xINTERPDF User Guide 0.1.0

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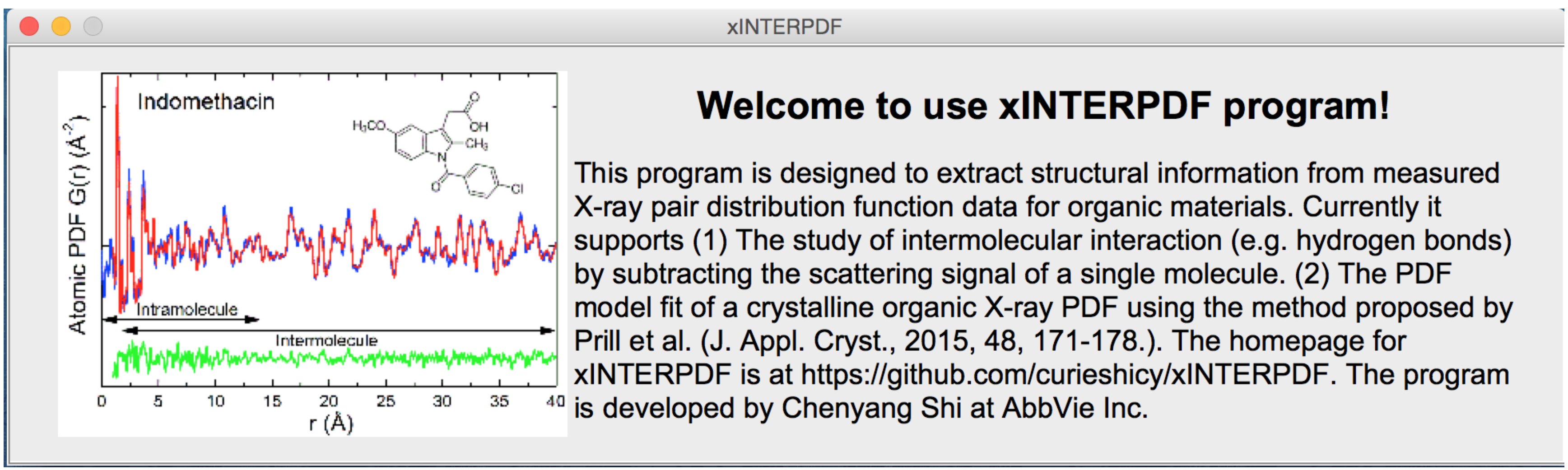
Overview

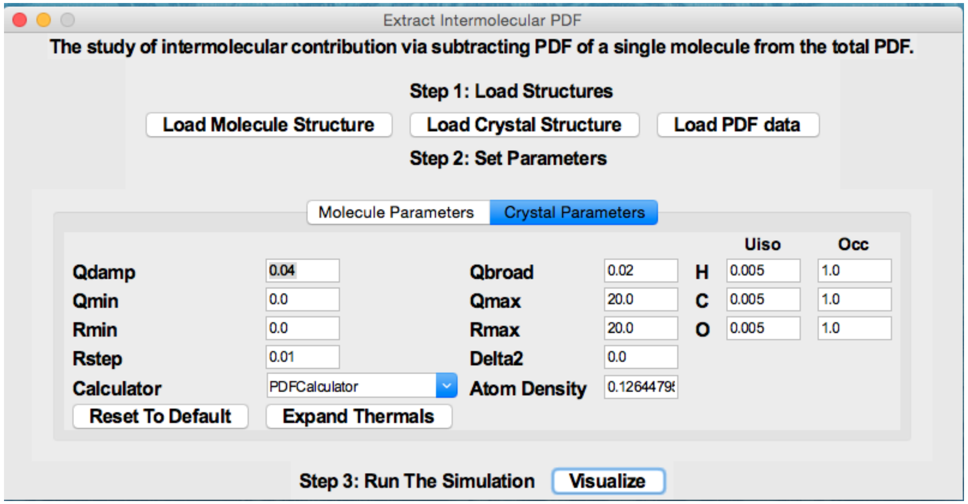
xINTERPDF is written in Python 2.7. It utilizes Tkinter and matplotlib modules for creating a Graphical User Interface (GUI) and plot visualization, and NumPy and SciPy for scientific calculations. It builds on DiffPy-CMI package (http://www.diffpy.org/products/diffpycmi/index.html) for analysis of synchrotron/laboratory X-ray total scattering data collected for organic materials. The homepage for xINTERPDF is at https://github.com/curieshicy/xINTERPDF.



Usage 1: Extracting Intermolecular PDF

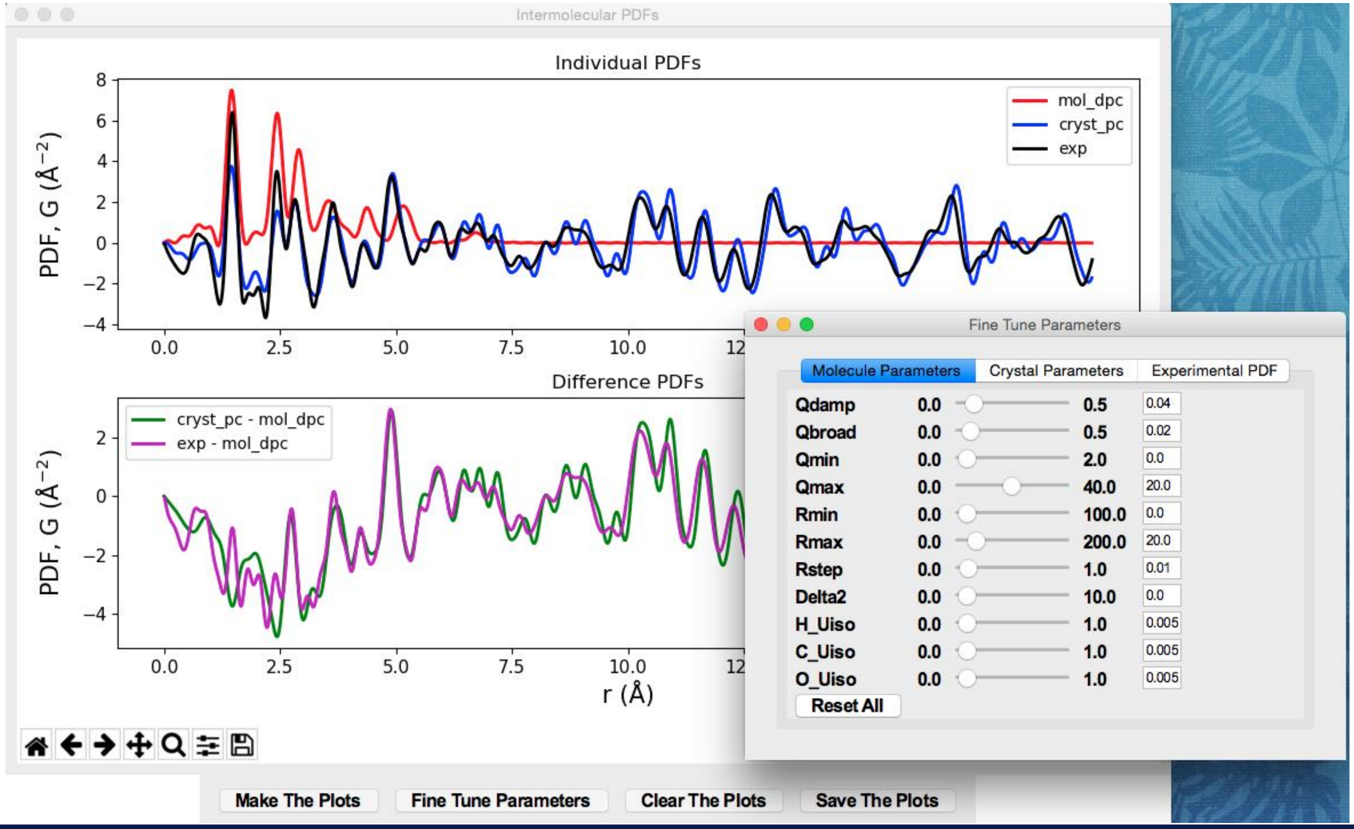
Users may use xINTERPDF to study the molecule-molecule interaction in organics. The program considers three common scenarios—the organic compound of interest is (1) crystalline (2) amorphous and (3) amorphous solid dispersion (two components). Shown below is an example when compound is crystalline, other two cases are similar.

To extract intermolecular interaction for crystalline organics, users first supply the structures for a single molecule (in xyz format) and a crystal (in cif format) and (optionally PDF data). Then in step 2, click <u>Expand Thermals</u> to bring up Uiso/Occ info. A variety of parameters for molecule and crystal will be specified by users. These include instrument parameters, thermal factors, occupancy and calculator to calculate PDF. In Step 3, hit <u>Visualize</u> to plot results.

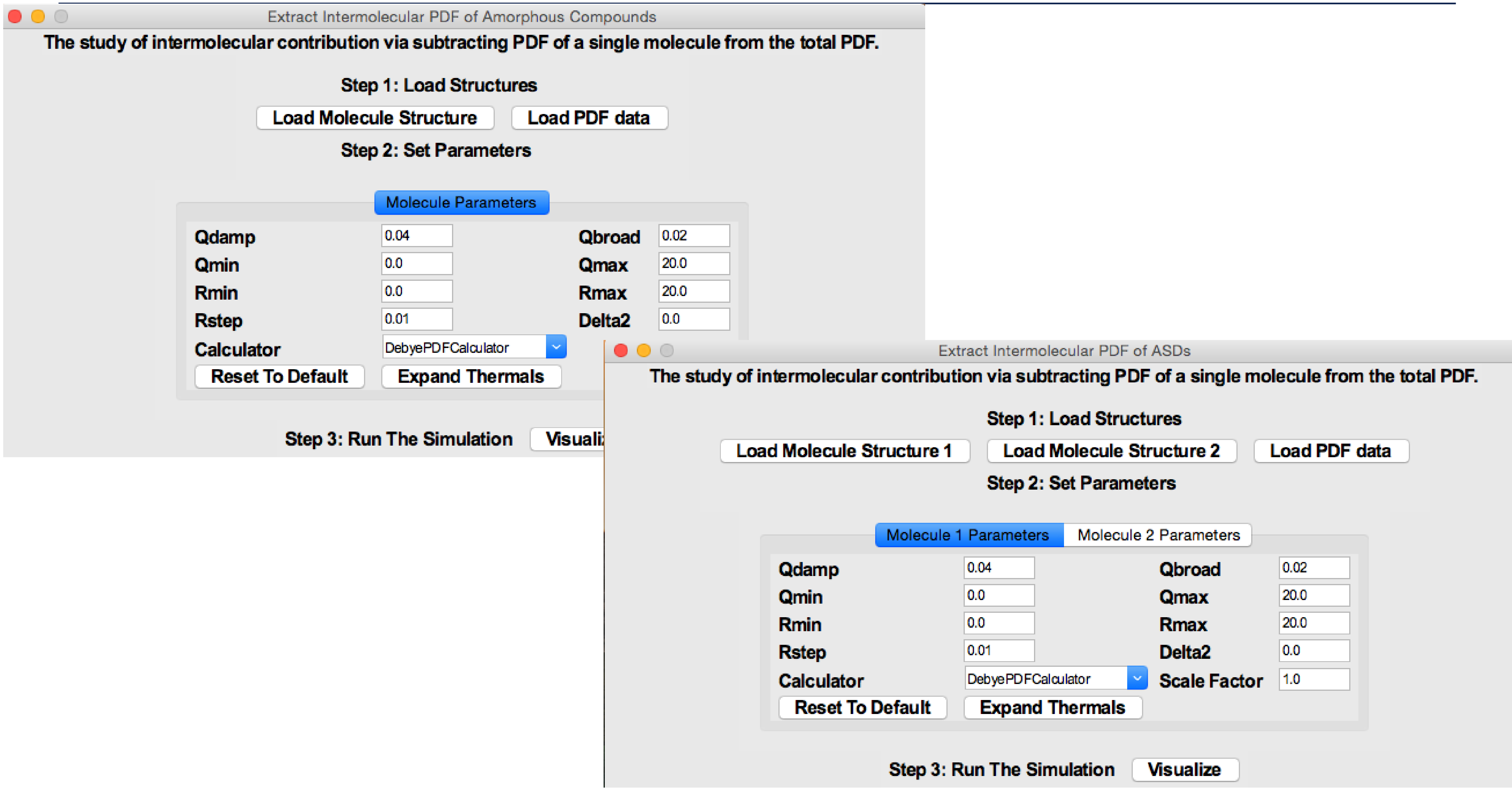


Usage 1: Extracting Intermolecular PDF

In the plot, the top panel shows the individual PDFs. In the example below, it shows the PDF (red) for molecule calculated by DebyePDFCalculator and PDF (blue) for a crystal using PDFCalculator. The experimental total PDF is shown in black. The bottom panel displays the theoretical/experimental intermolecular PDFs. Click <u>Fine Tune Parameters</u> to adjust the simulated plots. Hit <u>Save the Plots</u> to save raw data.



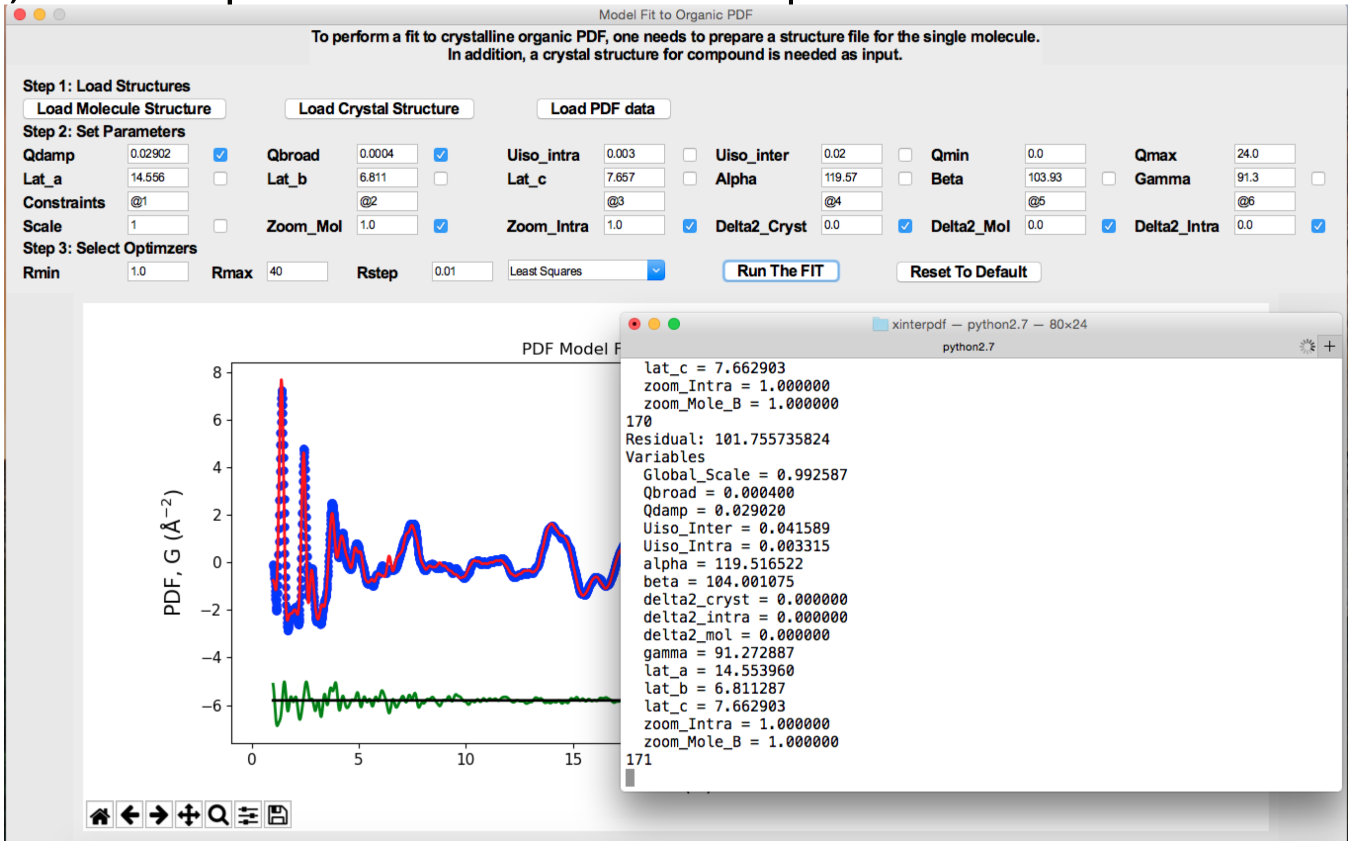
Usage 1: Extracting Intermolecular PDF



Similar to crystalline case, users can study intermolecular PDFs in amorphous compounds and amorphous solid dispersions. In both cases, only PDF(s) for molecule(s) is simulated and subtracted.

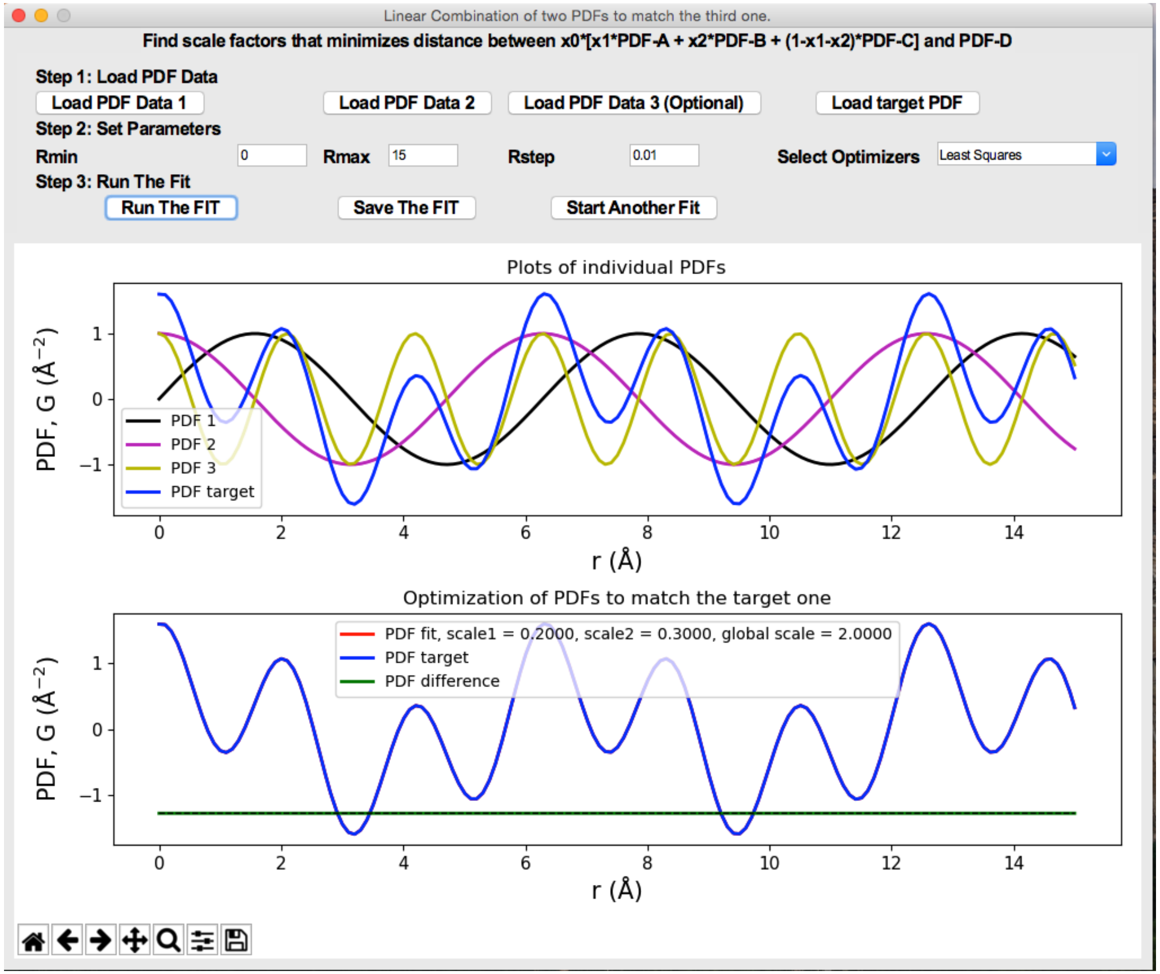
Usage 2: Model fit to organic crystalline PDF

Another capability of xINTERPDF is to perform a PDF fit to organic crystalline PDF. In Step 1, users load in structure files and PDF data. In step 2, various parameters are fixed or allowed to vary. In Step 3, the range of the fit and optimizers are further determined by users. Hit Run the FIT to start the refinement. After the fit is complete, the fit is plotted and fit results are printed on the terminal.



Usage 3: phase quantification

The program offers an easy functionality that takes in the PDFs of 2 or 3 pure materials and compares against a target PDF (e.g. physical mixture or amorphous solid dispersion of them). The scale factors are returned which encodes the info about phase fraction.



Installation

xINTERPDF can be installed on Linux and macOS 64 bit computers. The easiest way to install it is through **conda**. Here is an example of installing it on macOS 10.10.3.

(1) Download Anaconda Distribution for macOS at https://www.anaconda.com/download/?lang=en-us#macos. Select Python 2.7 version to install.

(2) Invoke a terminal, type **conda config --get channels** to check any channels that have been added. diffpy and xinterpdf are required. If you don't see both, type **conda config --add channels diffpy** and **conda config --add channels xinterpdf** to add them.

```
Chenyang — bash — 80x24
bash
Last login: Fri Feb  2 14:06:01 on ttys000
Chenyangs-MacBook-Pro:~ Chenyang$ conda -V
conda 4.3.30
Chenyangs-MacBook-Pro:~ Chenyang$ conda env list
# conda environments:
#
root                  *  /Users/Chenyang/anaconda2

Chenyangs-MacBook-Pro:~ Chenyang$ conda config --get channels
--add channels 'defaults'   # lowest priority
--add channels 'diffpy'
--add channels 'rdkit'
--add channels 'xinterpdf'   # highest priority
Chenyangs-MacBook-Pro:~ Chenyang$
```

Installation

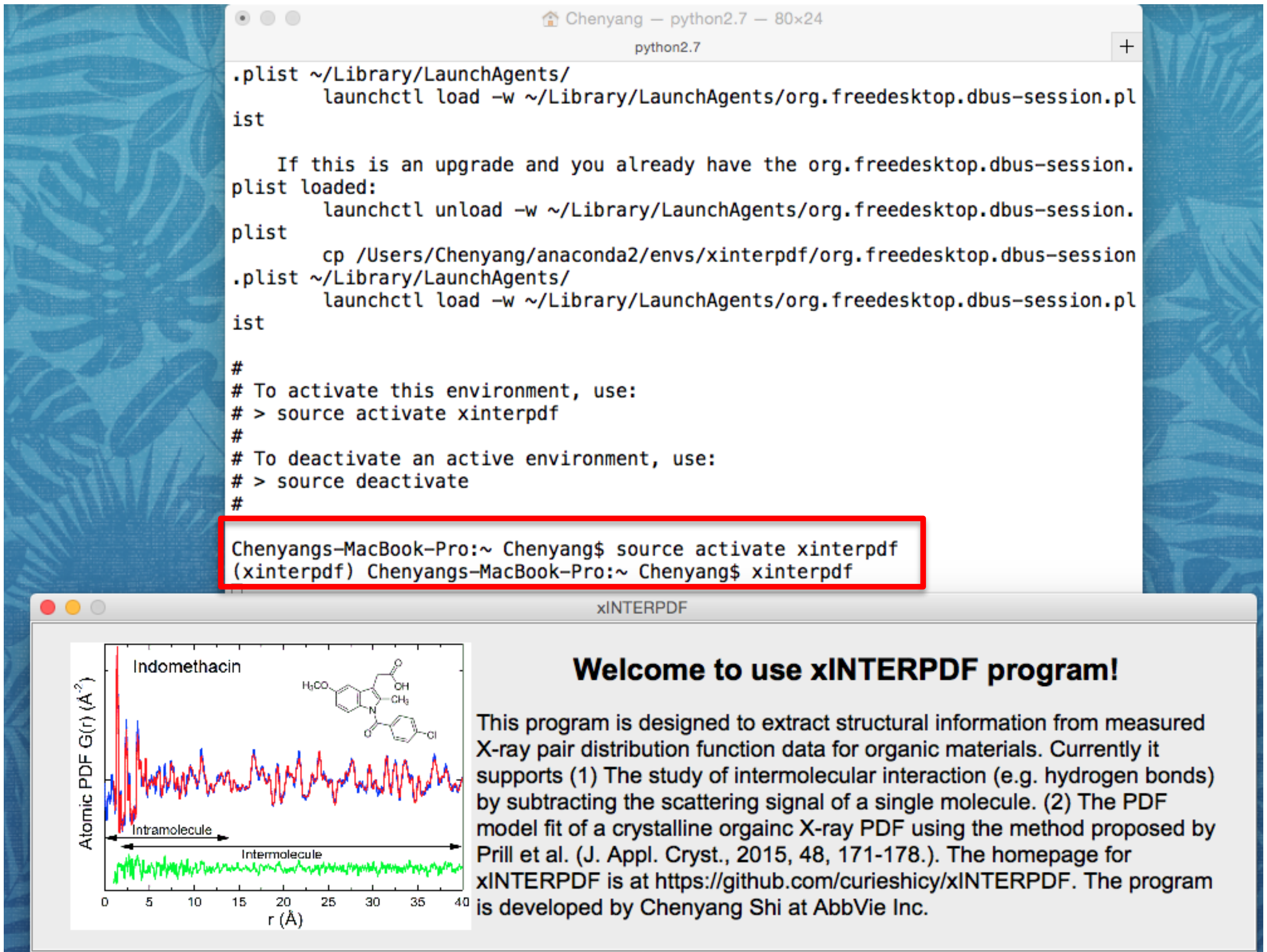
(3) Type **conda create –c curieshicy –n xinterpdf xinterpdf** to install it.

```
Chenyang — python2.7 — 100×50
python2.7
Chenyangs-MacBook-Pro:~ Chenyang$ conda create -c curieshicy -n xinterpdf xinterpdf
Fetching package metadata .......
WARNING: The remote server could not find the noarch directory for the
requested channel with url: https://conda.anaconda.org/xinterpdf

It is possible you have given conda an invalid channel. Please double-check
your conda configuration using `conda config --show`.

If the requested url is in fact a valid conda channel, please request that the
channel administrator create `noarch/repodata.json` and associated
`noarch/repodata.json.bz2` files, even if `noarch/repodata.json` is empty.
$ mkdir noarch
$ echo '{}' > noarch/repodata.json
$ bzip2 -k noarch/repodata.json
...........
Solving package specifications: .

Package plan for installation in environment /Users/Chenyang/anaconda2/envs/xinterpdf:

The following NEW packages will be INSTALLED:

    appnope:                          0.1.0-py27hb466136_0
    backports:                        1.0-py27hb4f9756_1
    backports.shutil_get_terminal_size: 1.0.0-py27hc9115de_2
    backports_abc:                    0.5-py27h6972548_0
    bleach:                           2.1.2-py27_0
    boost:                            1.61.0-py27_0
    ca-certificates:                  2017.08.26-ha1e5d58_0
    certifi:                          2018.1.18-py27_0
    configparser:                     3.5.0-py27hc7edf1b_0
    cycler:                           0.10.0-py27hfc73c78_0
    dbus:                             1.12.2-haa0f8f7_0
    decorator:                        4.2.1-py27_0
    diffpy-cmi:                       2.1-hfb420b8_0        diffpy
    diffpy.srfit:                     1.3-py27h491f910_0    diffpy
    diffpy.srreal:                    1.2-py27_0            diffpy
    diffpy.structure:                 1.3.5-py27_0          diffpy
    diffpy.utils:                     1.2.2-py27_0          diffpy
    entrypoints:                      0.2.3-py27hd680fb1_2
    enum34:                           1.1.6-py27hf475452_1
    expat:                            2.2.5-hb8e80ba_0
    freetype:                         2.8-h12048fb_1
    functools32:                      3.2.3.2-py27h8ceab06_1
    futures:                          3.2.0-py27h1b80678_0
    gettext:                          0.19.8.1-h15daf44_3
    glib:                             2.53.6-h33f6a65_2
    gsl:                              2.1-0                 diffpy
    html5lib:                         1.0.1-py27h5233db4_0
    icu:                              58.2-h4b95b61_1
    intel-openmp:                     2018.0.0-h8158457_8
```

```
Chenyang — python2.7 — 100×50
python2.7
    openssl:                          1.0.2n-hdbc3d79_0
    pandoc:                           1.19.2.1-ha5e8f32_1
    pandocfilters:                    1.4.2-py27hed78c4e_1
    pathlib2:                         2.3.0-py27he09da1e_0
    pcre:                             8.41-hfb6ab37_1
    periodictable:                    1.5.0-py27_0          diffpy
    pexpect:                          4.3.1-py27_0
    pickleshare:                      0.7.4-py27h37e3d41_0
    pip:                              9.0.1-py27h1567d89_4
    prompt_toolkit:                   1.0.15-py27h4a7b9c2_0
    ptyprocess:                       0.5.2-py27h70f6364_0
    pycifrw:                          4.3-py27_0            diffpy
    pygments:                         2.2.0-py27h1a556bb_0
    pyobjcryst:                       2.0.2-py27_2          diffpy
    pyparsing:                        2.2.0-py27h5bb6aaf_0
    pyqt:                             5.6.0-py27hf21fe59_6
    python:                           2.7.14-hde5916a_29
    python-dateutil:                  2.6.1-py27hd56c96b_1
    pytz:                             2017.3-py27h803c07a_0
    pyzmq:                            16.0.3-py27h91ccc67_0
    qt:                               5.6.2-h9975529_14
    qtconsole:                        4.3.1-py27hdc90b4f_0
    readline:                         7.0-hc1231fa_4
    scandir:                          1.6-py27h97aa1ee_0
    scipy:                            1.0.0-py27h793f721_0
    send2trash:                       1.4.2-py27_0
    setuptools:                       38.4.0-py27_0
    simplegeneric:                    0.8.1-py27h6db5e31_0
    singledispatch:                   3.4.0.3-py27he22c18d_0
    sip:                              4.18.1-py27h6300f65_2
    six:                              1.11.0-py27h7252ba3_1
    sqlite:                           3.22.0-h3efe00b_0
    srfit-sasview:                    3.1.2-py27_0          diffpy
    ssl_match_hostname:               3.5.0.1-py27h8780752_2
    subprocess32:                     3.2.7-py27h24b2887_0
    terminado:                        0.8.1-py27_1
    testpath:                         0.3.1-py27h72d81a5_0
    tk:                               8.6.7-h35a86e2_3
    tornado:                          4.5.3-py27_0
    traitlets:                        4.3.2-py27hcf08151_0
    wcwidth:                          0.1.7-py27h817c265_0
    webencodings:                     0.5.1-py27h19a9f58_1
    wheel:                            0.30.0-py27h677a027_1
    widgetsnbextension:               3.1.0-py27_0
    xinterpdf:                        0.1.0-py27ha494169_0  curieshicy
    xz:                               5.2.3-h0278029_2
    zeromq:                           4.2.2-ha360ad0_2
    zlib:                             1.2.11-hf3cbc9b_2

Proceed ([y]/n)?
```

Installation

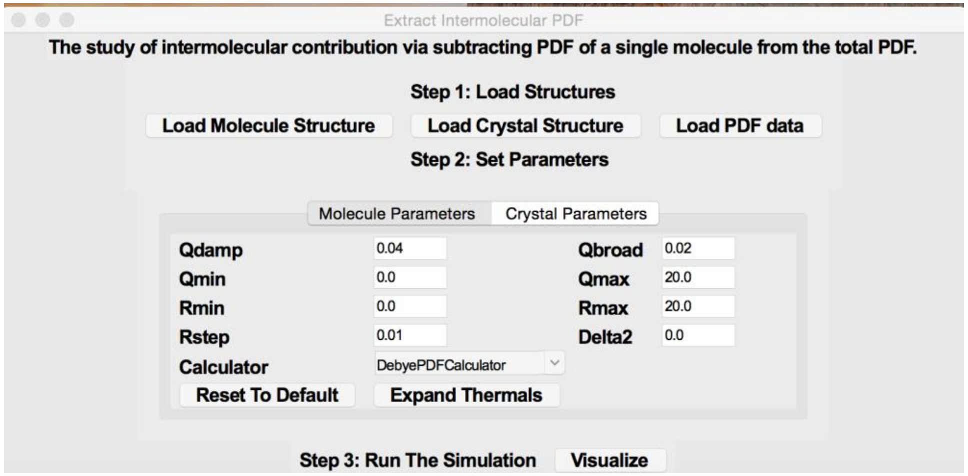
(4) Once the installation is complete. Type **source activate xinterpdf** to start the virtual environment and **xinterpdf** to invoke the main window of xINTERPDF.

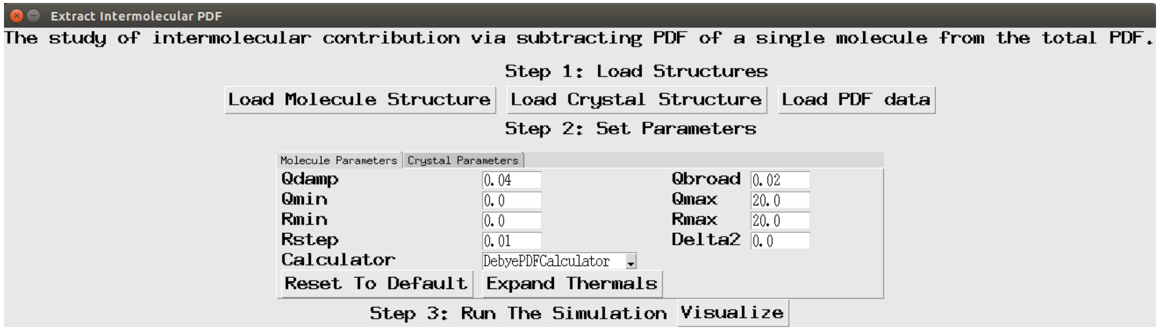


Installation (alternative)

If conda install failed, alternatively, one may download the raw files (Logo.gif and cli.py) at https://github.com/curieshicy/xINTERPDF/tree/master/Conda_Build_Recipe/xinterpdf. To start the program, in a terminal, navigate to the folder where you put both files, and type **python cli.py** to invoke the main window. Make sure you have installed Diffpy-CMI and matplotlib (2.0.2). Follow http://www.diffpy.org/products/diffpycmi/index.html to install DiffPy-CMI. If you have conda, matplotlib can be installed by **conda install matplotlib=2.0.2**.

Installation





Although xINTERPDF is distributed using the same Anaconda 2.7 across platforms (i.e. the same version for Python: 2.7.14, ttk: 0.3.1 and Tkinter: Revision 81008), the overall appearance of the GUI window in macOS 10.10.3, 64 bit (top figure) and Ubuntu 14, 64 bit (bottom figure) varies. Both platforms return consistent simulation results as expected. However, for a better user experience, as of now, it is recommended to install xINTERPDF on a macOS machine.

Technical Details

xINTERPDF uses **diffpy.srreal.pdfcalculator** module to calculate PDFs. (http://www.diffpy.org/diffpy.srreal/api/diffpy.srreal.html?highlight=pdfcalculator#diffpy.srreal.pdfcalculator.DebyePDFCalculator). Specifically PDF Calculator (PC) and Debye PDF Calculator (DPC) are used to simulate PDF in real and reciprocal spaces, respectively.

PDF Calculator (PC)

Given a unit cell, and with periodic boundary conditions applied, the PDF for a crystalline material can be calculated via

$$G(r) = \frac{1}{Nr}\sum_i \sum_{j\neq i}\left\{\frac{f_i f_j}{<f>^2}\exp\left[\frac{-(r-r_{ij})^2}{\sigma_{ij}{}^2}\right]\right\} - 4\pi r\rho_0$$

Where σ_{ij} is defined by

$$\sigma_{ij} = \sigma'_{ij}\sqrt{1 - \frac{\delta_1}{r_{ij}} - \frac{\delta_2}{r_{ij}{}^2} + Q_{broad}{}^2 r_{ij}{}^2}$$

Here, f_i, f_j and <f> are X-ray form factor for species i and j, and average value weighted by concentration. N is the number of atoms in the unit cell. ρ_0 is the atomic density. σ'_{ij} is the root mean squared displacement coming from the atomic displacement parameters (ADP) tensors of the atom-pair. δ_1 and δ_2 are corrections that can be separately used to account for correlated atomic motion and Q_{broad} is an instrumental broadening factor coming from the finite Q resolution of the experiment.

Debye PDF Calculator (DPC)

When using DPC to calculate PDF, first the reduced structure factor, F(Q), defined as Q[S(Q)-1], is calculated by Debye sum* and then it is Fourier transformed to obtain PDF, G(r). The relevant equations are listed below.

$$F(Q) = \frac{1}{N\langle f(Q)\rangle^2} \sum_{i,j} f_i(Q) f_j(Q) \frac{\sin Q r_{ij}}{r_{ij}} \exp\left[-\frac{1}{2}\,\sigma_{ij}^2\, Q^2\right]$$

$$F(Q) = Q[S(Q) - 1]$$

$$G(r) = \frac{2}{\pi} \int_{Q_{min}}^{Q_{max}} Q[S(Q) - 1] \sin(Qr) dQ$$

$$\sigma_{ij} = \sigma'_{ij} \sqrt{1 - \frac{\delta_1}{r_{ij}} - \frac{\delta_2}{{r_{ij}}^2} + {Q_{broad}}^2 {r_{ij}}^2}$$

Using DPC one can calculate PDF from any structure given known coordinates (typically in xyz format).

*Debye, P. (1915). *Ann. Phys.* **351**, 809-823.

More details see Chapter 3 of *Underneath the Bragg peaks: Structural Analysis of Complex Materials*, 2nd ed.; Elsevier: Amsterdam, The Netherlands, 2013.

Explanation of parameters

Q_{damp}: PDF Gaussian dampening envelope due to limited Q-resolution. Not applied when equal to zero. The Gaussian envelope is of the form

$$B(r) = e^{-\frac{(rQ_{damp})^2}{2}}$$

Q_{broad}: PDF peak broadening from increased intensity noise at high Q. Not applied when equal zero.

Delta 2: Coefficient for ($1/r^2$) contribution to the peak sharpening.

Q_{min}:

-PC: Lower bound of the experimental Q-range used. Affects the shape envelope.

-DPC: Lower bound of the Q-grid for the calculated F(Q). Affects the shape envelope.

Q_{max}:

-PC: Upper bound of the experimental Q-range used. Affects the termination ripples. Not used when is set to zero.

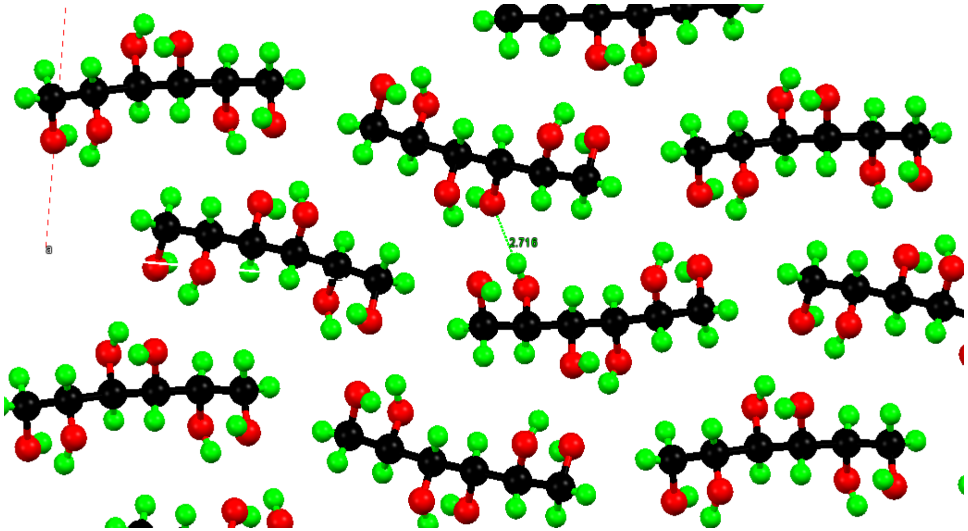
-DPC: Upper bound of the Q-grid for the calculated F(Q). Affects the termination ripples.

R_{min}: Lower bound of the r-grid for PDF calculation

R_{max}: Upper bound of the r-grid for PDF calculation.

R_{step}: Spacing in the calculated r-grid. r-values are at the multiples of rstep.

Example 1: Hydrogen bonds in D-mannitol



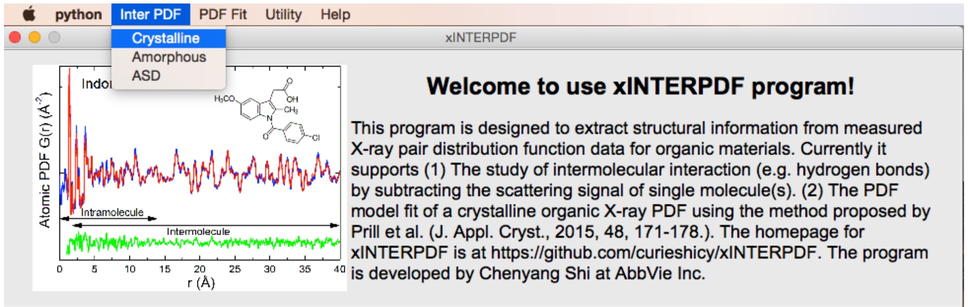
D-mannitol is a polyalcohol with rich hydrogen bonds. Based on its room temperature (283-303 K) structure as reported by Kim et al, the nearest O…O bond distance is ~2.72 Å.

Synchrotron X-ray total scattering was conducted on D-mannitol powder sample at 300 K. From a fit to PDF of cerium oxide, the instrumental resolution parameters are determined: Q_{damp}=0.02902 Å^{-1}, Q_{broad}=0.0004 Å^{-1}. A Q_{max} of 24 Å^{-1} was used for Fourier transform. The software program PDFgetX2 was used.

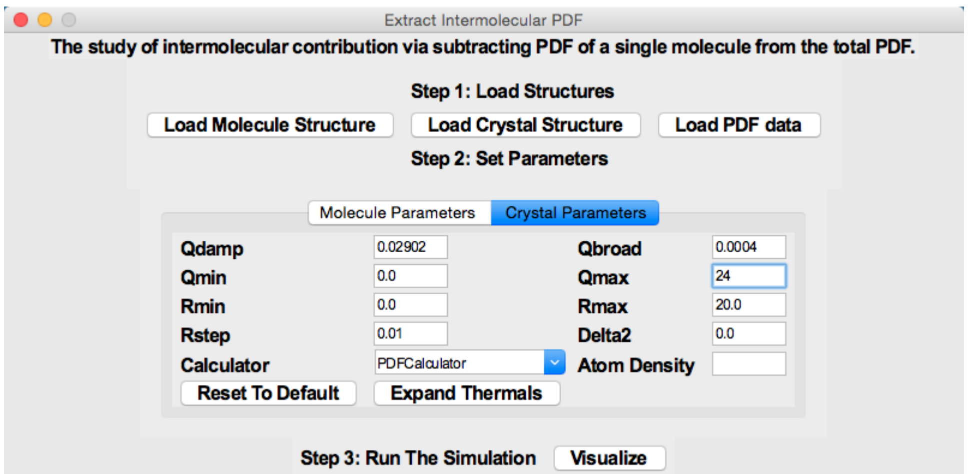
Examples files are available at
https://github.com/curieshicy/xINTERPDF/tree/master/Examples.

H. S. Kim, G. A. Jeffrey and R. D. Rosenstein, *Acta Cryst. B*, 1968, 24, 1449.
X. Qiu, J. W. Thompson and S. J. L. Billinge, *J. Appl. Cryst.* 2004, 37, 678.

Example 1: Hydrogen bonds in D-mannitol



After invoke the main window in a terminal, select from drop-down menu, **Inter PDF /Crystalline**, which brings up a new window titled **Extract Intermolecular PDF**.

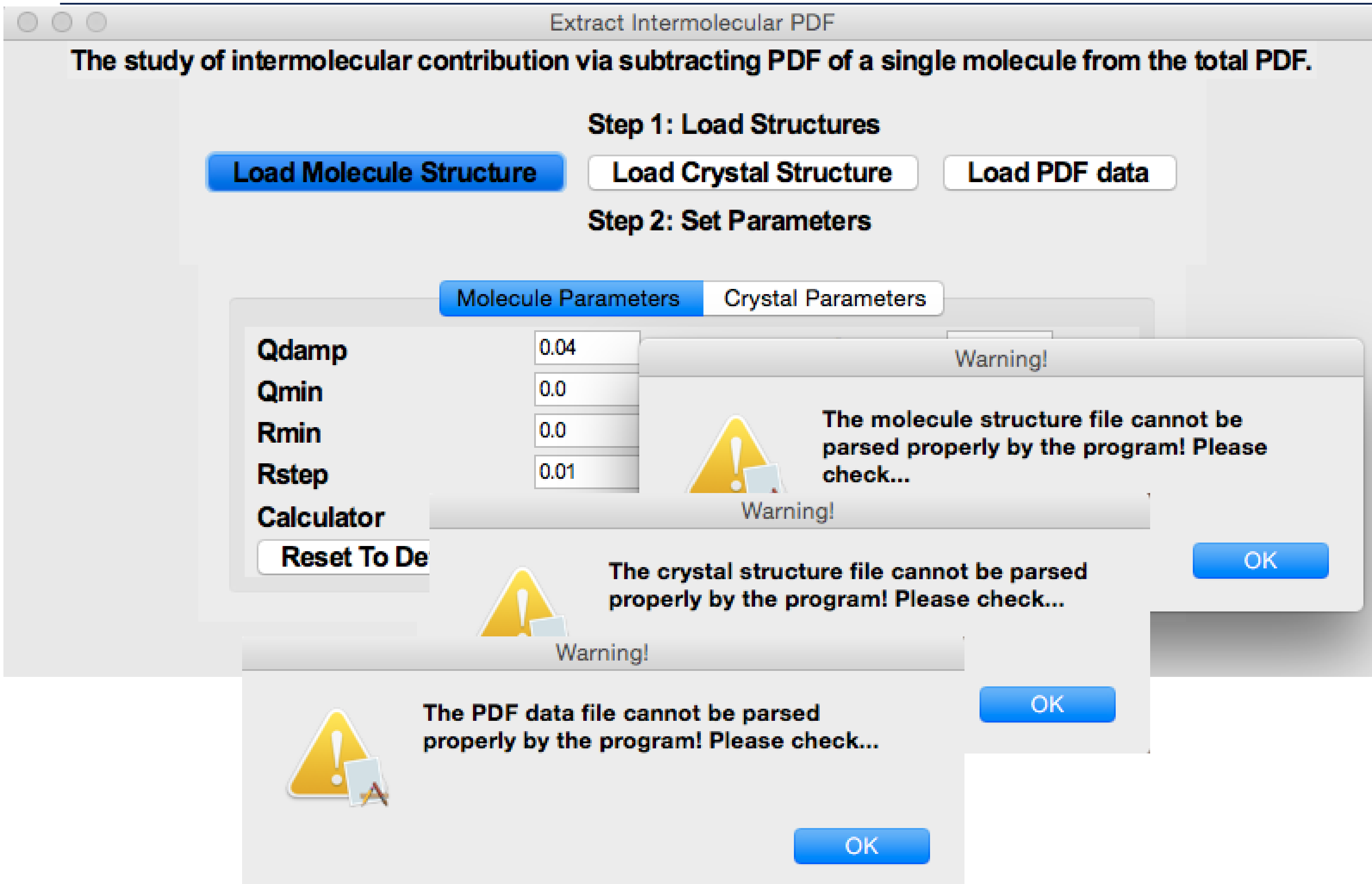


Following the Steps: first load in files for molecule (MAN.xyz), crystal (MAN.cif) and PDF data (MAN_300-00000.gr). In step 2, set Q_{damp} and Q_{broad} values to those determined from cerium oxide calibrant; set Q_{max} to 24 $Å^{-1}$.

For molecule DebyePDFCalculator is used; while for crystal, PDFCalculator is used. Click **Expand Thermals** for both molecule and crystal. Leave values at default.

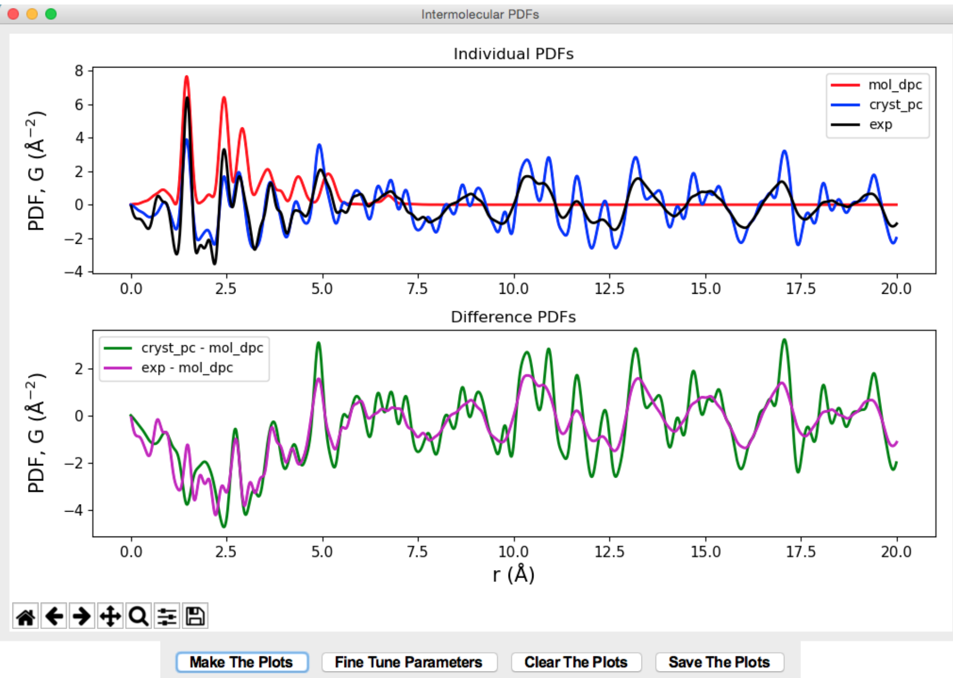
In step 3, click **Visualize** to see the plots.

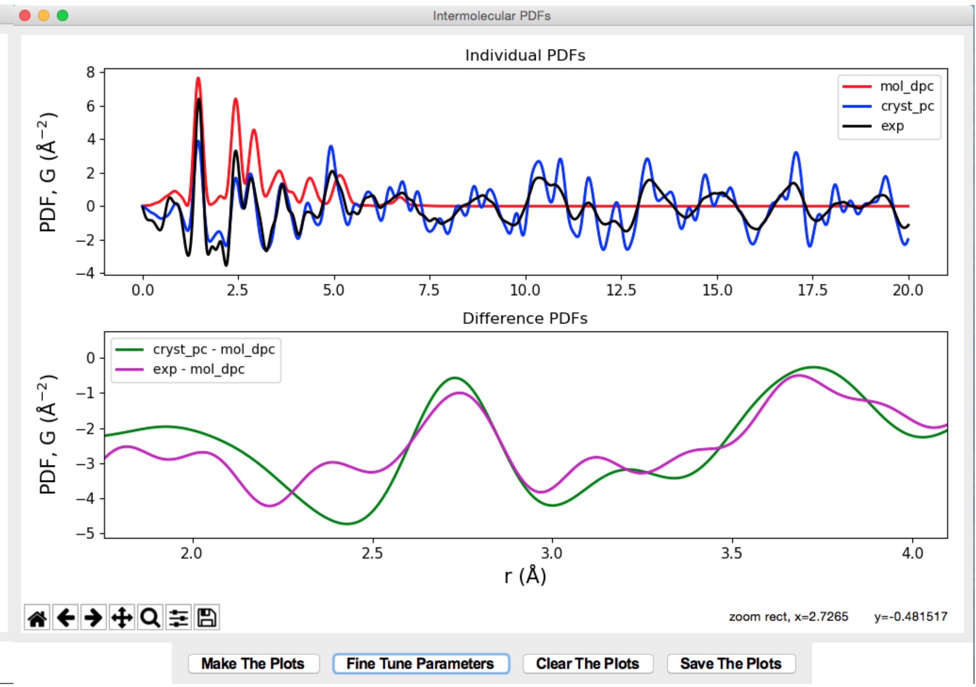
Example 1: Hydrogen bonds in D-mannitol



If any of the molecule/crystal structure file or PDF data cannot be recognized by the program, an error message will be displayed to alert the users.

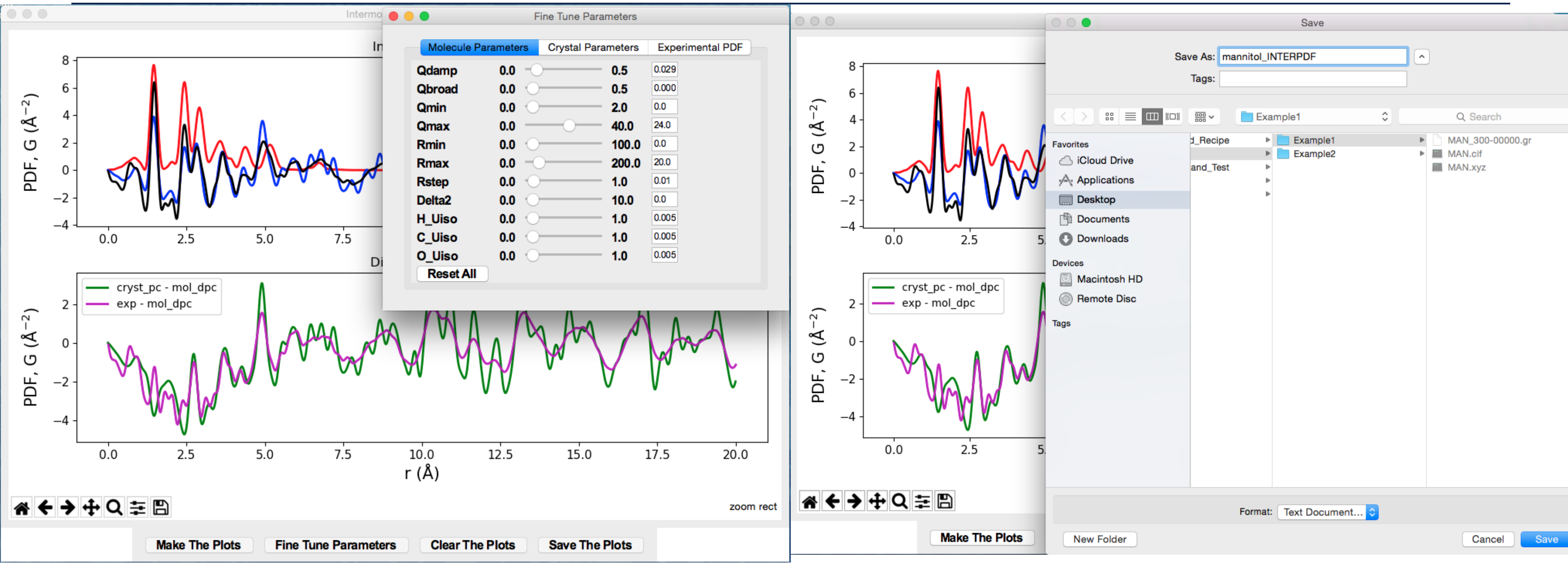
Example 1: Hydrogen bonds in D-mannitol





Click **Make The Plots**, the theoretical PDFs for molecule and crystal, together with experimental PDF are plotted in the top panel. In the bottom panel, the difference PDFs from experiment and theory are compared. Using magnifying tool in the embedded navigation toolbar, one can zoom into the peak around 2.7 Å. Hovering the mouse in the region, the peak positions for O…O is ~2.72 Å and ~2.74 Å, respectively.

Example 1: Hydrogen bonds in D-mannitol



Hit **Fine Tune Parameters** to bring about a window for fine tuning parameters. It has three tabs for molecule, crystal and experiment data, respectively. Users can either drag the scale bar or type a number in the entry box and hit Enter. The plots will update in real time.

Click **Clear the Plots** to erase the plots. Click **Save The Plots** to save all raw data.

Example 1: Hydrogen bonds in D-mannitol

mannitol_INTERPDF.txt

```
# ************************************************************************************************
# ************************************************************************************************
# ******Here are the raw data for the plotting the curves.****************************************
# ******You have chosen to use DeybePDFCalculator for molecule; PDFCalculator for crystal.*********
# ******You also have scaled the measured PDF by a factor of 1.000 ******************************
# ******From left to right, the data correspond to (1)r (2)m (3)c (4)e (5)c-m (6)e-m **************
# *************************************************************************************************
# *************************************************************************************************
#
0.000000000000000000e+00 0.000000000000000000e+00 0.000000000000000000e+00 -9.280011000000000509e-02 0.000000000000000000e+00 -9.280011000000000509e-02
1.000000000000000021e-02 6.212443191915230020e-03 -1.059388955578956237e-02 -1.841415000000000135e-01 -1.680633274770479413e-02 -1.903539431919152314e-01
2.000000000000000042e-02 1.222590932327609001e-02 -2.149921887044312432e-02 -2.726172000000000040e-01 -3.372512819371921433e-02 -2.848431093232761113e-01
2.999999999999999889e-02 1.786282325375071478e-02 -3.300927702376095507e-02 -3.569217000000000084e-01 -5.087210027751166985e-02 -3.747845232537507232e-01
4.000000000000000083e-02 2.296872986922959825e-02 -4.538209911720556683e-02 -4.358954999999999913e-01 -6.835082898643515814e-02 -4.588642298692295896e-01
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5.999999999999999778e-02 3.113916665704996936e-02 -7.348440170292774853e-02 -5.741665999999999714e-01 -1.046235683599777144e-01 -6.053057666570499373e-01
7.000000000000000666e-02 3.408136856581576307e-02 -8.943330360119053357e-02 -6.321792000000000522e-01 -1.235146721670062897e-01 -6.662605685658158361e-01
8.000000000000000167e-02 3.623690446715328861e-02 -1.066708208278051434e-01 -6.823230000000000128e-01 -1.429077252949584320e-01 -7.185599044671533431e-01
8.999999999999999667e-02 3.770188369346503393e-02 -1.251201272690600774e-01 -7.245664000000000549e-01 -1.628220109625251044e-01 -7.622682836934651096e-01
1.000000000000000056e-01 3.858763146288396451e-02 -1.446331717899595193e-01 -7.591143999999999670e-01 -1.832208032528434838e-01 -7.977020314628839870e-01
1.100000000000000006e-01 3.904458472449394424e-02 -1.649991428368153268e-01 -7.863909000000000038e-01 -2.040437275613092849e-01 -8.254354847244939064e-01
1.199999999999999956e-01 3.925448026295294546e-02 -1.859566010169879380e-01 -8.070112000000000396e-01 -2.252110812799408834e-01 -8.462656802629530128e-01
1.300000000000000044e-01 3.942080670153031569e-02 -2.072085892115682615e-01 -8.217503000000000446e-01 -2.466293959130985702e-01 -8.611711067015304089e-01
1.400000000000000133e-01 3.976139948555254544e-02 -2.284398564666100251e-01 -8.315048000000000439e-01 -2.682012559521625983e-01 -8.712661994855526171e-01
1.499999999999999944e-01 4.051142979510184011e-02 -2.493352073592800811e-01 -8.372540000000000537e-01 -2.898466371543819142e-01 -8.777654297951018592e-01
1.600000000000000033e-01 4.186383830073221041e-02 -2.695979199506459700e-01 -8.400197999999999832e-01 -3.114617582513781735e-01 -8.818836383007322421e-01
1.700000000000000122e-01 4.399199010123152481e-02 -2.889671668736874532e-01 -8.408276999999999557e-01 -3.329591569749189572e-01 -8.848196901012315152e-01
1.799999999999999933e-01 4.703481701861558784e-02 -3.072334262372494185e-01 -8.406723999999999863e-01 -3.542682432558650341e-01 -8.877072170186155464e-01
1.900000000000000022e-01 5.108940734433653486e-02 -3.242509790985316220e-01 -8.404865000000000252e-01 -3.753403864428681569e-01 -8.915759073443365601e-01
2.000000000000000111e-01 5.620585249988695187e-02 -3.399467522291140242e-01 -8.411155999999999633e-01 -3.961526047290009900e-01 -8.973214524998869290e-01
```
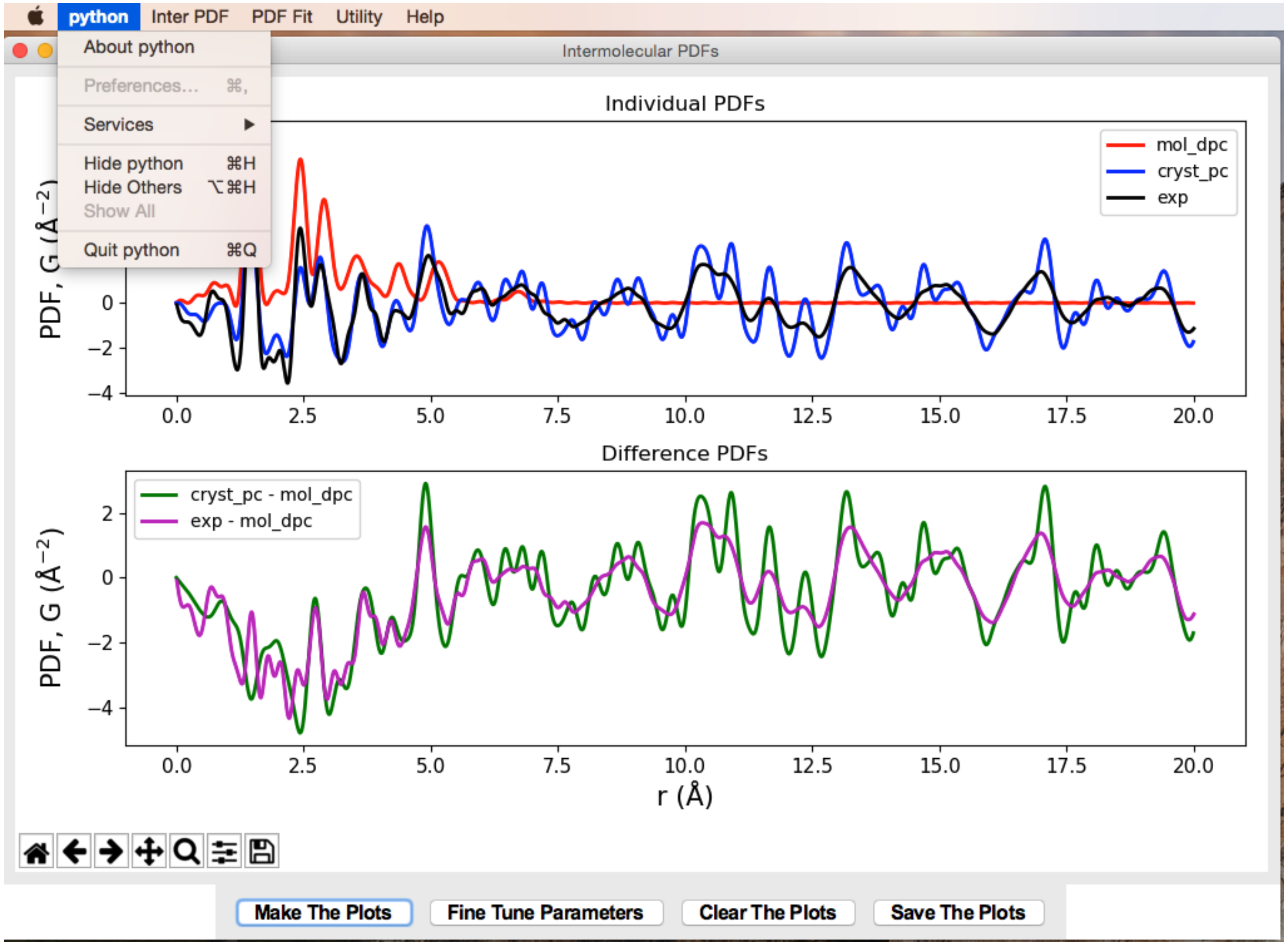
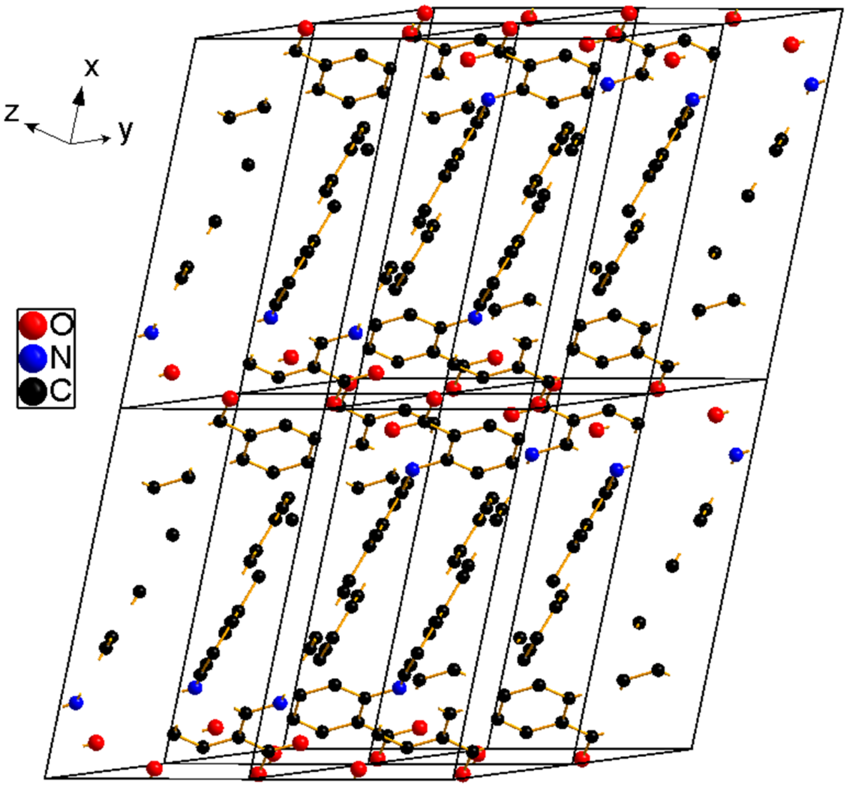

In the file that saved, the header explains the details of each column of data saved. In this example, it describes the Calculators used for simulating PDFs for molecule and crystal, and the scale factor used (in **Fine Tune Parameters** tab) for experimental PDF. Each column, from left to right, corresponds to, respectively, (1)the radial distance, (2) theoretical PDF for molecule, (3) theoretical PDF for crystal, (4) experimental PDF, (5) theoretical intermolecular PDF and (6) experimental intermolecular PDF.

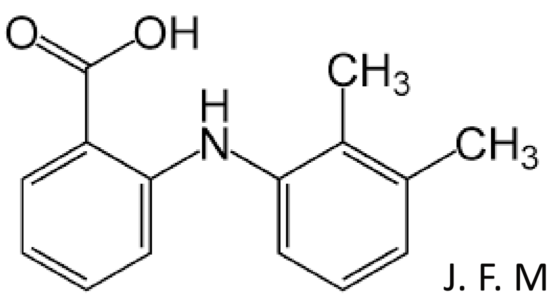
Example 1: Hydrogen bonds in D-mannitol



In the dropdown menu, click **Python---Quit Python** to quit. If terminal fails to respond, press Crtl + Z to kill the process.

Example 2: Model fit of MEF crystalline PDF



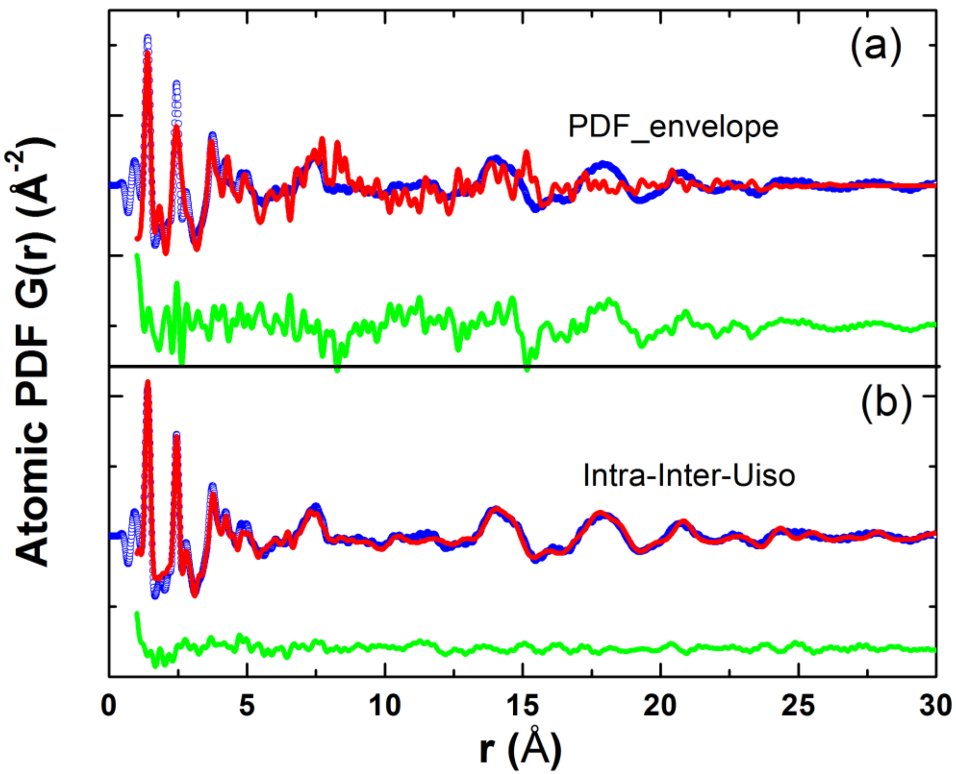


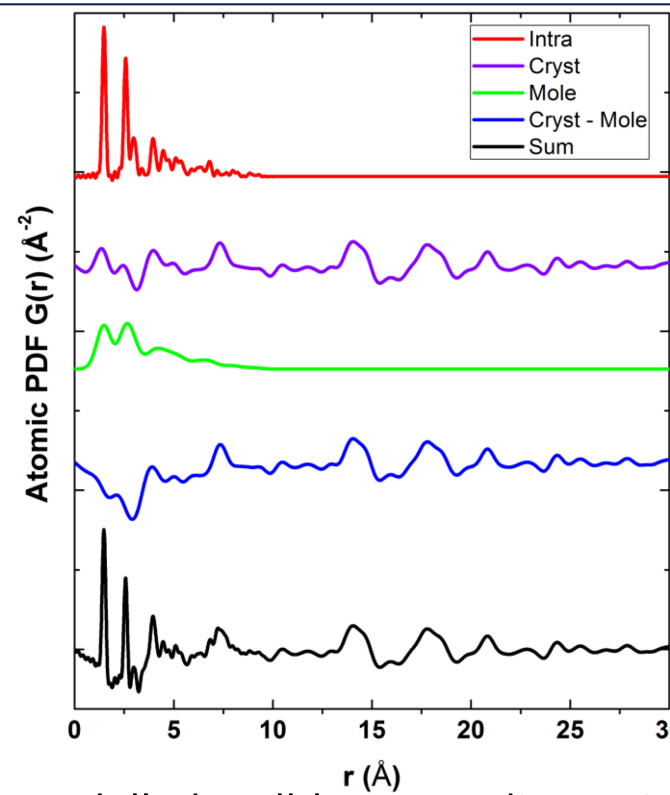
Mefenamic acid (MEF) is a nonsteroidal anti-inflammatory and analgesic drug used to treat mild pain, especially menstrual cramps. The crystal structure of mefenamic acid (Form I) was solved by McConnell and Company in 1976. It has a triclinic structure with a space group $\bar{P}1$.

Synchrotron X-ray total scattering was conducted on MEF powder sample at 300 K. From a fit to PDF of cerium oxide, the instrumental resolution parameters are determined: Q_{damp}=0.02902 Å^{-1}, Q_{broad}= 0.0004 Å^{-1}. A Q_{max} of 24 Å^{-1} was used for Fourier transform. The software program PDFgetX2 was used.

J. F. McConnell and F. Z. Company, *Cryst. Struct. Commun.* 1976, 5, 861-864.

Example 2: Model fit of MEF crystalline PDF

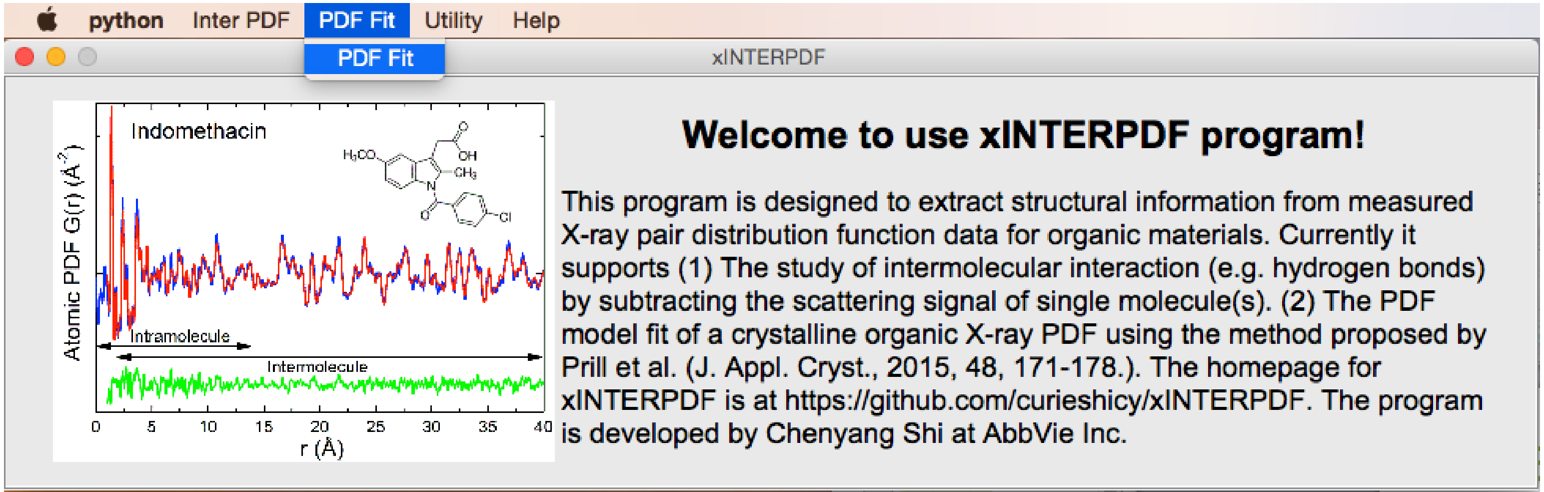




As Prill et al. reported, the PDF of organics cannot be modelled well by expanding unit cell as typically done for inorganic materials (left figure a), because the intermolecular forces are weaker than intramolecular ones. Instead, a model differentiating both intra- and intermolecular contributions is more appropriate. As shown in the breakdown of a total PDF for MEF (black curve in the right figure), it has contributions from intra- (red) and inter-molecules (blue), each with a distinct U_{iso} thermal factor.

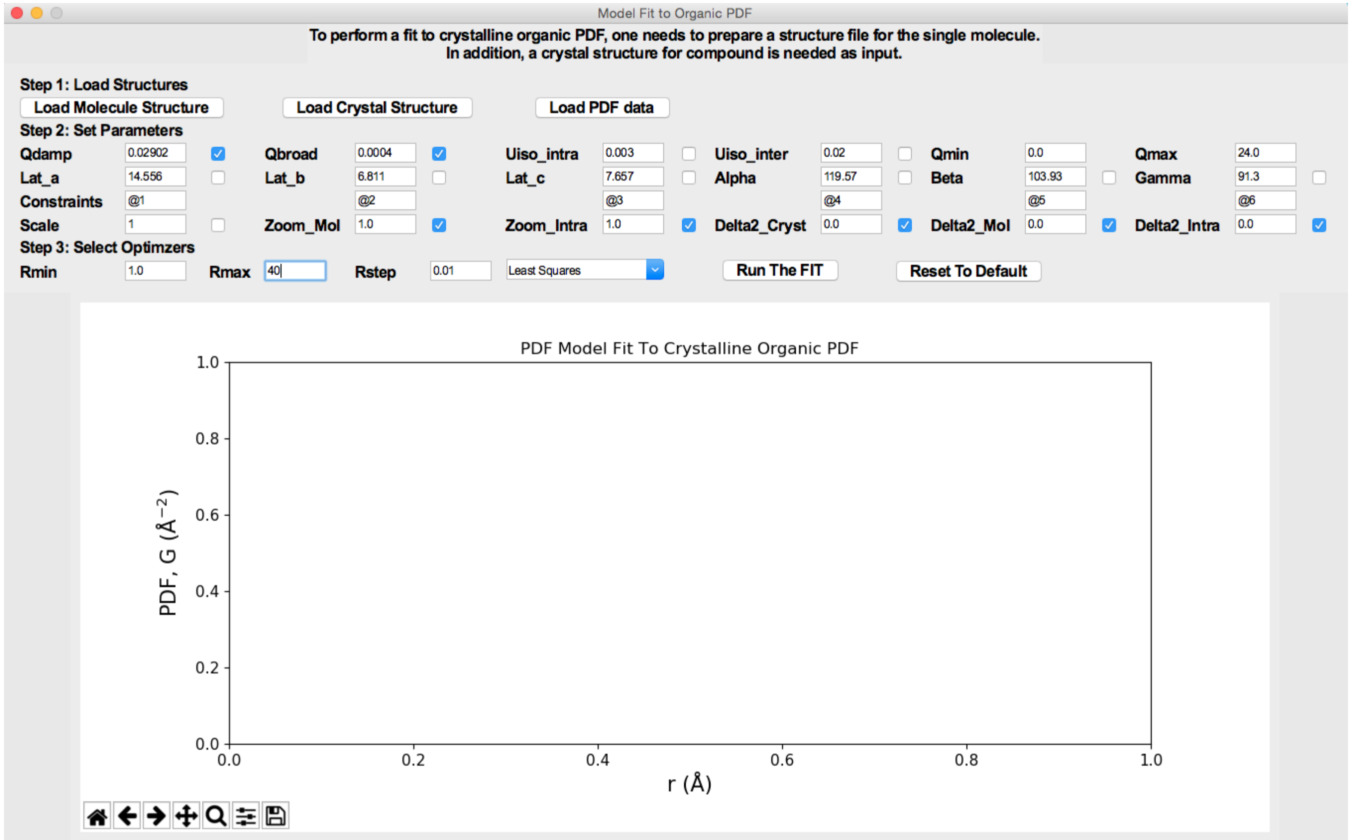
D. Prill, P. Juhás, M. U. Schmidt and S. J. L. Billinge, *J. Appl. Cryst.* 2015, 48, 171-178.

Example 2: Model fit of MEF crystalline PDF



To perform a PDF fit, in dropdown menu, click **PDF Fit/PDF Fit** to start the GUI window.

Example 2: Model fit of MEF crystalline PDF



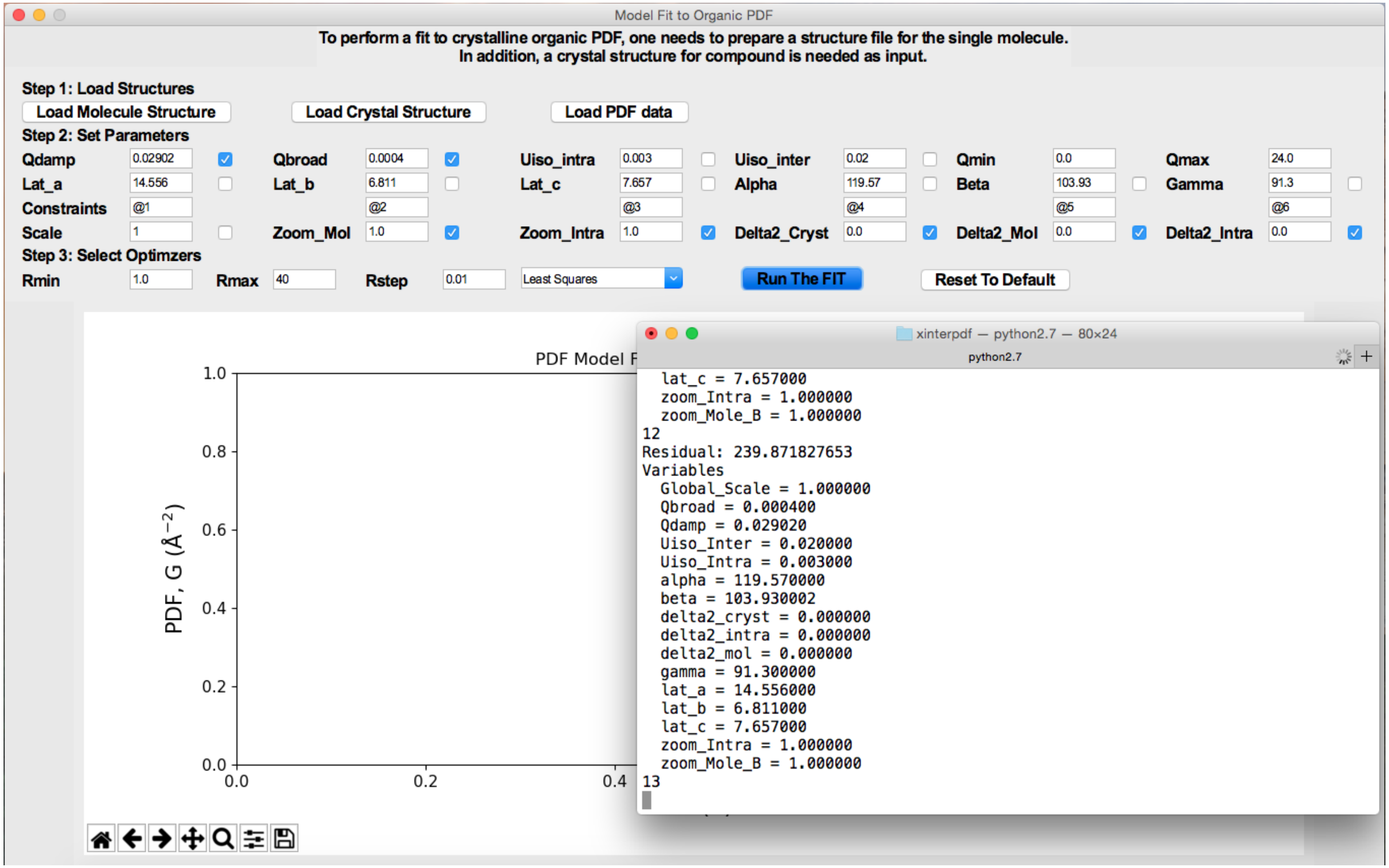
Following the steps, first load in structure files and PDF data (MEF.xyz, MEF.cif and MEF_300-00000.gr). In Step 2, specify the parameters. If a check box is marked, that parameter is fixed during the fit; otherwise is allowed to vary.

Below lattice parameters, there is a row for constraining them. For example, if it is a cubic structure, users can type @1 for **Lat_a**, **Lat_b** and **Lat_c**.

For a tetragonal structure, @1 for **Lat_a** and **Lat_b**, @2 for **Lat_c**. Similar syntax is applied to constrain the angles (**Alpha**, **Beta** and **Gamma**). Since MEF is triclinic, we need six different variables for lattice parameters. **Zoom_Mol** and **Zoom_Intra** give the possibilities to expand or shrink the molecule isotropically. The three delta 2 values can be further freed to explain for the r-dependent peak width (i.e. correlated motions). Refer to the right figure in Slide 22, for the meaning of **Mol** and **Intra**.

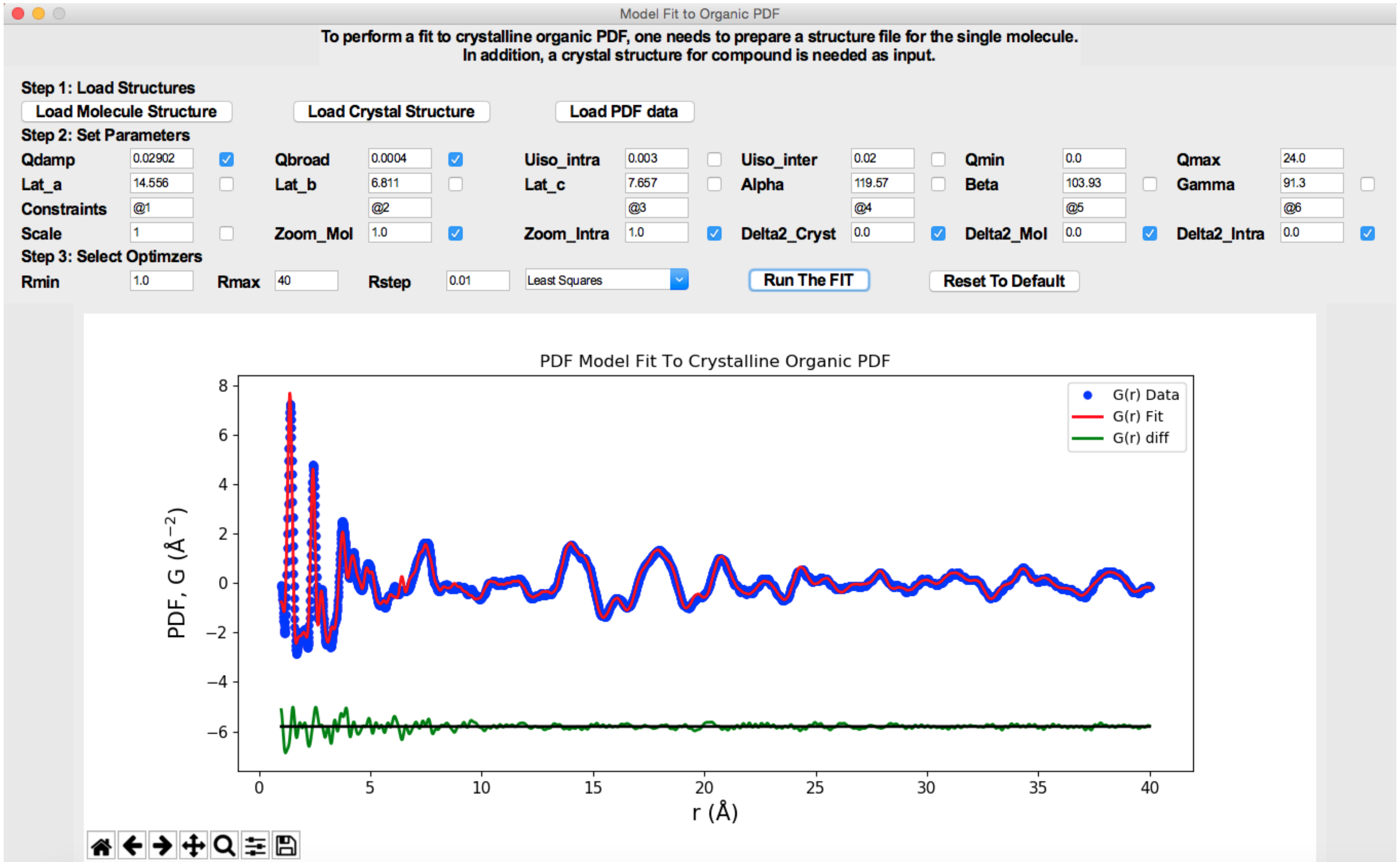
In Step 3, select the fit range and optimizer. Hit **Run The Fit** to start the run.

Example 2: Model fit of MEF crystalline PDF



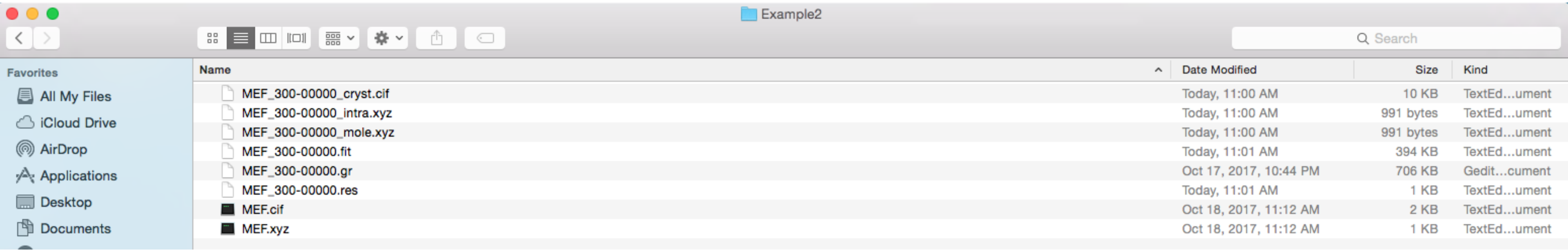
When the fit starts running, the terminal will update fit parameters in real-time.

Example 2: Model fit of MEF crystalline PDF



When the fit is complete, the fit result is plotted. Blue circles, red and green curves, correspond to measured, calculated and difference PDF, respectively.

Example 2: Model fit of MEF crystalline PDF



MEF_300-00000.res

```
Results written: Tue Feb  6 11:01:55 2018
produced by Chenyang

Cannot compute covariance matrix.
Some quantities invalid due to missing profile uncertainty
Overall (Chi2 and Reduced Chi2 invalid)
------------------------------------------------------------------------------
Residual       101.75573582
Contributions  101.75573582
Restraints     0.00000000
Chi2           101.75573582
Reduced Chi2   0.02619195
Rw             0.18472270

Variables (Uncertainties invalid)
------------------------------------------------------------------------------
Global_Scale  9.92587263e-01 +/- 0.00000000e+00
Qbroad        4.00000000e-04 +/- 0.00000000e+00
Qdamp         2.90200000e-02 +/- 0.00000000e+00
Uiso_Inter    4.15886353e-02 +/- 0.00000000e+00
Uiso_Intra    3.31484234e-03 +/- 0.00000000e+00
alpha         1.19516522e+02 +/- 0.00000000e+00
beta          1.04001075e+02 +/- 0.00000000e+00
delta2_cryst  0.00000000e+00 +/- 0.00000000e+00
delta2_intra  0.00000000e+00 +/- 0.00000000e+00
delta2_mol    0.00000000e+00 +/- 0.00000000e+00
gamma         9.12728874e+01 +/- 0.00000000e+00
lat_a         1.45539596e+01 +/- 0.00000000e+00
lat_b         6.81128742e+00 +/- 0.00000000e+00
lat_c         7.66290270e+00 +/- 0.00000000e+00
zoom_Intra    1.00000000e+00 +/- 0.00000000e+00
zoom_Mole_B   1.00000000e+00 +/- 0.00000000e+00

Variable Correlations greater than 25% (Correlations invalid)
------------------------------------------------------------------------------
No correlations greater than 25%
```

After the fit is complete, a variety of files will be saved automatically to the folder where structure files exist. These include structure files (.cif and .xyz files). The MEF-300-00000.fit contains raw data for plotting. MEF-300-00000.res contains a detailed summary of fit results. See the screenshot shown to the left.

Example 3: Find phase fraction by linear regression

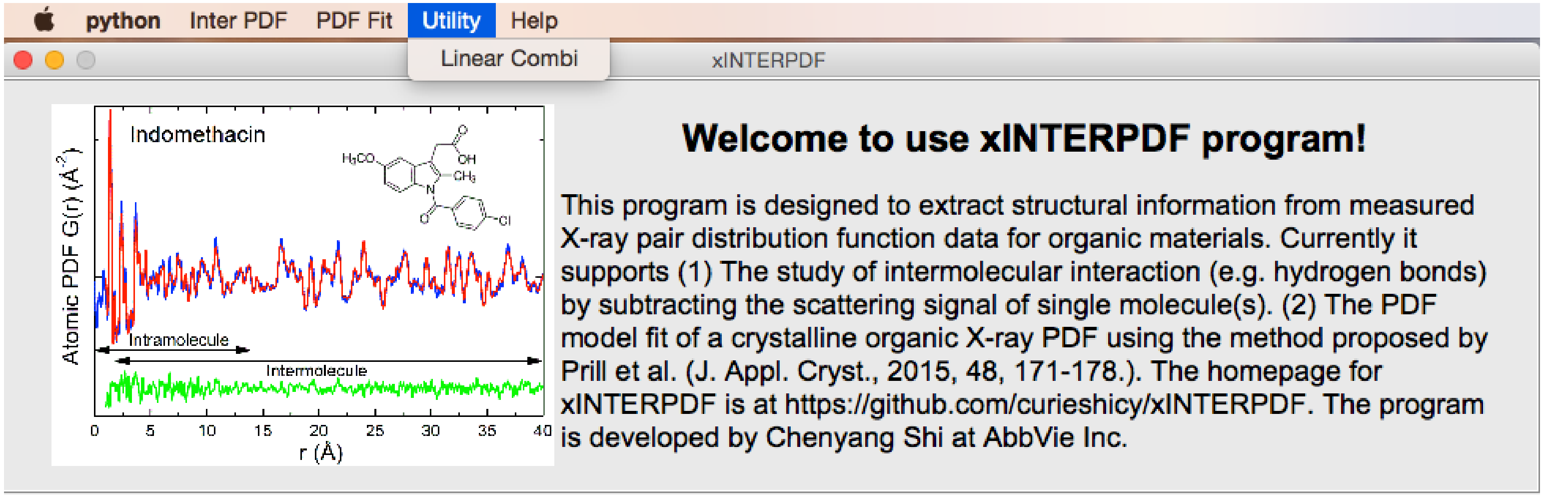
X-ray PDFs can be used for phase quantification. Given a measured total PDF, PDF_{total}, and separate PDF for each pure phase, e.g. in a three phase case, PDF_A, PDF_B, PDF_C. One may find phase fraction by minimizing the difference/maximizing the similarity between left hand side (LHS) and right hand side (RHS) of the following equation:

$$PDF_{total} = Global\_Scale * \{x1 * PDF_A + x2 * PDF_B + (1 - x1 - x2) * PDF_C\}$$

For minimization problem, the convergence criteria could be Least Squares, Least Absolute Deviation. For maximization problem, one finds the phase fractions that maximize the Pearson coefficient between LHS and RHS.

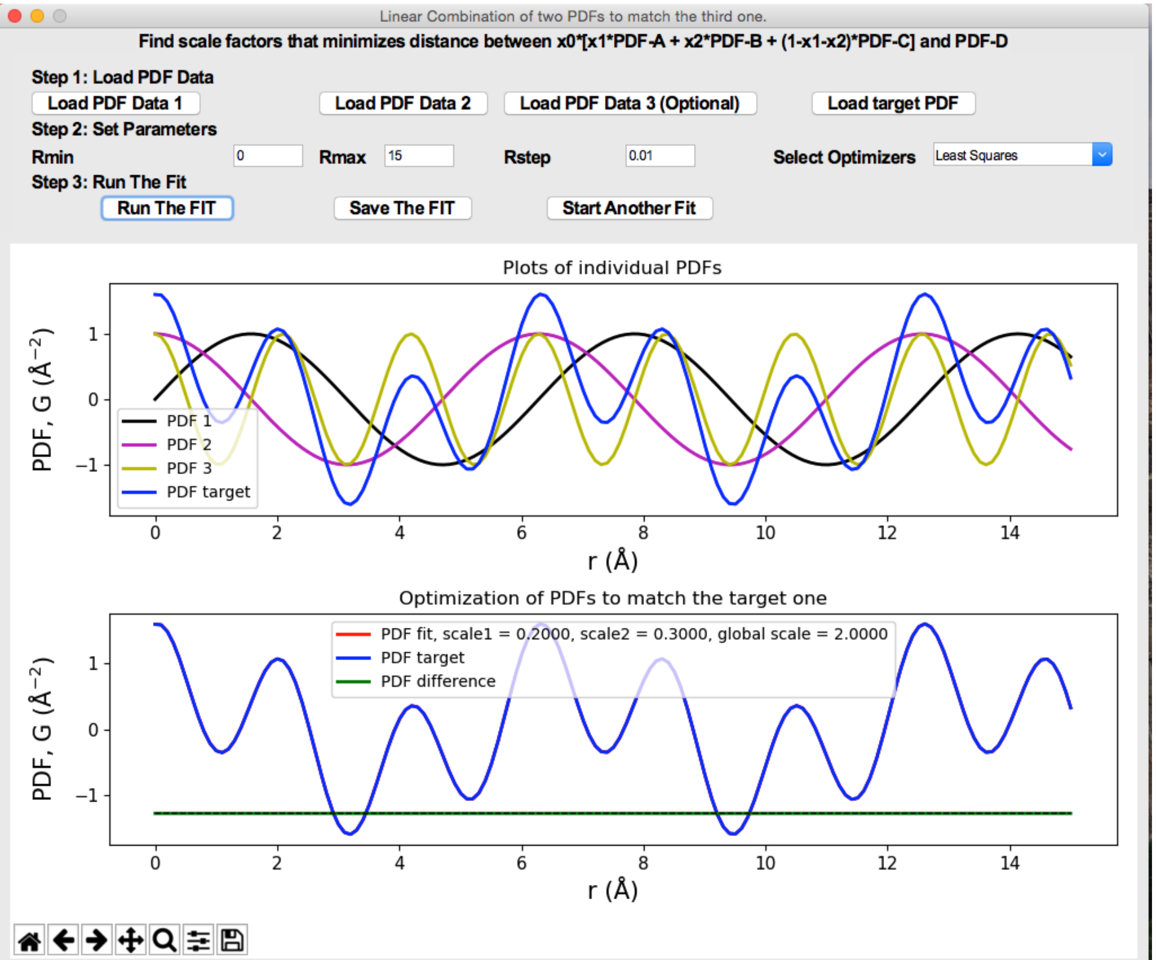
This exercise is particular important for differentiating amorphous solid dispersion (ASDs) and physical mixture of amorphous drug and polymer, i.e. test the miscibility of drug and polymer. If the final product is a physical mixture, one should be able to scale the PDFs of each component to match the total PDF. However, if it is a pure ASD, the linear combination of PDFs of end members should not yield a desired result. More details see A. Newman et al., *J. Pharm. Sci.* 2008, 97(11):4840-56.

Example 3: Find phase fraction by linear regression



To perform a linear fit, in dropdown menu, click **Utility/Linear Combi** to start the GUI window.

Example 3: Find phase fraction by linear regression



In step 1, users can either load in two PDFs or three PDFs to match against a target one. As a simple test, fours simulated curves are loaded, and they are

Y1 = sin(x)

Y2 = cos(x)

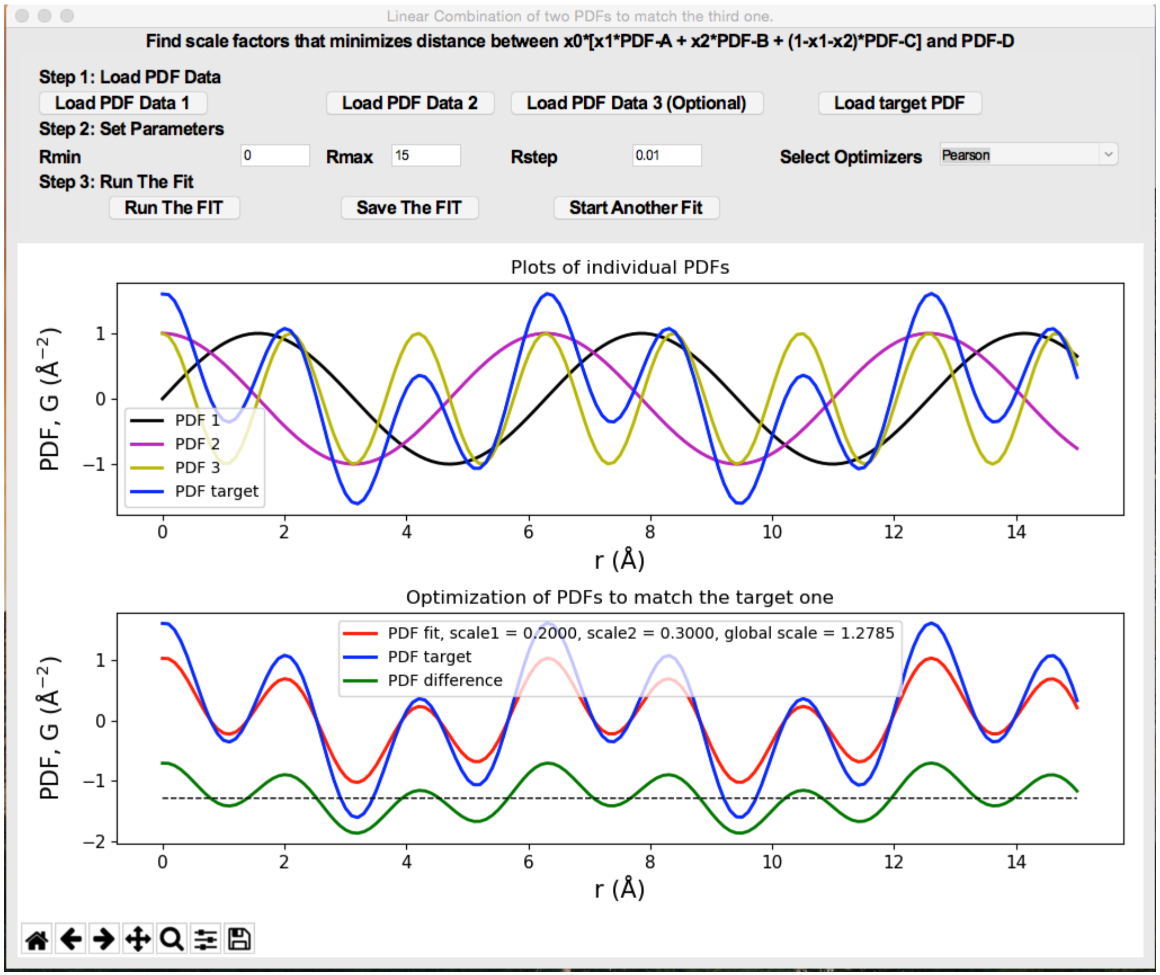
Y3 = cos(3x)

Y4= 2*(0.2*Y1 + 0.3*Y2 + 0.5*Y3)

In step 2 **Select Optimizers** to Least Squares, and use default Rmin, Rmax, and Rstep.

In Step 3, by hit **Run The FIT**, the individual PDFs are plotted in the top panel of the figure; in the bottom panel, the fit is displayed and the scale factors are shown. One may save the results by click **Save the FIT**.

Example 3: Find phase fraction by linear regression



Using Least Absolute Deviation as convergence criteria, the result is the same as using Least Squares. However, if we switch to Pearson, the scale factors for each phase is correct but not the overall global factor. This is because Pearson coefficient is insensitive to scaling.

Disclosure/Acknowledgement

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Notes

C.S. is the employee of AbbVie and may own AbbVie stock. The design, study conduct, and financial support for this research were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the publication. The author declares no competing financial interest.

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