A computer based simulation to demonstrate stem cell dynamics and regulation – a guide for presenters

Audience: Age 12+. For use at open days or festivals with a scientist facilitator (1 or 2 people sitting at the computer or could be projected onto a screen). Could also be used with school groups with a projected screen or with 1 or 2 students per computer.

Overview: This tool helps demonstrate the role of stem cells in maintaining a healthy body. It shows a dynamic population of stem and differentiated cells, with the number of each cell produced regulated by three feedback mechanisms. The three types of regulation can be turned on or off, showing the audience why regulation is needed and also how a level of redundancy in regulation can create a more robust system. The simulation also has a control for destroying 50% of the cells in the population, so that it can be seen how a system might recover from an injury and the role of stem cells in the recovery. A further two controls allow for the introduction of cancerous cells into the system. Above all, the simulation helps demonstrate how computer modeling is contributing to an understanding of stem cells and system dynamics. **In the zip folder you will find the Stem Cell Simulation Tool Java file, the tool manual and some background information about the biology of stem cells for public users.**

Getting started - Overview of the simulation windows:

When you open the 'StemCellSimulationTool' file, the three windows shown on the next page will open. A more detailed explanation of how each window works and the settings involved can be found in the 'manual' file, but personally I found it most useful to just have a play before reading the more detailed notes. **See next page**

start with a stem cell

Stem cell simulation tool:

A computer based simulation to demonstrate stem cell dynamics and regulation

The colour of the word ‘HEALTH’ corresponds to the health of the system. Green is healthy, red unhealthy and orange is in between. This change in colour corresponds to the changing range in the graphs.

Population of cells where blue are stem cells and green differentiated cells. The green cells fade in colour as they get older.

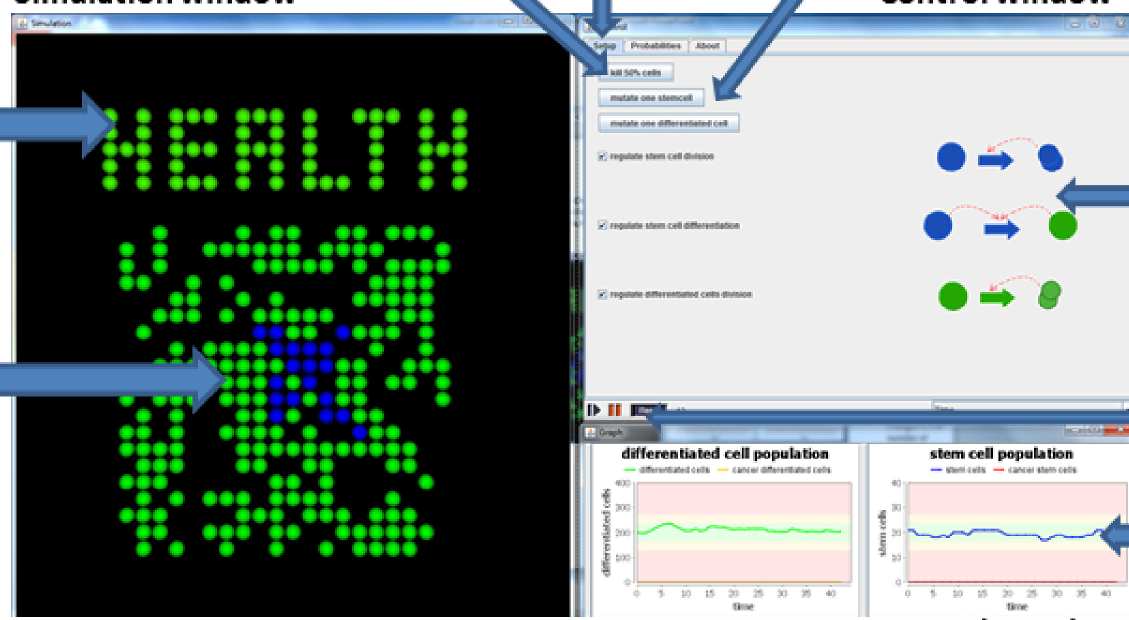
50% of the cells will be killed each time this button is pressed.

Set up tab: Main tab of the control window. Probabilities tab: Used for viewing and manipulating probabilities of cell fate.

Buttons which allow you to introduce a cancerous cell to the system.

Simulation window

Control window



Graph window

The three types of regulation corresponding to their respective feedback mechanism.

Play/Pause/Stop and Restart buttons

Graphs showing the changes in the number of each type of cell over time.

start with a stem cell

Stem cell simulation tool:

A computer based simulation to demonstrate stem cell dynamics and regulation

Working with the public: Three things to think about

Pitch: To help pitch appropriately I think about - What is the audience's background knowledge, understanding and perception of stem cells? What is the age of the audience? Are they likely to have studied stem cells at school? Have they been doing any other activities about stem cells that day? As a general rule start with basic information about stem cells (see level one of the key messages). People will generally tell you if they already know what you're telling them but are less likely to tell you that they don't understand. Maintaining a dialogue and looking for non-verbal cues (for example facial expressions) will help you monitor your audience's understanding. Try and avoid a monologue as it doesn't give you a chance to assess whether you are pitching the demonstration appropriately.

Time: How motivated and interested is your audience? What is their attention span? How much time has the audience before they move on to another activity?
It's probably worth planning an initial short 5 minute session which includes some introduction, demonstration and activity. For example using '***Our cells are in constant turnover' and 'If we are injured '*** described on the next page. This provides a complete story for the audience to take away, and maintains interest even if the audience are only with you for a short time. For audiences who have more time and / or interest then this can be built upon and the simulation can be explored in more depth.

A positive experience: As well as an understanding of the science shown by the simulation we want the audience to go away feeling curious and interested, having had a positive experience. This is where it helps to be reflexive to the feedback (both verbal and non-verbal) we get from the audience. By showing enthusiasm, positivity, humour, curiosity and approachability, we can change the experience of the audience.

start with a stem cell

Stem cell simulation tool:

A computer based simulation to demonstrate stem cell dynamics and regulation

Working with the public: What will you say?

There are several ways that you could introduce the simulation and lead the audience through its different components and over time you'll most certainly find one that suits you best for each audience that you come across. Here is an example of how I've demonstrated the simulation. It's broken up into sections so that sections can be selected based on the time available, the audience you have and their interests. I've worked through all of the sections consecutively with an adult audience and it took about 20 minutes.

1. Our cells are in constant turnover…

[OPEN UP ALL THREE WINDOWS ON SCREEN. SELECT PLAY THEN PAUSE SO THAT THE GROUP OF CELLS AND THE WORD 'HEALTH' CAN BE SEEN]
You probably know that your body is made from trillions of cells. Here we have a group of cells on the screen. Everyday new cells need to be made as old ones die– just think of when you wash yourself in the shower and that what is scrubbed off is not just dirt but dead skin cells. Also, we need new cells as new muscle and hair grows and wounds heal... Most cells can't replicate so we have reserves of cells, stem cells, found throughout the body that can make the new cells we need. As well as making different kinds of new cells, stem cells can also make copies of themselves so that the reserve doesn't run out. We can see the stem cells here in blue.
The differentiated cells, which have more specialised jobs, are shown here in green. To keep healthy we must keep a constant supply of stem cells and differentiated cells. We can see there is a healthy balance when the colour of the word HEALTH on the screen is green. [SELECT PLAY BUTTON, TO START THE SIMULATION] We can see here that our group of cells is staying healthy as we have the right balance of stem cells and differentiated cells. We can also see that the differentiated cells get older and die which is shown by their colour fading.

2. If we are injured…

Imagine we fell off our bike and started to bleed a lot. We would be losing a lot more cells than normal. Let's see what happens if we kill lots of the cells in our group [ASK AUDIENCE TO PAUSE AND TO KILL 50% CELLS, THEN A FURTHER 50%, THEN PRESS PLAY STEP BY STEP]. We can see our group of cells is out of balance as the word HEALTH is in red which shows there are not enough stem cells and differentiated cells (if we look at the graph we can see that its gone below the critical number that we need). But after a time the group of cells manages to get back to a healthy state. Can our body always regain a healthy balance? There is a limit to this recovery – for example if you've ever given blood you'll know that the amount taken is limited so that you can remain healthy whilst your body replaces the blood that has been donated.

start with a stem cell

Stem cell simulation tool:

A computer based simulation to demonstrate stem cell dynamics and regulation

Working with the public: What will you say?

3. Cells are regulated…

How does our body maintain this balance? How does our group of cells know what type of cell to make to bring the group back in balance? This happens as the cells are able to communicate with each other through signals and in this way the number and type of cell made is regulated. These signals – the feedback – are shown on the screen [SHOW THE THREE TYPES OF REGULATION IN THE CONTROL WINDOW]. Scientists can create computer programs like this, giving the cells 'rules', to test out ideas about how cells might work. By comparing the results with lab data, or by using the computer data to design experiments these methods are helping create a better understanding of cells.

4. Regulation has a back-up plan…

You'll see that there are three types of regulatory feedback. Let's see what happens to our group of cells and the graphs if we remove one, two or three of these [UNCHECK ONE, TWO OR THREE OF THE REGULATORY MECHANISMS]. We can see that there is some redundancy in the regulation. Regulation controlled by more than one feedback mechanism means that there is a better chance that our group of cells keeps in balance. This is what also happens in our bodies.

5. Stem cells are important…

But can this regulation always bring our group of cells back into balance? What about if there are no stem cells present? [UNCHECK THE TWO BOXES WHICH REGULATE STEM CELL PRODUCTION – 'REGULATE STEM CELL DIVISION' AND 'REGULATE STEM CELL DIFFERENTITION] Eventually, all of the differentiated cells die as there are no stem cells left to replenish the cells that have been lost. Scientists are thinking about ways of applying this knowledge in clinical therapies. For example, a chemical burn which destroys the entire stem cell reserve in the eye can leave a person blind as the eye is left unable to repair itself. By using stem cells from the 'good eye', a new cornea can be grown and be used for transplanting to the damaged eye. With the stem cell store replenished, the damaged eye can repair.

6. Cancer…

You'll have heard of cancer. You may even know someone who has had or has cancer. Let's see what happens when we introduce a cancer cell into our group of cells [MUTATE A STEM CELL INTO A CANCER CELL AND THEN SELECT PLAY BUT IN SINGLE TIME STEPS]. Red cells are cancer stem cells; orange cells are cancer differentiated cells. The problem with cancer cells is that they do not respond to regulatory feedback properly and so can divide uncontrollably. We can also see that the cancer cells don't always spread. Sometimes the cancer cell(s) die(s) which means that the cancerous cell doesn't cause a problem. We can also compare what happens if there is a cancer stem cell as opposed to a cancer differentiated cell (MUTATE A DIFFERENTIATED STEM CELL).

start with a stem cell

Stem cell simulation tool:

A computer based simulation to demonstrate stem cell dynamics and regulation

Working with the public: What will you say?

7. Probabilities…

[OPEN THE CONTROL WINDOW AND THE PROBABILITIES TAB]. We can see here the possible cell fates for each time step. We can also see the probabilities of each of these fates occurring. For example, we can see that stem cells are more likely to make copies of themselves than they are to die. We can alter these probabilities to see their effect on the group of cells as long as the probabilities add up to less than one (they don't add up to one as the cells sometimes do nothing!).

This is an example of how scientists might use a computer program to look at the effects of changing parameters might have on a system. This gives further insight into how cells work.

Key messages: A progression of concepts

The simulation can be used to convey many key ideas about stem cells, cell population dynamics and the use of modeling. I usually find it helpful to have these in mind and decide which ones I would most like to communicate whilst maintaining a flexibility to allow for the interests of the audience.

First level

- Our bodies are made of trillions of cells of many different types.
- During our life many cells die and new ones are made.
- A pool/ reservoir of stem cells are needed for new cells to be made.
- Stem cells can make copies of themselves or differentiate into different cell types.
- Scientists are using computer models to think about how stem cells and differentiated cells work.

Second level

- Some cells have a higher turnover rate than others eg skin compared to brain
- The number of stem cells and differentiated cells in our bodies is regulated.
- Regulation is achieved through feedback between cells.
- By creating different rules in a simulation we can test their outcomes and relate this to what is observed in experiments, or design experiments around the outcomes.

Third level

- Redundancy is incorporated into the regulatory system
- Cell fate is based on probability