COMPUTER SIMULATION FOR THE DEVELOPMENT OF IMMUNE CELLS

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OUTLINE

- Introduction
- Human immune system
- Case study
- Simulation
- Conclusion

INTRODUCTION

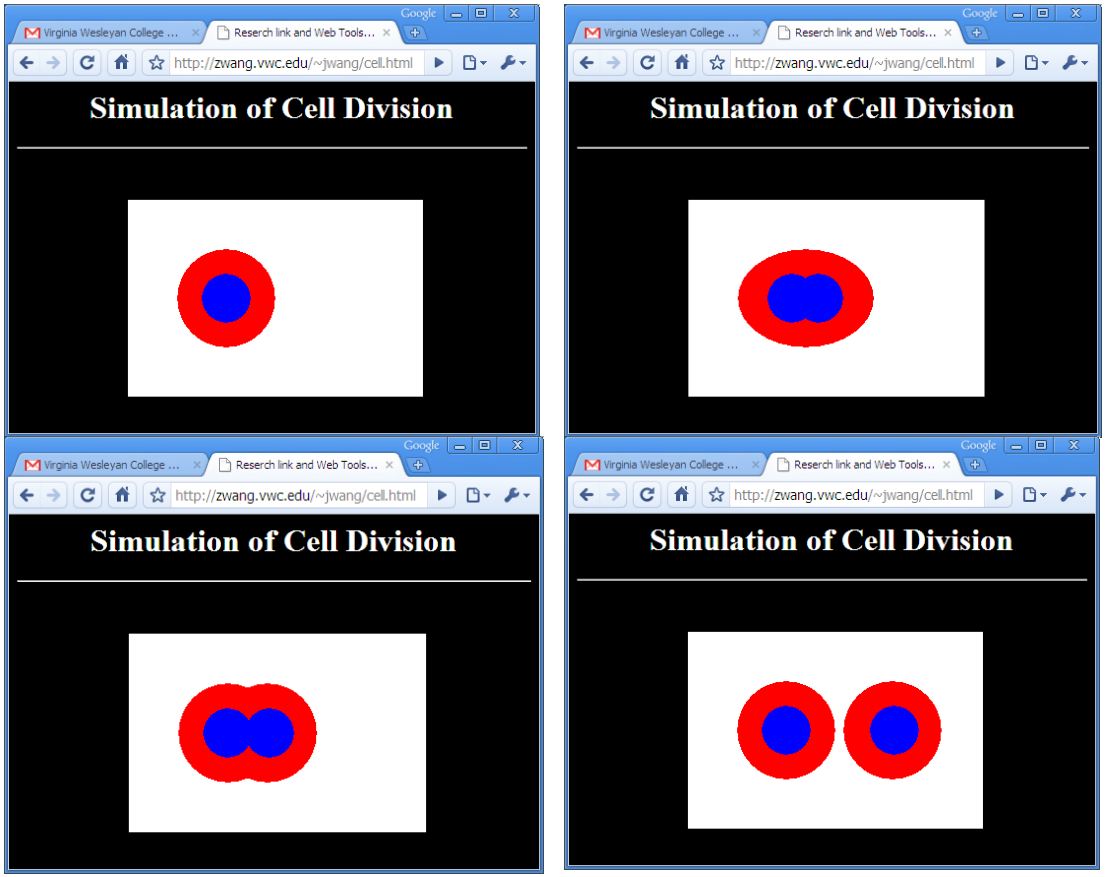
- Human cells and cancer
- Chemo may do more harm than good
- Human immune system
- Three states of immune system vs. cancer
  - Immune surveillance : safe state
  - Equilibrium state
  - Escape state
- Importance of computer simulation

CANCER

- A type of human cells
- Abnormal or bad cells
- Not killing human (!!!)
- Consuming nutrition and space
- Chance to become normal (very low, though)
- May be killed by normal cells (immune cells) or chemicals/laser
- Unknown mechanism (can’t simulate)

CANCER (CTD)

- Develop fast !!!



IMMUNE CELLS

- Components of the immune system
- May kill cancer and other infected cells
- Every body has them – Actually, a lot of
- Getting sick easily if they are weak
- May be stronger if you take care of them
- Looking younger and living a long, healthy life if you have a strong immune system

IMMUNE CELLS (CTD)

- Mainly white blood cells
- Natural killer cells (NK), T cells and B cells
- *Innate* and *adaptive* immune layers and mechanisms
- Innate layer – including NK cells; fast but limited power
- Adaptive layer – T and B cells; slow but more power

B CELLS

- B lymphocytes
- Initiated and matured in bone (B) marrow
- One of important immune cells
- When a body part is infected, the B-cell can stimulate the system to produce a great amount of antibody which can kill the infected cells

T CELLS

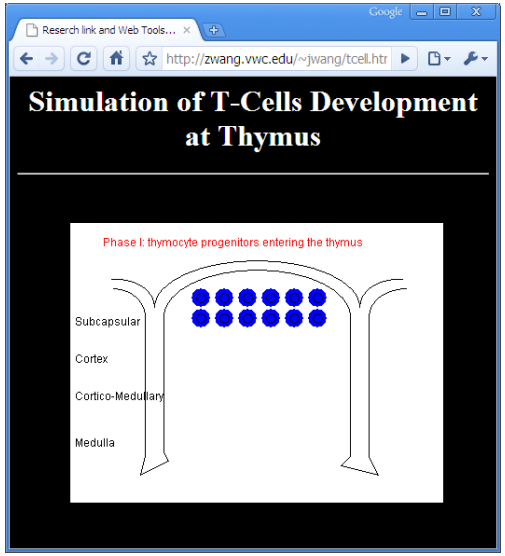
- T lymphocytes
- Initialized in bone marrow (like B cells) and matured in the thymus (T)
- T CD4 (or T4) cells and T CD8 (or T8) cells
- T4 cells, the helper cells, coordinate the immune response
- T8 cells, the killer cells, kill the bad or infected cells

CASE STUDY

- T cells play one of the most important roles in defending our body
- Simulation of the development of T cells
- The maturing process of T cells in thymus has two important stages:
  - Positive selection
  - Negative selection

T CELLS DEVELOPMENT

(a)



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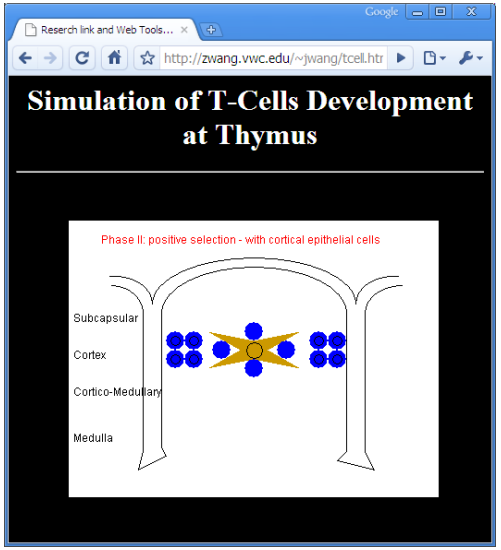

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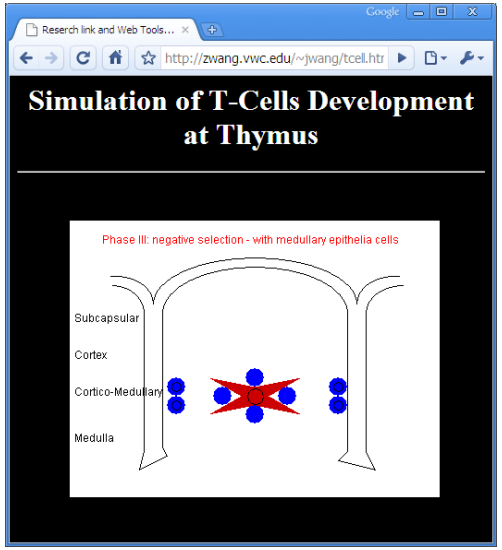
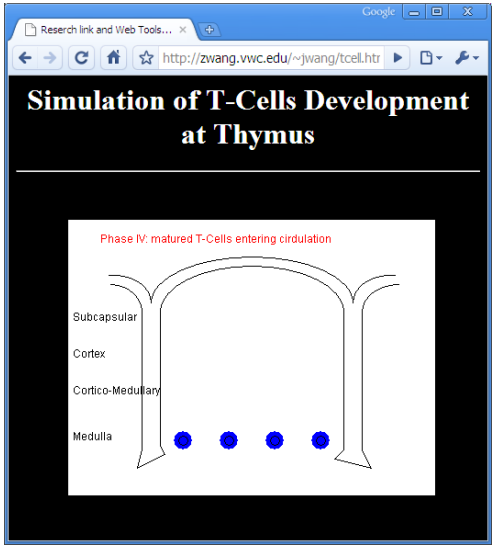


(d)



T CELLS DEVELOPMENT (CTD)

- Initial phase (a): The progenitors of T cells from bone marrow enter the thymus for maturing
- Positive selection phase (b): Only 1-2% of the cells, the *double positive thymocytes*, has the receptors that can interact with one of the MHC (major histocompatibility complex) class I or II isoforms, being selected to mature further, and leaving the majority to die

T CELLS DEVELOPMENT (CTD)

- Positive selection (b):
  - T4 cells interact with the MHC II molecules
  - T8 cells interact with the MHC I molecules
- Negative selection phase (c): deletes T cells being potentially auto-reactive to cause tissue damage and autoimmune disease
- Exit phase (d): T cells leave the thymus and enter the circulation

SIMULATION

- Based on the Java applets and threads.
- The function representing the thymus frame:

```
private void OutStruct(Graphics g)
{
     g.setColor(Color.black);
     g.drawString("Subcapsular", 5, 110);
     ...
     // left part
     g.drawArc(10, 60,80,60, 0, 100);
     g.drawArc(10, 70,70,60, 0, 90);
     ...
}
```

SIMULATION (CTD)

- The code segment for the initial phase when T cells progenitors entering the thymus:

```
OutStruct(g);
for(int i=0; i<6; i++)
      for(int j=0; j<2; j++)
      {
            g.setColor(Color.blue);
            g.fillOval(130+i*25, 70+j*22, 20, 20);
            g.setColor(Color.black);
            g.drawOval(135+i*25, 75+j*22, 10, 10);
      }
```

SIMULATION (CTD)

- Positive selection: cells to be deleted is in color blue and attaching to the epithelial cells

```
g.setColor(new Color(204, 153, 0));
g.fillPolygon(x3, y3, 8);
g.setColor(Color.black);
g.drawOval(192, 132, 17, 17);
// cells to be removed
g.setColor(Color.blue);
g.fillOval(155, 130, 20, 20);
g.fillOval(225, 130, 20, 20);
...
```

SIMULATION (CTD)

- Negative selection:

```
g.setColor(new Color(204, 153, 0));
g.setColor(new Color(204, 0, 0));
g.fillPolygon(x4, y4, 8);
g.setColor(Color.black);
g.drawOval(192, 182, 17, 17);
// cells to be deleted
g.setColor(Color.blue);
g.fillOval(155, 180, 20, 20);
g.fillOval(225, 180, 20, 20);
...
```

CONCLUSION

- Simulation of the development of T cells with Java applets and a thread object
- Better understanding of the adaptive immunity
- Four phases in the development of T cells
- Further research:
  - Simulation of B cells development
  - Simulation of measures improving the immunity