SpiralMaker User's Manual v 1.0

Miquel Marín-Riera[a], Miguel Brun Usan[a], Roland Zimm[b], Tommi Välikangas[a], Isaac Salazar-Ciudad[a,b*]

[a] Genomics, Bioinformatics and Evolution. Departament de Genètica i Microbiologia, Universitat Autònoma de Barcelona, Barcelona, Spain.

[b] Evo-devo Helsinki community, Centre of excellence in computational and experimental developmental biology, Institute of Biotechnology, University of Helsinki, PO Box 56, FIN-00014 Helsinki, Finland.

Index

Presentation

SpiralMaker is a modification of the EmbryoMaker: a general model of animal embryonic development capable of simulating complex developmental processes in 3D (Marín-Riera et al., 2015). SpiralMaker is only concerned with early cleavage, and it only implements one kind of cells (blastomeres), and the limited repertoire of cell behaviors they display. SpiralMaker does not consider gene regulatory networks (GRNs) as EmbryoMaker does. Because of that, many editing and plotting options that are available in the original EmbryoMaker have been disabled in the SpiralMaker.

1. Download Software:

The SpiralMaker software can be downloaded from

http://www.biocenter.helsinki.fi/salazar/software.html

2. Installation (Linux):

2.1 Software requirements:

-Freeglut libraries:

-http://freeglut.sourceforge.net/
-In Ubuntu this can be installed by running “apt-get install freeglut3-dev”

-Mesa Opengl libraries:

-http://www.mesa3d.org/
-They are normally already installed in most linux distributions

-gfortran compiler:

-https://gcc.gnu.org/wiki/GFortran
-In Ubuntu this can be installed by running “apt-get install gfortran”

2.2 Building:

Download the .tar file from the website and save it in the place you want to install the software. Uncompress the .tar file. You may do that by opening a terminal, going to the directory where the .tar file is stored and typing the following command:

```
tar -xzvf <SpiralMaker_directory>.tar.gz
```

where <SpiralMaker_directory> stands for the name the downloaded .tar file has at that moment. While in the terminal, enter the <SpiralMaker_directory> and simply run the *compile_SpiralMaker.sh* script. You may need to grant execution permissions to the script first, in that case type:

chmod +x compile_SpiralMaker.sh

then, to run the script type,

./compile_SpiralMaker.sh

the following output should be printed in the terminal:

descending
/<path_to_SpiralMaker_dir>/src/core
making object files
linking
cleaning
executables installed in bin/

The executable is named SMaker and is placed in the bin directory.

3. Command-line execution options:

This section provides a brief description of how to run the program executable:

Open a terminal and go to the directory where the simulator has been installed. Then type:

./Smaker 4cellstage

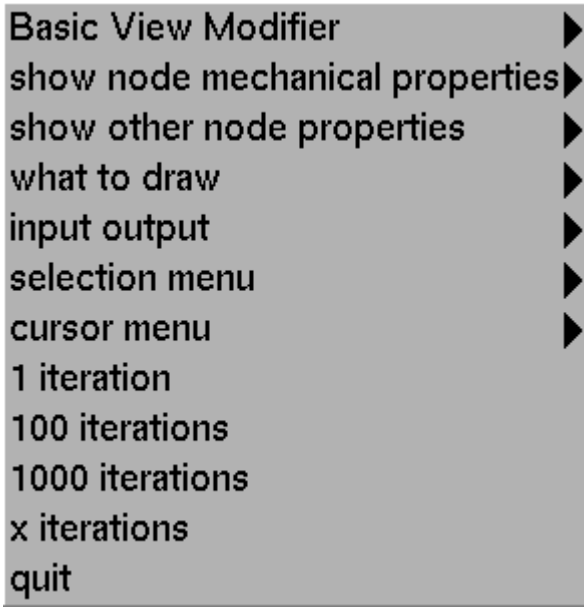
This runs the model with its full graphical interface and the default initial conditions (2500 nodes distributed in four equally sized blastomeres). The parameter values of these initial conditions are one example of those generating a *Trochus*-like blastula (Rot=0.4, w_{SACHS}=0.5, w_{SACHS}=1=16.0 and k^{asym}=2.0). These parameters can be modified by opening the *4cellstage* file (in the bin/ directory) and manually changing the parameter values in the lines 31-36 of the file.

4. Running SpiralMaker with its graphic interface: (Linux)

After the program is executed a window will arise displaying the initial conditions in 3D. This is the simulated blastula. The user can run a number of iterations (by choosing specific options in the menu) and see how this blastula changes over developmental time. The user can also modify how the blastula is viewed and how it is drawn. When pressing the right button a menu will appear. The

following pages detail these options in detail:

4.1. Principal Menu options:



4.1.1. *Basic View Modifier:* This option shows a submenu with options to modify the view of the model results. By default pressing the left mouse button and moving the mouse would rotate the embryo but other options in this menu allow the mouse to do different things on the view. These options are described in section 4.2.1.

4.1.2 *Show node mechanical properties.* This menu allows to display mechanical node properties in two ways, through the color of nodes or through drawing semitransparent spheres over nodes whose size reflect the value of the property. There are also several options to tune the display of each of the two methods. Node coloring and transparent spheres are independent, thus one can display a different node property with each method, but not more than one with the same method at once. See section 4.2.2.

4.1.3 *Show other node properties.* This menu allows to display non-mechanical node properties such as node type, gene expression, etc. This can be displayed in two ways, through the color of nodes and through drawing semitransparent spheres over nodes whose size reflect the value of the property. There are also several options to tune the display of each of the two methods. Node coloring and transparent spheres and independent, thus one can display a different node property with each method, but not more than one with the same method at once. 4.2.3

4.1.4 *What to draw:* This option shows a submenu with a list of options to choose which parts of the embryo are shown in the display and how are those shown. These options are described in detail in section 4.2.4.

4.1.5 *Input Output:* This option shows a submenu with a list of options to save the current state of the embryo into a file or to read previous states from a file. See section 4.2.5.

4.1.6 *Selection menu:* This menu shows different options to select nodes or cells. This is useful to simply track nodes or cells over time, but also allows to use the editor options (section 4.2.6) on them, and to plot their gene expression over time using the *gene plotting options* menu (section 4.1.9).

4.1.7: *Cursor menu:* This menu includes all options regarding the control of the cursor, a tool mainly used to select nodes (see Section 4.1.6) or to mark a reference point in space. See section 4.2.8.

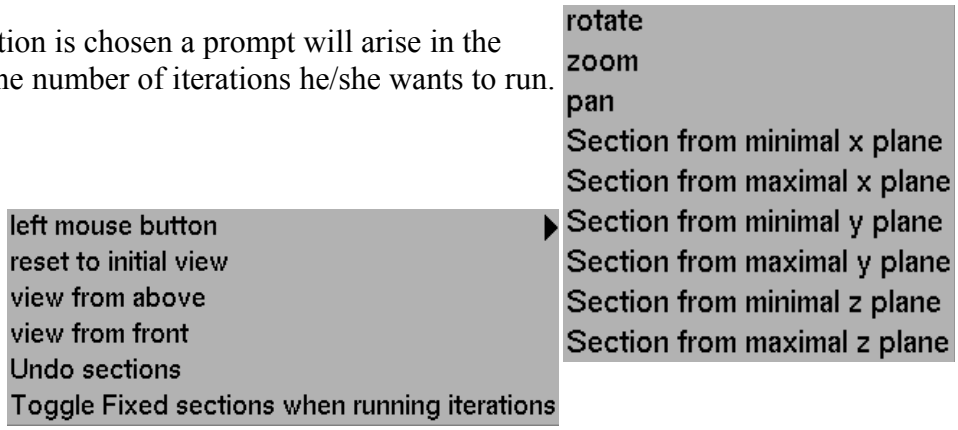
4.1.8 *1 iteration*. Runs the model for 1 iteration. After this is chosen, the window will lock while this number of iterations are running in the simulator. When these are run the current state of the embryo will be shown in the window and the use will win control on the display again. Notice that depending on the number of nodes and the running options this iteration may take more or less time.

4.1.9. *100 iterations.* As above but the model is run for 100 iterations.

4.1.10. *1000 iterations.* As above but the model is run for 1000 iterations.

4.1.11 *x iterations.* When this option is chosen a prompt will arise in the terminal. The user should enter the number of iterations he/she wants to run.

4.1.12. *Quit.* Quits the simulator.



4.2. Submenu options:

4.2.1 *Basic View Modifier* Menu

4.2.1.1 *Left mouse button* Submenu. By choosing one of the options the user decides what happens when dragging with the left mouse button.

4.2.1.1.1 *Rotate*. The camera rotates. This is the default option.
4.2.1.1.2 *Zoom*. Zoom the camera in an out.
4.2.1.1.3 *Pan*. Moving the camera point of rotation.
4.2.1.1.4 *Section from the Minimal x plane.* The mouse will section the embryo as it is moved, starting from the node with the minimal x position. This is very useful to see the interior of the embryo. By default all sections will be undone when the simulation resumes (i. e. running some iterations). Sections can be kept over time with the (see section 4.2.1.6 to set it otherwise)
4.2.1.1.5 *Section from the Maximal x plane.* As above but starting from the node with the maximal x position.
4.2.1.1.6 *Section from the Minimal y plane.* As above but starting from the node with the minimal y position.
4.2.1.1.7 *Section from the Maximal y plane.* As above but starting from the node with the maximal y position.
4.2.1.1.8 *Section from the Minimal z plane.* As above but starting from the node with the minimal z position.
4.2.1.1.9 *Section from the Maximal z plane.* As above but starting from the node with the maximal z position.
These different directions of sectioning can be combined to section the embryo from different sides.

4.2.1.2 *Reset to initial view.* This shows the embryo from the same default view than when the program was started.

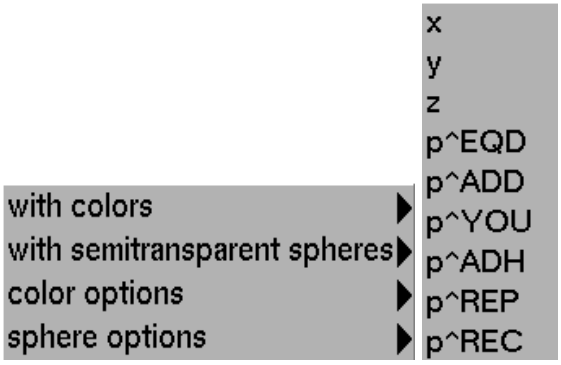
4.2.1.3 *View from above.* Adjusts the view to be from top (from large z values)

4.2.1.4 *View from front.* As above but to see from the front.

4.2.1.5 U*ndo sections.* All sections will be undone and the whole system will be visible

4.2.1.6 *Toggle fixed sections when running iterations.* This allows to switch between keeping the sections during simulations time, or being undone when some iterations are run. By default this option is set to the second case.

4.2.2 *Show node mechanical properties* Menu.



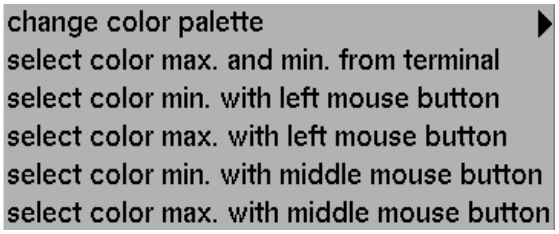
4.2.2.1 *with colors* Submenu. This submenu allows you to select a mechanical node property to be displayed as node color.

4.2.2.2 *with semitransparent spheres* Submenu. This submenu allows you to select a mechanical node property to be displayed as semitransparent spheres of different radius over each node.

4.2.2.3 *Color options* Submenu. This submenu allows to set different options regarding the coloring of nodes.

4.2.2.3.1 *Change color palette S*ubmenu. Allows you to choose between 4 different color palettes.

4.2.2.3.2 *Change color max. and min. from terminal.* This option will change the minimum and maximum values of the node property selected taken into account for coloring each node. All values below the minimum value will have the same minimum color (depending on the palette) and all values above the maximal value will have the same maximum color. The minimum and maximum values will be entered via terminal in the same line separated with a space, in the respective order.

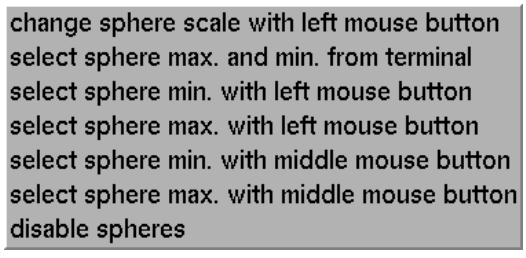


4.2.2.3.3 *Change color min. with left mouse button.* This button allows to change the minimum value described above simply dragging the mouse with the left button.

4.2.2.3.4 *Change color max. with left mouse button.* This button allows to change the maximum value described above simply dragging the mouse with the left button.

4.2.2.3.5 *Change color min. with middle mouse button.* This button allows to change the minimum value described above simply dragging the mouse with the middle mouse button (this means pressing the scrolling wheel, not actually scrolling).

4.2.2.3.6 *Change color max. with middle mouse button.* This button allows to change the maximum value described above simply dragging the mouse with the middle mouse button (this means pressing the scrolling wheel, not actually scrolling).



4.2.2.5 *Sphere options* Submenu. This submenu allows to set different options regarding the semitransparent sphere display of nodes properties.

4.2.2.6.1 *Change sphere scale with left mouse button*. Allows to change the maximum radius of spheres by dragging the mouse with the left button.

4.2.2.6.2 *Change sphere max. and min. from terminal.* This option will change the minimum and maximum values of the node property selected taken into account for setting semitransparent sphere radius for each node. All values below the minimum value will have a

sphere radius of 0 and all values above the maximal value will have a sphere radius equal to the sphere scale (1 by default). The minimum and maximum values will be entered via terminal in the same line separated with a space, in the respective order.

4.2.2.6.3 *Change sphere min. with left mouse button.* This button allows to change the minimum value described above simply dragging the mouse with the left button.

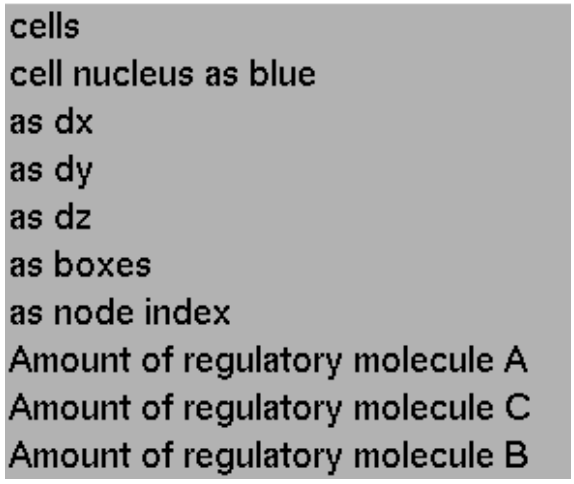
4.2.2.6.4 *Change sphere max. with left mouse button.* This button allows to change the maximum value described above simply dragging the mouse with the left button.

4.2.2.6.5 *Change sphere min. with middle mouse button.* This button allows to change the minimum value described above simply dragging the mouse with the middle mouse button (this means pressing the scrolling wheel, not actually scrolling).

4.2.2.6.6 *Change sphere max. with middle mouse button.* This button allows to change the maximum value described above simply dragging the mouse with the middle mouse button (this means pressing the scrolling wheel, not actually scrolling).

4.2.2.6.7 *Disable sphere.* This option disables the display of semitransparent spheres.

4.2.3 *Show other node properties* Menu. It is exactly the same as the previous menu (4.2.2), except for the node properties you can set in each of the three submenus ("*with colors*" and "*with semitransparent spheres*"). The following descriptions doesn't refer to all the submenus and options, since they are the same as in the previous menu. Instead the node properties that available for display in this menu are described.



4.2.2.1 *Cell.* The cell index of the cell the node belongs to is displayed.

4.2.2.2 *Cell nucleus as blue.* Nodes specified as nuclei will have a value of 0, the rest will have a value of 1.

4.2.2.3 *As cell cycle.* The value of the cell property P^{PHA} of the cell the node belongs to will be displayed.

4.2.2.4 *As dx*. The distance a node has moved in the x axis will be displayed.

4.2.2.5 *As dy*. The distance a node has moved in the y axis will be displayed.

4.2.2.6 *As dz*. The distance a node has moved in the z axis will be displayed.

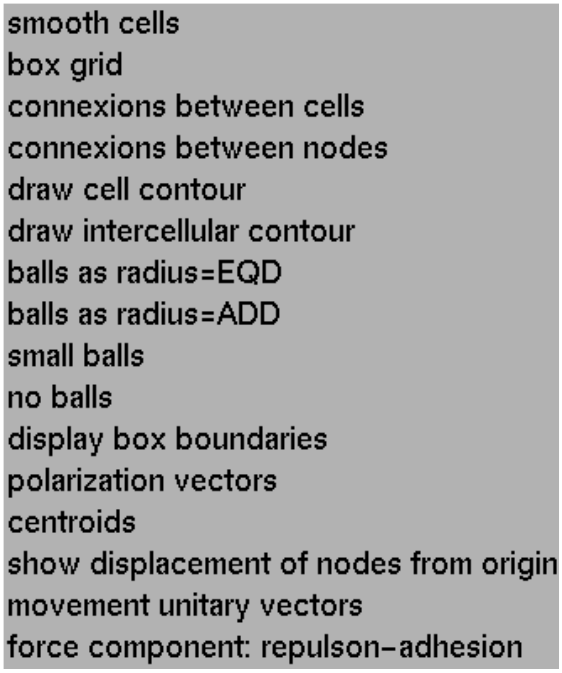
4.2.2.7 *As dtotal*. The total distance a node has moved will be displayed.

4.2.2.8 *As node index*. The index within the node matrix will be displayed.

4.2.2.9 *Amount of regulatory molecules* . The variable displayed will be the amount of a certain molecule expressed in each node. There will be one of those options for each regulatory molecule (A, B or C) described in the system to be simulated (it may change in different developmental simulations).

4.2.3 What to draw Menu

Note that some drawing options will not have a visible effect if other things are drawn in front (most notably one should chose to draw small balls only if one wishes to see the other options). Note also that these options activate a specific drawing when chosen and deactivate it when chosen again.



4.2.3.1 *Smooth cells.* Draws the smoothed surface of the cells based on a 3D-Delaunay triangulation.

4.2.3.2 *Box grid*. Draws a 3D grid around the embryo. The distance between grid points is proportional to the maximal ADD of the nodes in the embryo.

4.2.3.7 *Connexions between cells*. Draws a lines between those nodes from different cells that are in physical contact. These lines are red between nodes of different epithelial cells and green between apical nodes of the epithelium and mesenchymal nodes.

4.2.3.8 *Connexion between nodes*. Draws red lines between the nodes of the same cell.

4.2.3.9 *Draw cell contour*. Draws cellular contours by rendering surfaces between neighboring nodes of the same cell using a 3D Delaunay triangulation.

4.2.3.10 *Draw intercellular contour*. Complements the previous option by also rendering surfaces between nodes belonging to different cells, displaying thus the space occupied by a compact tissue.

4.2.3.11 *Balls as radius=EQD*. Nodes are draw as balls of radius equal to the EQD node property of each node.

4.2.3.12 *Balls as radius=ADD*. Nodes are draw as balls of radius equal to the ADD node property of each node.

4.2.3.13 *Small balls*. Draws the nodes with very small balls. Very useful for the visualization of forces or connections between nodes.

4.2.3.14 *No balls*. Doesn't draw the balls. Very useful for the visualization of forces or connections between nodes.

4.2.3.15 *Display box boundaries.* Shows the boundaries of the display box. Only elements inside this box will be displayed. The display box is useful to make sections of the system.

4.2.3.16 *Polarization vectors*. Draws a line for the polariztion vector of each cell.

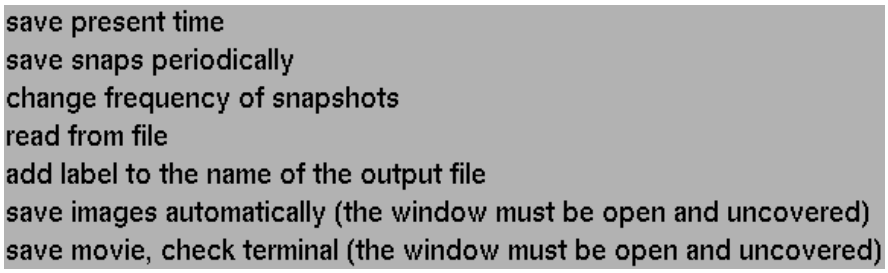
4.2.3.17 *Centroids.* Shows the centroids (this is average of the positions of the nodes in a cell) of each cells by a white ball.

4.2.3.18 *Show displacement of nodes from origin.* Shows a line from the initial position of the node to its actual position. For nodes that arise by growth this initial position is the position at which that node was created

4.2.3.19 *Movement unitary vectors.* Shows a line for each node in the direction in which it moved in the last iteration.

4.2.3.20 *Force components: repulsion and adhesion.* Shows a line for each node in the direction in of the repulsion and adhesion forces affecting the nodes in the last interation.

4.2.4 Input Output Menu.



4.2.4.1 *Save present time*. Save a present state of the embryo. This includes all model parameters (including the genetic ones) and also all node and cell properties.
When this file is read, either from the graphical interface or by calling the simulator with that file in the command line, everything is recovered (including the iteration number). In that sense this file can be used as the initial conditions for other simulator runs. The file is saved in a directory within the "output" directory in the directory where the simulator has been executed. The directory and the file have a random name that includes the date when it was run. This name is the same than the name of the window. The output file is a text file and it can be open by any plain text editor. The meaning of the values saved in it are explained in the same file and can be directly used by the user (as an alternative way to change the embryo's state).

4.2.4.2 *Save snaps periodically.* By choosing this option the state of the embryo is automatically saved into a different file every 1000 iterations.

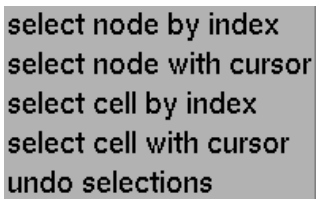
4.2.4.2 *Change frequency of snapshots*. This options prompts a message in the terminal where the user should introduce the iterations intervals in which snaps are taken.

4.2.4.5 *Read from file.* A prompt would arise in the terminal asking the user to introduce the name and address of the file the user wants to read.

4.2.4.6 *Add label to the name of the output file.* Adds a label, given trough the terminal, at the end of the output files saved.
4.2.4.5 *Save images automatically.* Snapshots of the system will be taken during simulation time. The amount and frequency of snapshots is set automatically.

4.2.4.6 *Save movie, check terminal*. Same as previous option, but you need to specify the amount and frequency of snapshots via terminal.

4.2.5. Selection menu.



4.2.5.1. *Select node by index*: When selected, the user should enter in the command line the index(es) of the node(s) to be selected. When the last selected node has been introduced, the user has to type '-1' to end selection. When a node is selected, it will be coloured in white or yellow, and some of its basic properties (such as position or energy) will be shown in the terminal. The last node selected will always be colored in yellow, and will be the one set for using the editor options (see section 4.2.5) and the moving options (see section 4.2.10). The rest of the selected nodes, if any, will be colored in white

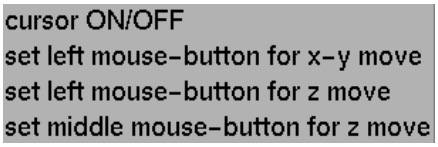
4.2.5.2. *Select node with cursor*. This option allows the user to select nodes using the cursor. By default the cursor is moved in the x-y plane by dragging the mouse with the left button. Pressing the DOWN key will toggle between x-y movement and z movement by dragging the mouse with the left button. In order to select node, approach the cursor to the desired node and press the mouse middle button (press the scroll wheel, but don't scroll the wheel).

4.2.5.3. *Select cell by index*: As in 4.2.7.1, but in here what the user should enter in the command line are the index(es) of the cell(s) to be selected.

4.2.5.4. *Select cell with cursor*: As in 4.2.7.2, but in here what is selected is the cell that is closest to the cursor.

4.2.5.5. *Undo selections*: All selected elements (not only the latter one) are unselected.

4.2.6. Cursor menu.



4.2.8.1. *Cursor ON/OFF*: Toggle cursor function. It is set OFF by default. When activated, the cursor appears in the display window as a red-solid ball, which can be moved by the user across the system to select nodes and cells (see section 4.2.5.2). Notice that, since the cursor appears in a corner of the window, it can be necessary to move it to make it visible. By default, the cursor is moved in the x-y plane by dragging the mouse with the left button, and is moved in the z axis by dragging with the middle mouse button (pressing the scrolling wheel).

4.2.8.2. *Set left mouse-button for x-y move*: When selected, the cursor can be displaced in the x-y plane whith the left mouse-button. This is the cursor displacement mode by default.

4.2.8.3. *Set left mouse-button for z move*: When selected, the cursor can be displaced in the z plane whith the left mouse-button. The user can also alternatively switch between cursor displacements in the x-y or z plane (4.2.6.2 or 4.2.6.3 options) by pressing the "DOWN key" in the keyboard.

4.2.8.4. *Set middle mouse-button for z move*: As in 4.2.6.3, but using the middle mouse-button instead of the left mouse-button.

Enjoy