier transform during the background-extraction process allows this peak to be minimized without removing too much intensity from the main peak.

Besides the manual extraction of EXAFS oscillations, semi-automatic extraction can be performed either with predefined parameters or by optimizing the results of superposition for a family of graphs.

1.3. Model fitting to the data

LASE allows EXAFS oscillations to be fitted in k-space using weighted or unweighted least squares. Amplitudes and phase shifts must be provided, either extracted from reference compounds or theoretically computed using *FEFF*6 (Zabinsky *et al.*, 1995). Fit quality is checked graphically and using the usual fit criteria based on the squared sum of differences between the data (y) and the model (y^*) (see Booth, 2024): the absolute sum of squares $\sum_{i=1}^{n}(y_i - y_i^*)^2$, the absolute weighted sum of squares $\sum_{i=1}^{n}[(y_i - y_i^*)/s_i]^2$ (where s_i is the standard deviation of y_i) and their counterparts expressed after division by the total number of points or the number of points minus the number of fit parameters. *LASE* also warns when unusual values are obtained, based on user-defined bounds for each fitted parameter, or if the number of fitted parameters exceeds the Shannon–Nyquist theorem limit.

1.4. Structural model visualization

Fitting is based on the scattering paths model, as used in *FEFF*6. *LASE* offers tools to import and visualize the structural part of the model, such as Protein Data Bank (PDB) file format import. For crystalline samples, *LASE* knows the 230 space groups described in Volume A of *International Tables for Crystallography*. After selecting the excited atom, a *FEFF* input file can be constructed. *FEFF* paths can be viewed in the structural model and similar paths can be averaged.

1.5. Handling maps

Besides graphs, *LASE* can handle maps that are their 2D equivalents. This allows XAS mapping experiments to be visualized, analysed and simulated in *LASE*.

2. Handling experimental errors

LASE was developed to provide a complete handling of experimental errors. The influence of both statistical and systematic errors can be studied using disjoint but complementary sets of tools.

2.1. Statistical error estimation and propagation

Each graph (x, y) can be associated with a graph containing standard deviations for x or y or both values, and associated degrees of freedom. Since these graphs can be user-defined, any method to estimate error bars described in Booth (2024) may be used. However, the standard way to obtain them is to average a set of experimental spectra and associate with each point of the average the usual unbiased variance estimator, $s_i^2 = [1/(n_i - 1)] \sum_{j=1}^{N}[y_{i,j} - (1/n) \sum_{k=1}^{N} y_{i,k}]^2$, where n_i is the number of available values of (x_i, y_i) couples (typically, the number of spectra) associated with $n_i - 1$ degrees of freedom.

If a graph has error bars, any operation performed on the graph will also be performed (after suitable adaptation) on its error bars, so the result also has error bars. This is achieved using the error-propagation theorem, which states that if $\mathbf{X}$ is a random vector with expectation $\mu_{\mathbf{X}}$ and covariance matrix $\Sigma_{\mathbf{X}}$ then, if the first-order Taylor expansion of f around $\mu_{\mathbf{X}}$ holds, the random vector $\mathbf{Y} = f(\mathbf{X})$ has covariance matrix $\Sigma_{\mathbf{Y}} = \mathbf{J}_f(\mu_{\mathbf{X}})\Sigma_{\mathbf{Y}}\mathbf{J}_f^{\mathrm{T}}(\mu_{\mathbf{X}})$, where $\mathbf{J}_f$ is the Jacobian matrix of f. The result is exact for linear transformations, such as all background-removal and Fourier-transform steps (Curis & Bénazeth, 2000), and is approximated otherwise. If needed, complete covariance matrices are constructed, as in Fourier-transform steps.

Error bars can be used as weights in the least-squares fit. Assuming a normal distribution of the errors, this corresponds to a maximum-likelihood fit.

Two methods can be used to obtain the fit-parameters covariance matrix based on these error bars. Firstly, the covariance matrix can be obtained as the inverse of the Hessian matrix of the fit, which is appropriate in maximum-likelihood fits and hence if error bars were used as weighting. Secondly, the error bars can be used to perform Monte Carlo simulations by generating pseudo-experimental spectra and fitting them, leading to a nonparametric covariance matrix (semi-parametric bootstrap, see Curis & Bénazeth, 2005; for an example of its application, see Curis *et al.*, 2012).

2.2. Systematic error simulation

LASE can simulate an X-ray absorption spectroscopy experiment, in transmission or fluorescence mode, by defining

the sample, beam and detector characteristics. Effects such as spatial or energetic beam inhomogeneity, sample inhomogeneity and detector nonlinearity can be included in the simulation if the user provides suitable information (for instance, graphs of detector response for detector nonlinearity, maps of beam intensities for beam spatial heterogeneity *etc.*). In fluorescence mode, self-absorption is handled by the simulation code; see Curis, Osán *et al.* (2005) for details of the simulation algorithm. Briefly, the sample is approximated by a rectangular parallelepiped with regular voxels, each with its own absorption coefficient. A punctual beam, either incident or fluoresced, is then propagated along all of the voxels that it crosses and at each step its intensity is corrected for the absorption by the voxel (and the voxel then fluoresces at several energies according to the fluorescence yields). By integration over all voxels, this gives the simulated signal, which is then transformed using the detector characteristics. Non-punctual beams are seen as a set of punctual beams placed on a rectangular grid, each with its own intensity, and integration is performed on all of these beams.

By assigning theoretical or experimental absorption coefficients to the sample in the simulation, the influence of any systematic effect from the experiment on the measured spectrum can be estimated (for an application to grain-size effects in fluorescence, see Curis, Osán *et al.*, 2005). Coupling to the fitting procedure above allows an estimation of the systematic error-induced bias on the fitted parameters. Note that this does not cover systematic errors in the theoretical absorption coefficient computation used as the basis for the simulation, only systematic errors introduced by the experimental setting.

The effects of systematic errors on *ab initio* amplitude and phase shifts may be explored either by using different computation options or, to a lesser extent, when using real structural data and the path quasi-equivalence, changing the combined path amplitude and phase from the shortest to the longest path of the combination.

3. Conclusion

Compared with other XAS analysis packages, *LASE* presents a set of novel approaches that may prove to be useful in EXAFS analysis. These include the following.

(i) Complete handling of statistical uncertainties, with propagation through all data-extraction steps, including Fourier transform.

(ii) Use of a trapezoidal approximation of the Fourier transform, which avoids interpolation of the data on a constant step grid and allows error propagation.

(iii) 3D visualization of structural models and scattering paths, with tools to simplify *FEFF* models obtained from crystallographic data.

(iv) Monte Carlo simulations to estimate uncertainties in the fitted parameters.

(v) Experiment simulation to evaluate the influence of systematic effects.

LASE has successfully been used in several applications related to biology and bioinorganic chemistry: the degradation of hydroxyapatite-based bone implants (Chassot *et al.*, 2001), the degradation of platinum-based antitumor drugs (Curis *et al.*, 2000, 2001), the study of an arsenide-based medication for leukaemia (Nicolis *et al.*, 2002; Curis, Nicolis *et al.*, 2005), the development of a copper-based medication for Menkes disease (Deschamps *et al.*, 2003), and studies of gadolinium complexes used in magnetic resonance imaging (Agondanou *et al.*, 2007) and ruthenium-based antimalarial complexes (Curis *et al.*, 2012). Other fields have also used LASE, such as solid-state chemistry (Laget *et al.*, 2003).

References

Agondanou, J.-H., Nicolis, I., Curis, E., Purans, J., Spyroulias, G. A., Coutsolelos, A. G. & Bénazeth, S. (2007). *Inorg. Chem.* **46**, 6871–6879.

Booth, C. H. (2024). *Int. Tables Crystallogr. I*, ch. 5.8, 672–675.

Chassot, E., Oudadesse, H., Irigaray, J., Curis, E., Bénazeth, S. & Nicolis, I. (2001). *J. Appl. Phys.* **90**, 6440–6446.

Curis, E. & Bénazeth, S. (2000). *J. Synchrotron Rad.* **7**, 262–266.

Curis, E. & Bénazeth, S. (2005). *J. Synchrotron Rad.* **12**, 361–373.

Curis, E., Dubar, F., Nicolis, I., Bénazeth, S. & Biot, C. (2012). *J. Phys. Chem. A*, **116**, 5577–5585.

Curis, E., Nicolis, I., Bohic, S., Somogyi, A., Simionovici, A. & Bénazeth, S. (2005). *Phys. Scr.* **2005**, 870.

Curis, E., Osán, J., Falkenberg, G., Bénazeth, S. & Török, S. (2005). *At. Spectrosc.* **60**, 841–849.

Curis, E., Provost, K., Bouvet, D., Nicolis, I., Crauste-Manciet, S., Brossard, D. & Bénazeth, S. (2001). *J. Synchrotron Rad.* **8**, 716–718.

Curis, E., Provost, K., Nicolis, I., Bouvet, D., Bénazeth, S., Crauste-Manciet, S., Brion, F. & Brossard, D. (2000). *New J. Chem.* **24**, 1003–1008.

Deschamps, P., Zerrouk, N., Nicolis, I., Martens, T., Curis, E., Charlot, M.-F., Girerd, J.-J., Prangé, T., Bénazeth, S., Chaumeil, J.-C. & Tomas, A. (2003). *Inorg. Chim. Acta*, **353**, 22–34.

Ebel, H., Svagera, R., Ebel, M. F., Shaltout, A. & Hubbell, J. H. (2003). *X-ray Spectrom.* **32**, 442–451.

Kuzmin, A. (1995). *Physica B*, **208–209**, 175–176.

Kuzmin, A. (2024). *Int. Tables Crystallogr. I*, ch. 6.2, 728–733.

Laget, V., Jeffcoate, C. S., Isaacs, H. S. & Buchheit, R. G. (2003). *J. Electrochem. Soc.* **150**, B425–B432.

MacGillavry, C. H., Rieck, G. D. & Lonsdale, K. (1985). *International Tables for X-ray Crystallography*, Vol. III, 2nd ed., pp. 171–173. Dordrecht: Kluwer Academic Publishers.

McMaster, W. H., Kerr Del Grande, N., Mallett, J. H. & Hubbell, J. H. (1970). *At. Data Nucl. Data Tables*, **8**, 443–444.

Newville, M., Līviņš, P., Yacoby, Y., Rehr, J. J. & Stern, E. A. (1993). *Phys. Rev. B*, **47**, 14126–14131.

Nicolis, I., Dacher, P., Guyon, F., Chevallier, P., Curis, E. & Bénazeth, S. (2002). *J. Trace Microprobe Tech.* **20**, 565–570.

Zabinsky, S. I., Rehr, J. J., Ankudinov, A., Albers, R. C. & Eller, M. J. (1995). *Phys. Rev. B*, **52**, 2995–3009.