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Analytical Chemistry, PLEN, KU, 2017-2026

Tutorial for the Excel spreadsheet ChromSimGC and ChromSimGCxGC

This workbook and the associated Visual Basic Macros (VBA) can be used to predict gas chromatograms for 20 compounds and 2 columns selected from 451 compounds or 61 commercial GC-columns. For the 2D-version, in addition, please read *Short manual 2D GC.docx.*

ChromSimGC works on both Mac and Windows computers.

Check for updates on my homepage bosvensmark.dk.

You do not need to know about the Solvation Parameter model (Abraham's model) and the Linear Solvent Strength model (LSS) to use this spreadsheet - but the chromatograms are calculated using the Solvent Parameter model to calculate the retention factors for up to 20 compounds on 2 columns at a time (or 20 compounds on one pair of columns in 2D GC). The Linear Solvent Strength model mathematics is used to calculate the chromatograms for isothermal or temperature programmed GC in Excel. The VBA macro simulates the chromatograms by digital simulation using the plate theory for chromatography, and this allows simulations where the log(retention factor)'s are not a linear function of temperature.

The Excel sheet can only calculate for a simple linear temperature program, whereas the VBA and macro can simulate any temperature program you want.

OBS: The predictions in Excel are slightly wrong, because the LSS-model is valid for a gradient in HPLC, where the gradient progresses through the column, whereas the temperature in GC is the same for the whole length of the column at any time during the temperature program. This error is maximum 0.5*t_M for late eluting peaks. A correction has been added, so the average error is much smaller, but may now be in both directions.

Also – for retention times greater than the program (isotherm at max temp, tR > t(iso) + t(pgm)), there is an additional small error in the retention times.

For accurate work you need to use the simulation in VBA, even for linear temperature programs!

These errors do not occur for isothermal runs.

There are 5 chromatograms in the sheet:

1) **Dark green:** Linear log(k) vs temperature
2) **Light green:** First- second or third order polynomial fit of log(k) vs temperature
3) **Dark blue:** Linear log(k) vs temperature
4) **Light blue:** First, second or third order polynomial fit of log(k) vs temperature
5) **Reference:** May be one of the chromatograms 1-4 or any input you like.

All user input are in the white cells. If you want to modify the other cells you must unprotect the sheet first (no password).

1) Predict retention times with a linear model for *log(t)* vs *T* (LSS in Excel sheet GC)

This is the simplest function, and is very fast. But – the predictions will only good in the case where *log(k)* vs *T* is strictly linear in the whole temperature range (and includes the small error in retention times explained above). You can either:

- Compare 2 different columns with the same temperature program
- Compare 2 different temperature programs on the same column
- Compare 2 different programs on 2 different columns (may be used for optimization of GC)

To use this function:

1) **Enter names of the analytes in the cells C6:C25.** Each name must be identical to the name of one of the compounds in the table in the sheet *Compounds.* The only exception is that the case of the letters does not matter, i.e. both *Hexadecane* and *hexadecane* is ok. You will get a warning if the spelling is wrong.
2) **Enter the relative concentrations cells B6:B25**. Usually use 1 for a compound and 0 for rows without data. You can also use this to remove or amplify a compound for peak identification.
3) **Enter the names of the 2 columns in cell E29 and E31.** The name must be identical to one of the columns you can see in the Table 4.
4) **Enter the parameters for two gradients in** F29:N29 for column 1 (green chromatograms) and F31:N31 for column 2 (blue chromatogram) respectively. The meaning of the parameters should explain themself (for the parameter *Beta-ratio* see next point). Note though that only a single linear gradient is allowed, but you may add an isotherm start at *To* °C in the cells next to *t(iso)*. A complex temperature program can be simulated in VBA, se next section. If the chromatogram is longer than the program (B31 > J29 or J31) an isotherm part is added in this time. You can see the gradients in the plot to the right. If *Tmax <= To* an isocratic run will be calculated and *t(iso)* and *Tmax* are not used.

5) **Beta-ratio.** The Solvation Strength Parameters are for the chemical properties of the columns, but the same column type can be made with different physical dimensions, i.e. capillary diameter and thickness of the stationary phase. This is described in the parameter $\beta = V_{mobile\ phase} / V_{stationary\ phase}$. So if your column has another β than the columns used for the table values, all retention factors will change by a constant ratio, which you can enter here. Ratio > 1 means more retention.

6) **The c-term.** The literature data for the columns contains a c-term which in some cases has a discontinuity for log(k) as function of temperature. For this reason, there is the option to use an average value for *c* for all temperature. Enter 0 or 1 I Table 1 in sheet *Columns* to select literature date (*litt.*) or an average (*mean*).
7) **The amplification and offset** (*Amplify* and *Offset*) are used to amplify and position the chromatograms in the graph. Try different values to see the effect. Use 0 to hide a curve.
8) **Finally you may enter the retention times for a reference chromatogram** in the cells E6:F25. If you do not have a reference chromatogram (e.g. experimental values) you can set one of the calculated chromatograms as a reference by use of the button to the right of the graph. To remove the reference, just delete the values in E6:F25. If you only have retention times for a reference, you may copy the widths from one of the calculated chromatograms for comparison.
8) **The chromatograms can be seen in the graph**, and the retention times, peak widths, relative retention etc. in the tables below it B60:I106.

Please note that the peak order in the tables may be different from the elution order. In this case it is advised to sort the input according to the elution order – so press the button for sorting of the input just above the graph. The sorting of the input is according to the reference chromatogram.

Now you can try to change the input and see the results immediately. Try making a program for the blue chromatogram. Start with the same parameters as the green chromatogram and try different variations. You may also play with the other parameters for the columns, intensity and offset.

If you want to optimize the gradient you may get help by looking in the plots of *log(k)* vs *T* in the sheet *SPmodel.* Here you can also see a linear and a quadratic fit to judge if the linear fit seems good enough.

Advanced users: In cell A155:O177 there is a scheme for a *What-If-Analysis*, i.e. you can get many results for variation of a single input parameter. It is a little complicated but just follow the instructions in the spreadsheet and/or use the help function in Excel for *Data Table.* This function seems not to work unless you unprotect the sheet first: Go to *Review* and click *Unprotect sheet*. Protect the sheet again afterwards. Do only work for LSS data not for VBA smulations.

If you want to predict chromatograms using a nonlinear *log(k)* vs *T* relation, you must use the *VBA macros*, see next section.

2) Predict retention times with a nonlinear model for *log(t)* vs *T* (VBA Excel sheet GC)

One simulation takes a few seconds to one minute depending on the computer power and the parameters for the simulation (see *observations* below). The predictions can be much more accurate than the linear calculations in Excel in the case **when *log(k)* vs *T* is not strictly linear** in the whole temperature range. The 0.5 x t_M error for late eluting peaks is also absent in the simulation.

To use this function:

1) **Enter the degree for the polynomial fit of *log(k) vs T*** in cell L30 and L32 for the green and blue column respectively.
2) **Press the button *Update green* or *Update blue*.** The macros associated with these buttons simulates the chromatograms and returns the resulting retention times and peak widths in cell B86:I105. The progress of the simulation can be seen in the status bar at the lover left corner of the window.
3) **All chromatograms can be seen in the graph**, and the retention times, peak widths, relative retention etc. in the table below it B84:I106.
4) **If you change any run parameter or the polynomial order** a warning will be shown in cell J7 or J9 asking you to ***Update green* or *Update blue*.** This indicates that the retention times in chromatogram #2 and #4 do not correspond to the parameters in the spreadsheet. After the macro have been run the cells will indicate that this is ***ok* or *ok*.**
5) That's all.

The simulations will use the same parameters for the compounds, the two columns and the temperature program as the Excel calculations, unless you decide to simualte a complex temperature program, see next section.

If the simulation takes too long time, press and hold *Escape* and then press *Ok* in the message window. The program may stop with an error message if the simulation is too long. Close the

spreadsheet and reduce the number of theoretic plates for the simulation in the sheet *Macro input* as explained below.

Complex temperature programs

You can simulate almost any temperature program by VBA, but then you need to modify the sheet *Macro input*, and the simulation will no longer automatically simulate the same program as given in sheet *GC*. Only the VBA simulation will use the new complex program.

- Enter the data in the tables for the green and blue complex program (instructions given below the table)
- Set cell F19 or Q19 equal to 1 to use the complex program. (F19 or Q19 = 0 is used for temperature programs from sheet *GC*).

Run the simulation

Now you can try to change the input parameters and see the results after pressing the Update button whenever the Update warning is given. You may see the following observations if you try:

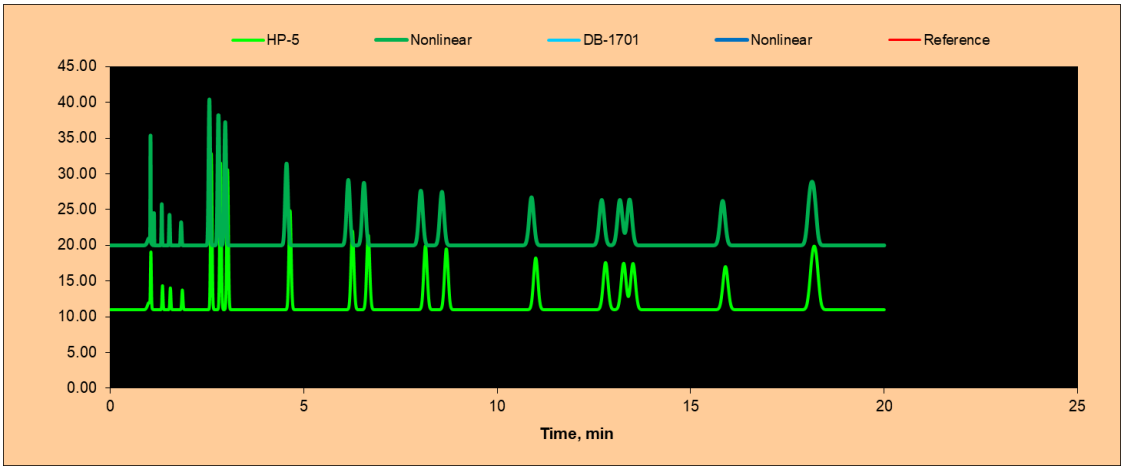
3) Observations: The error in Excel calculations due to gradient *vs* temperature program

The LSS-model is valid for gradient elution in HPLC. In HPLC the gradient progresses through the column, i.e. the elution strength is a function of both time and position within the column.

In GC the temperature changes in the whole lengths of the column at the same time.

Predictions with LSS (progression of the program through the column) will give retention times that are too high. **The error increases with retention times up to 0.5*t_M for late eluting peaks. A correction has been added to reduce this error, but it may now be in both directions**.

To test this set the degree for the Non-Linear simulation in L30 to 1 and press *Update green*. The difference can be seen in the graph and table cell K86:K105: (HP-5 is LSS, NonLin 1 is VBA simulation)



$\Delta t_R(1)$ Lin-Non
0.01
0.01
0.02
0.02
0.03
0.05
0.05
0.06
0.09
0.11
0.11
0.12
0.11
0.11
0.10
0.10
0.09
0.07
0.06
0.06
0.12

Error in Excel for t_M = 1 min:

4) Observations: VBA simulations *vs* Excel calculations

Use the same column for both chromatograms, fx HP-5 and HP-5 in cell E29 and E31. Then make an isotherm run for column 1 and a temperature program for column 2. Fit the parameters according to the analytes you have chosen so you have two reasonable good chromatograms. Use a relative short *tmax* in cell B31, i.e. 10-20 min. For the isothermal run, some peaks may have a longer retention time, but just forget about them in the graph.

Then set the polynomial order equal to 1 in L30 and L32 and run the simulation by pressing *Update* button. Now both Excel and simulation will predict the chromatograms for identical runs, i.e. a linear fit of log(k) vs T. But you can see small differences in the numbers when you compare the results from Excel in cell B68:I81 and the results from the simulation in cells B86:I105, as explained below.

The peak widths in the beginning of the chromatograms are somewhat smaller in the simulation than in the Excel calculations. The correct ones are the simulated numbers based on the plate theory. In the Excel calculation the number of theoretic plates *N* is assumed to be independent of the retention factor, but in reality the peak width depends on the retention factor by a factor sqrt(k/(k+1)). This is normally not observed in experimental chromatograms because extra-column broadening affects the early eluting narrow peaks more than later eluting broader peaks, thus compensating the theoretical effect. For late eluting peaks the widths may also be broader because of the nonlinear fit though.

The peak retention times for the same peak are slightly different for some of the peaks. This is because the simulation is only an approximation and the error in the approximation depends on the number of theoretic plates used in the simulation. The error is inverse proportional to the number of plates *N*, but unfortunately the CPC-time for the simulation depends on the number of plates squared N^2. For N = 200 in the simulation the error is ~1 % and the simulation of 20 analytes and *tmax* = 40 minutes takes about 4 s on my PC. You may change the number of plates used in the simulation in the sheet *Macro input* in cells A2 and/or L2. Try N = 100 and 500 in addition to 200 and see the effect (*N* max is 1000 at present).

The number of plates in the simulation is *NOT* identical to the number of theoretical plates *N* in cell B30 in the sheet *GC.* Actually the simulation is performed with relative few plates (cell A2 and L2 in *Macro input*) and then the simulated peak widths are corrected by a factor sqrt(*N(simulation)/N(real)*).

For peaks eluted after the end time of a temperature program i.e. if there is an isotherm hold at the final temperature, the retention times calculated by Excel are wrong and the simulated retention times are again correct. This is because the retention times here cannot be calculated by the Linear Solvent Strength model, so I have made a homemade approximation in Excel, and this approximation is obviously not very good – so if you need accurate results here you can only trust the simulations.

The table values for the columns and the compounds in the sheets *Compounds* and *Columns* are taken from literature and the references are given in sheets. Unfortunately the whole temperature range is not always covered in the same experiment thus This means, that there may be some disagreements between the data for the low and high range of temperatures. For this reason you should look carefully on the plots

of the model fits in the sheet *SPmodel*. For this reason the c-term in the model can be replaced by an average in order to smoothen the transition between low and high temperature. Input 0 or 1 in Table 1 sheet *columns* to select literature data or an average of data for all temperatures.

Troubleshooting Excel workbooks

Here is solutions to some of the problems encountered with the workbooks:

Workbooks downloaded from Absalon (or the internet in general) do not allow execution of macros.

To fix it save the workbook and open the saved workbook.

Sometimes it is necessary to allow macros in the properties for the workbook. Right click the workbook, open Properties and click *Unblock* then *Apply* and finally *Ok.*

If you get an error massage about the execution of a macro:

First you must reset the error:

- Click *End* in the error message window - or
- Click *Debug* in the error message window
- With *Debug* you can see the line in the macro with the error. Click *Reset* (the blue square in the toolbar above the code in the VBA Editor) or *Run -> Reset*.

Compile Error: *Sub or Function not defined* and Run-time error '*1004*'

This error occur when a macro is called, and the Add-In *Analysis ToolPack - VBA* or the Add-In *Solver* is not activated.

To fix it:

- Go to the spreadsheet and click *File -> Options -> Add-ins*
- Now a window opens. Go to the bottom and click *Go...* next to *Manage: Excel Add-ins*
- In the Add-ins window be sure to check the boxes next to the following Add-ins:
  - Analysis ToolPack
  - Analysis ToolPack – VBA
  - Solver Add-in

If you get an error again:

- Click *Ok* or *Debug*
- Click *Reset* (the blue square in the toolbar above the code)
- Click *Tools -> Reference* and a new window opens
- Check the box next to *Solver*
- Check the box next to *atpvbaen.xls*
- Click *Ok*, go to the spreadsheet and try to click the button causing the error again

Sheets do not react properly on changes:

Sometimes the sheets go into *manual calculation mode* by an unknown error. This means that the sheets are not recalculated when cells are changed. To fix this go to the menu *Formulas*, click the down arrow for *Calculation Options*, and click on *Automatic*. In manual mode the sheets will recalculate each time F9 are pressed.