

# 1 How to use Meltim

## 1.1 About Meltsim

Meltsim is a software which modelize the dna melting. It was developed by Blake and Bizzaro according to the Poland algorithm. The original software is for windows and can easily be found on the web. The source code is also available on the web, and one can compile Meltsim under Linux by removing all the windows user interface. This have been done by Petter Urkedal, and the Meltsim code was then compiled on a Linux machine.

Meltsim code is written in Pascal. A graphical user interface in Python can be used to modify parameters faster, but this is not necessary.

## 1.2 Basic run

The source code file is meltdna.pas. This one can be used directly and the parameters can be modified directly in the source code. To run Meltsim, one should first create a dna-sequence file, and then specify its name in the Meltsim code main procedure.

Thus the user essentially needs only two files: meltdna.pas and the sequence file.

The names of the output files should also be specified by the user, as well as the melting numerical parameters ( $c$ ,  $\sigma_0$ , temperatures, etc.). This should be done at the end of the source code.

```
begin { TMeltThread.Execute }
  index :=0;
  PARAMC := 1.75;
  SIGMAP := 1e-5;
  SALT := 0.075;{ sodium concentration}
  TSTEP := 0.1;{ temperature increment}
  TS := 40; { starting temp.}
  TF := 120; { final temp.}
  outputdir := './';
  OutFile1Name := 'melt.mlt'; { EMltFile }
  OutFile2Name := 'melt.int'; { EIntFile}
  LogFileName := 'melt.log'; { ELogFile }
  (*GetParameters;*)
  (*GetFileNames;*)
  {procedure execute      : reads parameters from a file}
  {procedure execute_loop : loop the code over one parameter}
  execute;
  writeln('Sequence melt.');
```

end.

### 1.3 Meltsim output

Meltsim has three output: one .log file, which recall the melting parameters, one .int file, which contains the melting curve histogram and one .mlt file, which contains the melting curve's derivative histogram. The curves can be drawn using Gnuplot for example.

### 1.4 File interface

Re-compiling the code each time a parameter is changed can be a cause of time wasting and may be unsafe.

To avoid re-compiling many times, one can read the parameters from a file. Two parameters files have been created:

melt\_param.dat contains the parameters values

melt\_files.dat contains the input/output filenames.

The first one will be read to set the melting parameters and the second one will state the sequence file name and the output base name.

### 1.5 User interface

One can also use the user interface to change the parameters faster. The interface file is melt.py.

### 1.6 Commands

Here are the main commands needed to run Meltsim:

- \_ To run NORDITA's version of Meltsim, just type `./meltdna`.
- \_ To run the user interface, enter `python melt.py`
- \_ The output files can be plot with Gnuplot entering `plot 'filename'`.

The figure 1 shows the Meltsim interface built with Python. The user can configure the values of loop exponent, cooperativity effect, salt concentration, initial/final temperatures and temperature increment. The right side of the interface holds four buttons with the following actions

1. Melt it! runs the simulation
2. Melting curve prints the melting curve on screen
3. Save datas saves the output melting curve in the Datas sub-directory.
4. QUIT or escape key, quits the application.



Figure 1: Python User Interface for Meltsim.

The names of the melting files should be entered in the `melt_files.dat` file. In the following way.

```
sequence.seq
melt
```

This example will melt the sequence file `sequence.seq` and generate three output files, `melt.mlt`, `melt.int` and `melt.log`. *Be careful* not to put spaces after the file names otherwise they won't be read correctly. It is also important to set the output base name as `melt` when using the user interface.

## 2 Main results using Meltsim

In this section we will see how the different parameters influence the melting curve generated by Meltsim. We will see that the only parameters relevant to vary are the loop exponent and the cooperativity effect.

### 2.1 Effect of loop exponent parameter

The loop exponent parameter  $c$  is known to be responsible of the transition order's value. However, varying the loop exponent did not always change the melting curve aspect. This strongly depended on the cooperativity effect parameter, as we will see in the following paragraph. The figure 2 shows the effect of  $c$  for a cooperativity effect  $\sigma = 0.08$ .

### 2.2 Effect of cooperativity effect parameter

When varying the cooperativity effects parameter, we notice that the transition is modified. The extreme case, for  $\sigma = 1$ , shows a very smooth transition. For  $\sigma$  lower than  $10^{-3}$  the transition is always sharp, whatever the loop exponent is.

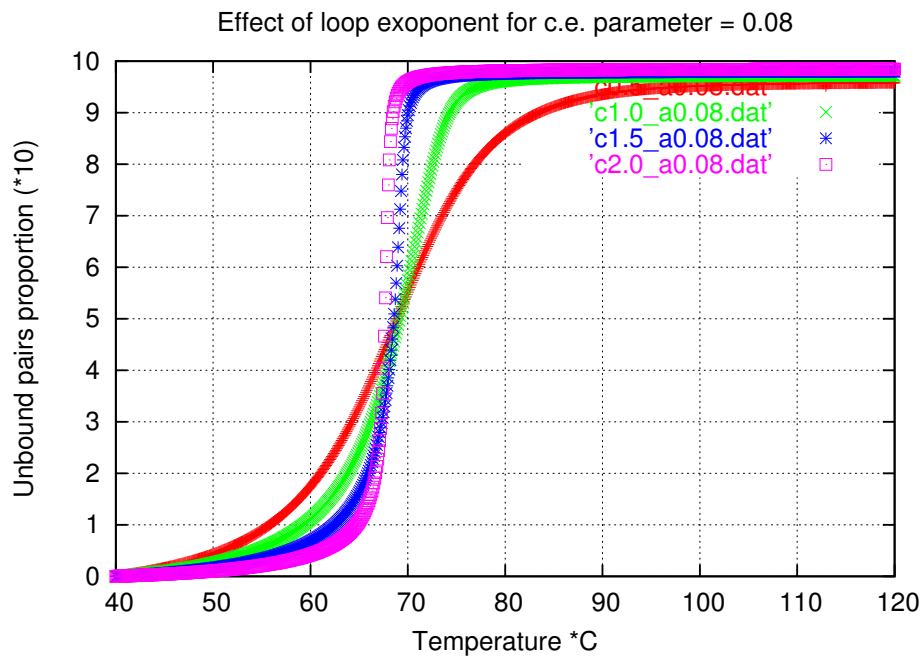


Figure 2: Influence of  $c$  on the melting curve for  $\sigma = 0.08$ . The sequence melted is a two thousand long poly-A.

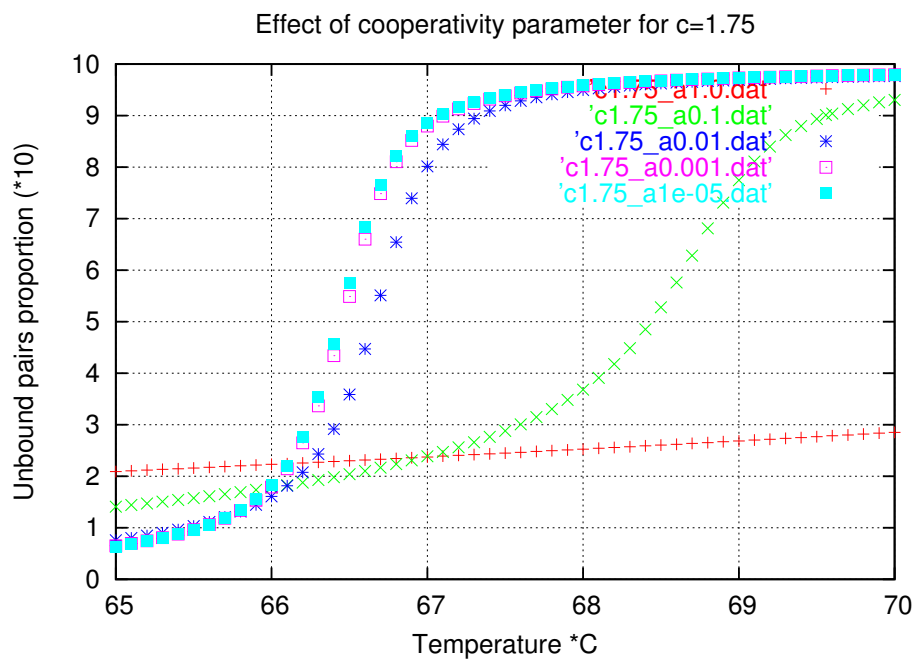


Figure 3: Influence of  $\sigma$  on the melting curve for  $c = 1.75$ . The sequence melted is a two thousand long poly-A.

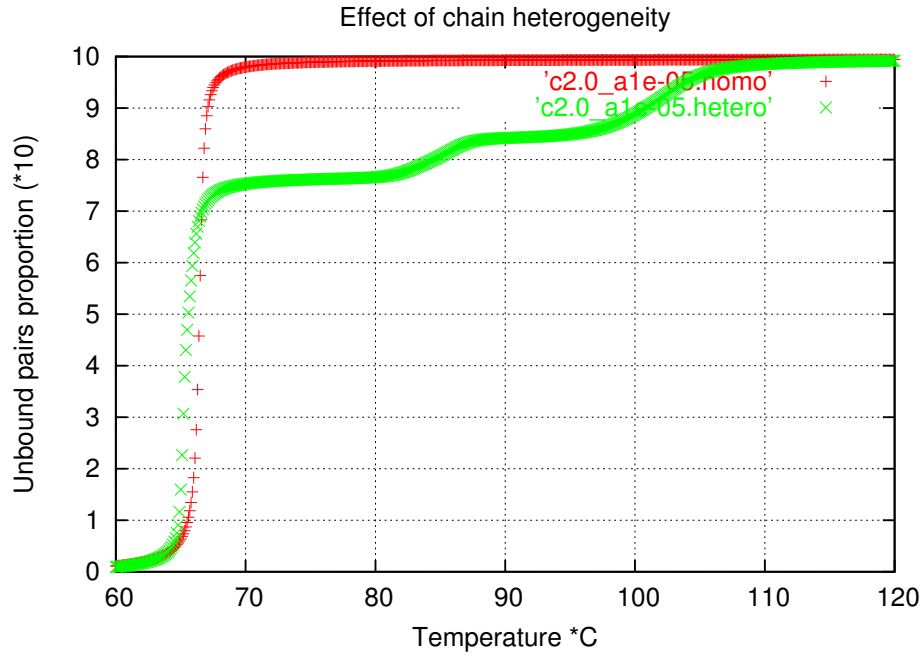


Figure 4: Influence of chain homogeneity. For a non homogeneous chain, the melted curve has several steps.

### 2.3 Effect of dna chain homogeneity

A usual dna chain is composed both of A-T and G-C pairs. Their binding energies are different and one naturally expect that a very inhomogeneous chain will present a melting curve with several steps. The simulation confirmed this expectation as it can be seen on figure 4.

### 2.4 Effect of dna chain length

One can read in Poland and Sheraga (p.234) that when the chain length increases the transition becomes sharper.

### 2.5 Temperature step and salt concentration

We noticed that the variation of those parameters was not relevant. For small variations, no changes can be noticed on the melting curves. High variations of the salt concentration modify the transition temperature. As we can see in the figure 5, a lower salt concentration correspond to a lower transition temperature.

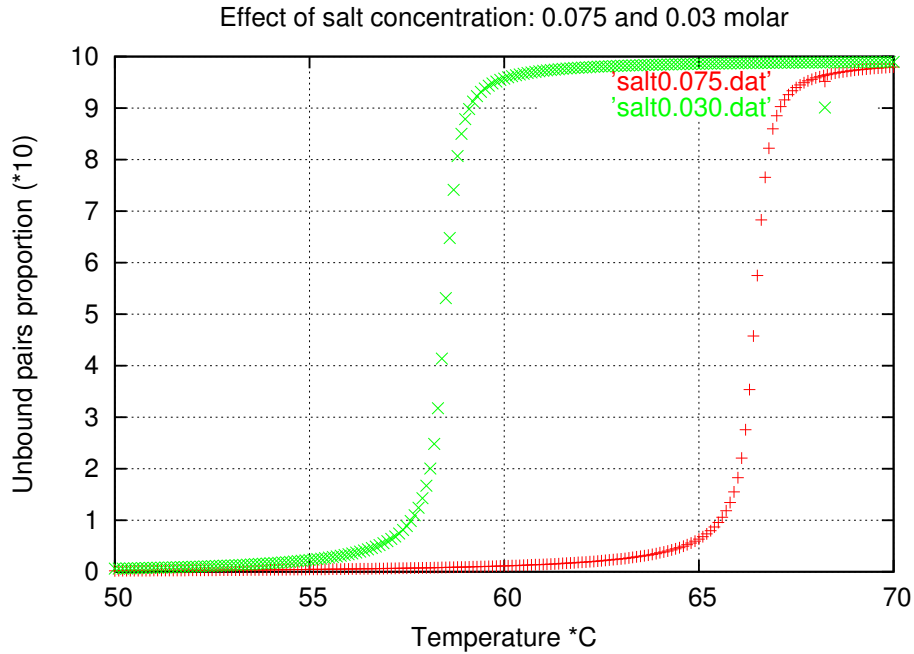


Figure 5: Influence of salt concentration on the melting temperature.

### 3 Conclusion

The Meltsim dna thermal denaturation simulator provide fast melting simulation and allows the variation of various parameters. The transition obtained in the most realistic case ( $c = 1.75$ ,  $\sigma = 10^{-5}$  and  $[Na] = 0.075/mol$ ) is very sharp and let think that the transition is first order. Although in various calculations the loop exponent parameter seems to rule the transition order, we noticed that its effect disappears for small values of cooperativity effects (in general for  $\sigma < 10^{-2}$ ). When  $\sigma$  is set to 1, the transition can be either first or second order, either inexistent. One may notice that this phenomenon was already predicted by the mean field approach. Comparisons between the two models can justify or not the hamiltonian approach in modeling dna's behaviour.