Cellular Automata Modeling of Tumor Growth Using Object-Oriented Methods

Reporter: Kalinicheva Marya
Organization: BMSTU (Russia)
Department: Medical-technical Information Technologies
Supervisor of Studies: Kotin V.V.

Subject of modeling: tumor

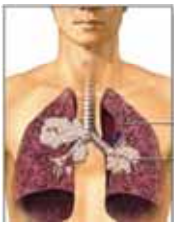
Tumor is a mass of abnormal tissue with:

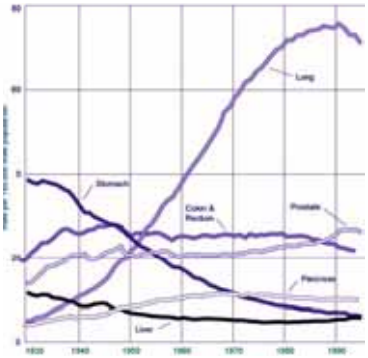
- no purposeful function
- tendency to independent and unrestrained growth
- the potential to invade and destroy neighboring tissues and create metastases

Cancer: some facts and figures

Risk factors:

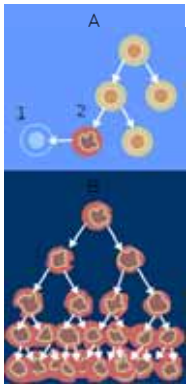
- Smoking (90% of lung cancer)
- Air pollution
- Radon gas
- Genetic factor





Biological properties of tumor cells

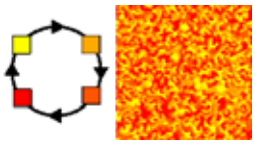
- Acquisition of self-sufficiency in growth signals
- Loss of sensitivity to anti-growth signals
- Loss of capacity for apoptosis
- Loss of capacity for senescence, leading to **limitless replicative potential** (immortality)
- Acquisition of sustained angiogenesis, allowing the tumor to **grow beyond the limitations of passive nutrient diffusion**
- Acquisition of **ability to invade** neighbouring tissues
- Acquisition of **ability to build metastases** at distant sites
- **Loss of capacity to repair genetic errors**, leading to an increased mutation rate (genomic instability)



Method: Cellular Automata

Cellular automaton (pl.: cellular automata) is a discrete model studied in computability theory, mathematics, theoretical biology and microstructure modeling.

Model concists of:
- Grid of *cells*
- Finite number of states

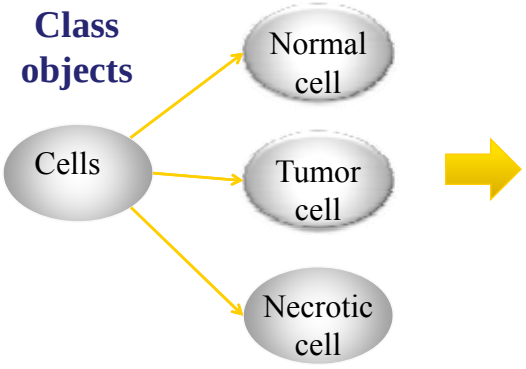


Advantages:
- Describing complex community's behavior using behavior rules for each its member
- In case of cancer modelling CA can give the geometry of tumour
- Verbal model of cells' behavior is exactly embodied in CA rules

Cellular automata using OOP methods

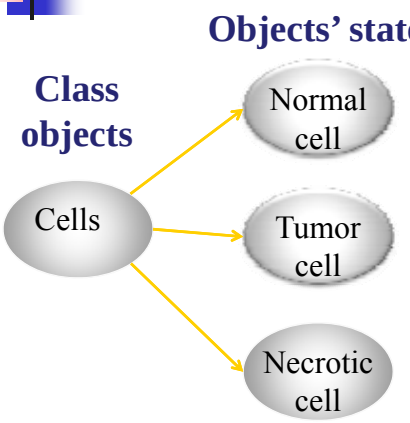
Objects' states

Class objects



Methods:
- Apoptosis
- Division
- Migration
- Mutation

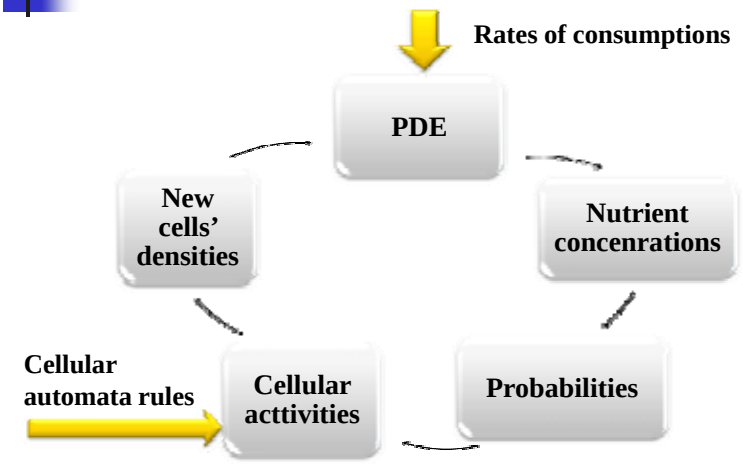
Cellular automata using OOP methods



Attributes:

- Position (x,y)
- Lifetime
- Mitosis period
- Rates of consumpion
- Capacity to mutation
- Capacity to repair genetic errors
- Replicative potential

Cellular Automata Life Cycle



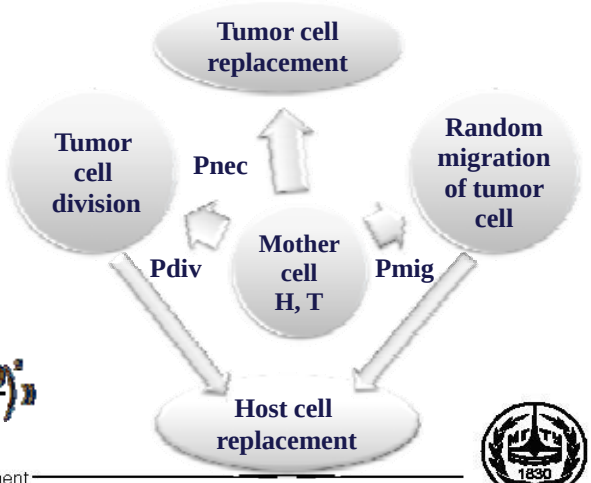
Cells division, death and movement in cellular automata model

Cellular automata probabilities

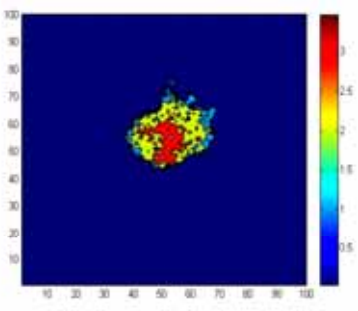
$$P_{nec} = \exp\left(-\left(\frac{m(i,j)}{(T(i,j)+H(i,j))\cdot 5}\right)^{n}\right)$$

$$P_{div} = 1-\exp\left(-\left(\frac{m(i,j)}{(H(i,j)+T(i,j))\cdot 5}\right)^{n}\right)$$

$$P_{mig} = 1-\exp\left(-(T(i,j)+H(i,j))\cdot 5\cdot\left(\frac{m(i,j)}{m_{mig}}\right)^{2}\right)$$



Results in simple tissue



Tumour cells' distribution after 30 iterations

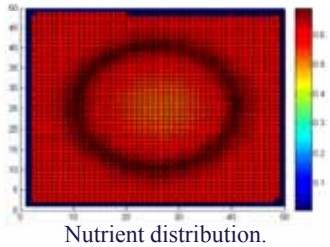
Model parameters

- Lifetime: 5-7 days
- Mitosis period :16-24 hours
- Main resource is glucose
- Pathological cells consume the resource in 10 times more than normal cells

On tumor shape influence:

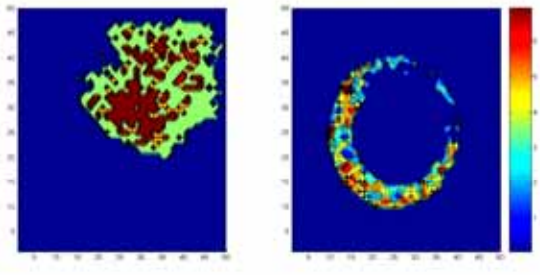
- The relative rates of tumor cells nutrient consumption
- The original tissue density
- Host cells rate of consumption

Results of modeling in complex tissue



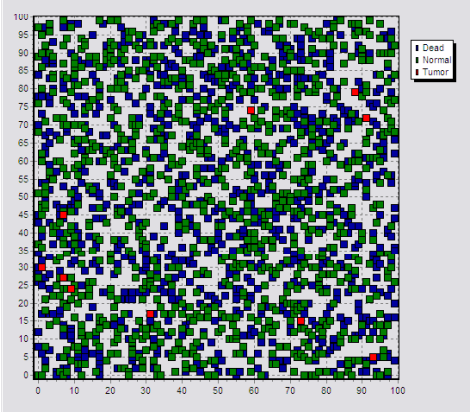
Nutrient distribution.
Colour represents relative concentration

Normal and patological cells' distribution



Distribution of normal (right) and tumour (left) cells

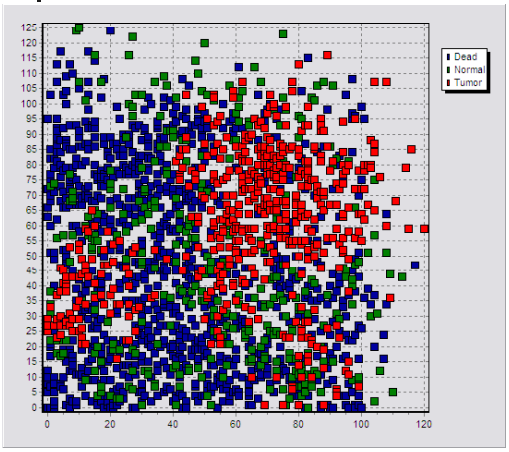
Modeling using OOP



Initial cells' distribution

- 10 tumor cells
- 1000 normal cells
- 1000 necrotic cells
- Square domain 100x100 CA cells
- Lifetime is 5 cycles for normal and 20 cycles for tumor cells

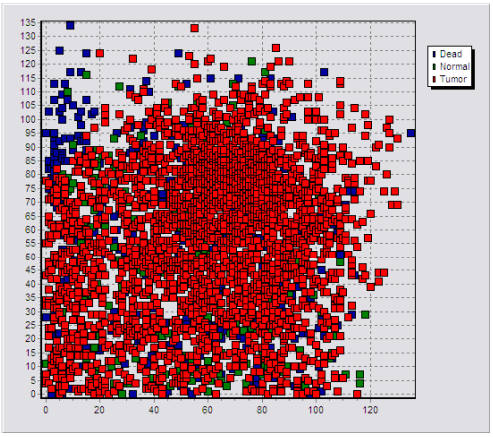
Modeling using OOP



Cells' distribution after 35 cycles

- Totally 2048 cells
- 531 tumor cells
- 369 normal cells
- 1142 necrotic cells
- Two tumor focuses

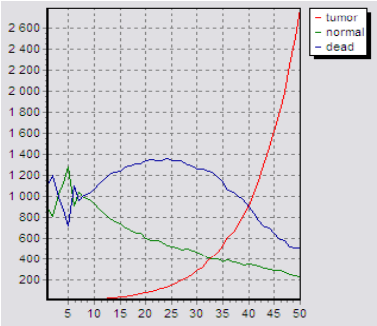
Modeling using OOP



Cells' distribution after 50 cycles

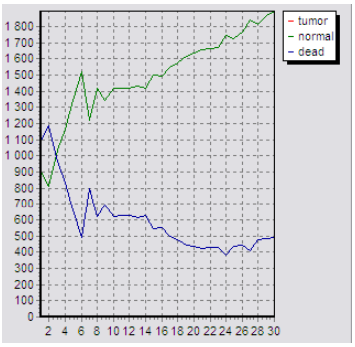
- Totally 3837 cells
- 2785 tumor cells
- 216 normal cells
- 512 necrotic cells
- Tumor focuces united

Results



Unlimited resource and loss of capacity to apoptosis lead to exponential tumor growth

Normal tissue growth (is linear)



Conclusions

- Cellular automata modeling conception perfectly coordinates with biological description of tumor growth.
- Object-oriented programming allows to build a flexible model built on cellular automata conception, and to complicate the automata rules without total model rebuilding.
- Futher model development may include building 3D-model, adding immune cells and limiting resources, adding chemotherapy influences ect.

References

1. Arkushina E.M., Kotin V.V. The Computer Modelling of Normal and Pathological Tissue Growth using Cellular Automata Conception. Biomedical electronics, №10, 2007, p. 52-57
2. Ershov U.A., Kotin V.V., Kirillova S.K., Kabisov R.K. Cancer Deseases Revealing on the Basis of Tumour Growth Kinetic Analysis and Increase of Efficiency. Biomedical electronics, №10, 2005
3. Ershov U.A., Kotin V.V., Starchenko V.M. Modelling of Local Tumour Growth using Cellular Automata Conception. Scientific and Technical Conference "Medical Technology on Guard of Health" Collected Articles 02.10-09.10.2005. M: MSTU, 2005
4. Litvitsky P.F. Physiopathology. V.1. GEOTAR-MED, 2002
5. Georgiady S.G., Kotlyarov P.M . Computer-aided tomography signals of diffuse lung diseases
6. D.G.Mallet, L.G. De Pillis. A cellular automata model of tumor-immune system interactions. Journal of Theoretical Biology 239 (2006) 334-350
7. Ferreira Jr., S.C., Martins, M.L., Viela, M.J., 2002. Reaction-diffusion model for the grouth of avascular tumour. Phys. Rev. E 65 021907
8. Greenspan, H.P., 1972. Models for the growth of a solid tumor by diffusion. Stud. Appl. Math. 51, 317–338.
9. Kuznetsov, V., Knott, G., 2001. Modelling tumor regrowth and immunotherapy. Math. Comput. Modell. 33 (12/13), 1275–1287
10. Anufriev I.E, Smirnov A.B. MATLAB 7. , 2005. 1104p.
11. Mandelbrot, B.B. (1982). The Fractal Geometry of Nature. W.H. Freeman and Company.
12. http://info.cancerresearchuk.org/images