Generate Mixtures
Getting started, basic operations

Sidebar

All data contained in a project, such as spectra and peak lists are located in the sidebar. **Double-clicking** on an item will open its properties popup.

Display

A display can contain multiple overlaid spectra which share the same axes. To show/hide a single spectrum, click on its toolbar button. If you close a display, you can open a spectrum by **dragging and dropping** it into the drop area from the sidebar or by **right-clicking** on a sidebar item and selecting **Open as module**. You can also add additional spectra to a spectrum display module later on, or drag several spectra into the drop area together to open them simultaneously.

Mouse

- Pan  ->  **Left-drag** in display
- Zoom in/out  ->  **Scroll wheel** in display
- Context menu  ->  **Right-click**
- Select a peak  ->  **Left-click** on a peak symbol “X”
- Move a peak  ->  select first, then **middle-click and drag**

Shortcuts

The program uses several shortcuts, for example **MK** for creating a mark at the current mouse position. You will need to press the first letter on your keyboard e.g. M, followed by the second letter, e.g. K (case insensitive). Press **Esc** to cancel the first letter.

For more commands and operations

Main Menu → Help → Tutorials → Beginners Tutorial

OR

Main Menu → Help → Show Shortcuts
Mixture Generation

In order to decrease the experimental resources in NMR screening, a common approach is to analyse several compounds against a target at the same time. This is can translate into a very crowded spectrum that leads to difficult, error prone and time-consuming interpretation of spectra.

In this section you will learn how to create cocktails of one dimensional reference spectra with minimal peak overlap. The new mixtures can be manually analysed and exported to Excel, ready to be printed and prepared in the lab.

The tutorial uses 20 synthetic spectra, representing the reference spectra of 20 small molecules.

Open Project

Open the MixtureGeneration.ccpn project in the ScreenTutorial directory of the tutorial sample data. You can do this in one of the following ways:

• Drag the project from your file browser into the the sidebar or drop area

OR

• Go to Main Menu → Project → Open... and select the project

OR

• Use the shortcut Ctrl+O (or Cmd+O on a Mac) and select the project
Set up Mixture Generation

- Go to Main Menu → Screen → Generate Mixtures or use shortcut GM

The calculation will be conducted by simulated annealing (SA). You can change the SA parameters by clicking on the gear icon. For the tutorial we will keep the default parameters.

- Select the **Number of Components** selection method to choose how many components you want in each mixture. (**Number of Mixtures** allows the creation of a set number of mixtures with components equally distributed among them.) The project contains 20 reference spectra, therefore select any value between 2 and 10 in the option number of Mixtures or between 2 and 20 for number of Components on the slider or in the spin box. Five components per mixture is a common choice.

- Leave the **minimal distance between peaks** at 0.01ppm. The algorithm will try to return mixtures where two adjacent peaks from separate spectra are separated by at least the selected value.

- Select the **Spectrum Group** you want to use to create the mixture, in this case: **SG:References**
**Set up Peak Picking**

- Go to the Pick Peaks Setup tab. Here you can select whether or not to pick the peaks first or use previously picked peaks. See Section 3 above on 1D Peak Picking for more details.
- Select **Water** from the drop-down as a solvent region to exclude.
- Click **Perform** to start the calculation.
Mixtures Analysis

The module mixture analysis will be opened automatically. If you close it, you can reopen it with Main Menu → Screen → Mixture Analysis or shortcut MI.

The table on the left-hand side of the module lists all the mixtures with scores. The scores are derived from placing a penalty on the distance between the best-resolved peak and its closest neighbour. The more overlapped the peaks, the higher the score. A score of 0.0 means there are no overlapped peaks in the mixture.

The table also lists the number of components and overlapped peaks present in each mixture. It can be sorted into ascending or descending order by clicking on the table header column.

Use the four tabs on the right to do a full inspection of the mixture selected in the table on the left:

The **Component Peaks** tab has a toolbar containing the spectrum component of each mixture.

- Click a button to show the PeakList. If a substance is linked to the spectrum, the molecular structure will be shown on the right.
- Use the **Components Structure** and **Components Info** tabs to visualise additional mixture properties.
Mixture Generation

Mixtures Management

The Mixtures Management tab will allow you to move components between mixtures by hand to try to improve scores or create new mixtures.

- Select an option from the pulldown menu on the right, e.g. New empty mixture or any other mixture. Drag and drop the components between the windows and click the Predict button to recalculate the scores, then Apply to get the new mixtures.

Once you are happy with your mixtures you can export them to an Excel file using the export button in the top right corner.
Contact Us

Website: www.ccpn.ac.uk

Suggestions and comments: ccpnmr3@gmail.com

Issues and bug reports: https://www.ccpn.ac.uk/forums

Cite Us

Mureddu, L. et al. CcpNmr AnalysisScreen, a new software programme with dedicated automated analysis tools for fragment-based drug discovery by NMR. J. Biomol. NMR (2020)