## A Membrane Computing View on Tumours

Miguel A. Gutiérrez-Naranjo, Mario J. Pérez-Jiménez, Agustín Riscos-Núñez, Francisco J. Romero-Campero

Dpto. de Ciencias de la Computación e Inteligencia Artificial E.T.S. Ingeniería Informática, Universidad de Sevilla Avda. Reina Mercedes s/n, 41012, Sevilla, España {magutier, marper, ariscosn, fran}@us.es

**Abstract.** In this paper we discuss about the potential usefulness of P systems as natural tools for modelling tumours. This is done both from a macroscopic point of view, by considering the tumour as a growing mass of cells, as well as from a microscopic point of view, by studying molecular signalling pathways. In each of these approaches we work with appropriate variants of P systems

## 1 Introduction

Natural Computing is a field that tries to abstract ideas and new paradigms for introducing models of computation inspired by Nature. One of the branches within this field is Membrane Computing, presented by Gh. Păun in [16], where the basic computing devices are the so-called *membrane systems* or P systems.

Roughly speaking, a P system consists of a cell-like membrane structure in the compartments of which one places multisets of objects which evolve according to given rules in a synchronous non-deterministic maximally parallel manner<sup>1</sup>. P systems offer two levels of parallelism: on the one hand, the rules within a membrane are applied simultaneously; on the other hand, these operations are performed in parallel in all the membranes of the system.

To sum up, P systems have the following properties:

- P systems can be considered as structures of nested processors placed in a tree-structure i.e., we can consider computations on many scales.
- If we consider P systems where membranes can be dissolved, divided or created, we usually obtain a geometrical shape too irregular to be described in traditional geometrical language, both locally and globally.
- Computations in P systems are obtained by the application of a finite set of rules. The application of these rules allows to obtain a configuration  $C_{n+1}$  from another configuration  $C_n$ .
- The computation of a P system is discrete, i.e., it is a process performed *step* by *step*.

<sup>&</sup>lt;sup>1</sup> A layman-oriented introduction can be found in [18], a formal description in [17], and further bibliography at [24].

In this paper we address the issue of using P systems in order to provide a better understanding of tumours. From an intra-cellular point of view, one can try to express the molecular interactions happening in the cytoplasm of a tumoral cell by means of P systems. We will recall some ideas from [20], where the EGFR signalling pathway is studied, but we are not going to focus on this approach. We will also consider a macroscopical point of view, looking at the whole tumour.

The rapid growth and resilience of tumours make it difficult to believe that they behave as disorganised and diffuse cell mass and suggests instead that they are emerging, opportunistic systems. If this hypothesis holds true, the growing tumour and not only the single cell must be investigated and treated as a self-organising complex dynamic system. This cannot be done with currently available in vitro/in vivo models or common mathematical approaches.

We follow here a number of recent studies (see [1, 3, 5, 10, 11, 14, 21, 22]) postulating that tumours have a *fractal* shape. The massive parallelism, the synchronous application of the rules, and the discrete nature of their computation, among other features, lead us to consider P systems as natural tools for dealing with fractals. Several examples of fractals represented by P systems are presented, and we propose to use P systems as a new tool for representing and simulating the fractal nature of tumours.

The paper is organised as follows. First we deal with tumours at macroscopic level. We recall de definition of P systems with membrane creation in Subsection 2.1, and we explain how the evolution of a P system can be linked to the construction of a classical fractal, the Koch curve. Subsection 2.3 concludes the macroscopic approach, and it addresses random fractals, which are closer to the real shape of tumours. Section 3 is devoted to the intracellular scenario of tumoral cells. In this case we recall the definitions of continuous P systems and we briefly present the EGFR signalling pathway in Subsection 3.2.

## References

- 1. J.W. Baish, R.K. Jain: Fractals and cancer. Cancer Research, 60 (2000), 3683–3688.
- M.F. Barnsley: Lecture notes on iterated function systems. Proceedings of Symposia in Applied Mathematics, AMS, 39 (1989), 127–144.
- A. Brú, J.M. Pastor, I. Fernaud, I. Brú, S. Melle, C. Berenguer: Super-rough dynamics on tumour growth. *Physical Review Letters*, 81, 18 (1998), 4008–4011.
- 4. A. Bunde, S. Havlin, eds.: Fractals in Science. Springer-Verlag, 1995.
- 5. S.S Cross: Fractals in pathology. Journal of Pathology, 182 (1997), 1-8.
- M. Dekking, J.L. Véhel, E. Lutton, C. Tricot, eds.: Fractals: Theory and Applications in Engineering. Springer-Verlag, 1999.
- K. Falconer: *Fractal Geometry*. Mathematical Foundations and Applications. John Wiley & Sons, 1990.
- M.A. Gutiérrez-Naranjo, M.J. Pérez-Jiménez, F.J. Romero-Campero: Simulating avascular tumours with membrane systems. In *Third Brainstorming Week on Memebrane Computing* (M.A. Gutiérrez-Naranjo, A. Riscos-Núñez, F.J. Romero-Campero, D. Sburlan, eds.), RGCN Report 01/2005. Fénix Editora, Sevilla, 2005, 185–195.

- M.A. Gutiérrez-Naranjo, M.J. Pérez-Jiménez: Fractals and P Systems. In Proceedings of the Fourth Brainstorming Week on Membrane Computing, Vol. II (C. Graciani Díaz, Gh. Păun, A. Romero-Jiménez, F. Sancho-Caparrini, eds.), Fénix Editora, (2006), 65–86.
- K.M. Iftekharuddin, W. Jian, R. Marsh: Fractal analysis of tumour in brain MR images. *Machine Vision and Applications*, 13 (2003), 352–362.
- A. Kikuchi, S. Kozuma, K. Sakamaki, M. Sito, G. Marumo, T. Yasugi, Y. Taketani: Fractal tumour growth of ovarian cancer: Sonographic evaluation. *Gynecologic* Oncology, 87, (2002), 295–302
- 12. H. von Koch: Sur one courbe continue sans tangente, obtenue par une construction géometrique élémentaire. Arkiv för Matematik, 1 (1904), 681–704.
- H. von Koch: Une méthode géometrique élémentaire pour l'étude de certaines questions de la théorie des courbes planes. Acta Mathematica, 30 (1906), 145–174.
- G. Landini, J.W. Rippin: How important is tumour shape? Quantification of the epithelial-connective tissue interface in oral lesions using local connected fractal dimension analysis. *Journal of Pathology*, 179 (1996), 210–217.
- 15. B.B. Mandelbrot: *The Fractal Geometry of Nature*. W.H. Freeman, New York, 1982.
- Gh. Păun: Computing with membranes. Journal of Computer and System Sciences, 61, 1 (2000), 108–143.
- 17. Gh. Păun: Membrane Computing. An Introduction. Springer-Verlag, Berlin, 2002.
- Gh. Păun, M.J. Pérez-Jiménez: Recent computing models inspired from biology: DNA and membrane computing. *Theoria*, 18 (2003), 72–84.
- H.-O. Peitgen, H. Jürgens, D. Saupe: Fractals for the Classroom. Springer-Verlag, 1992.
- M.J. Pérez-Jiménez, F.J. Romero. A study of the robustness of the EGFR signalling cascade using continuous membrane systems. In J. Mira, J.R. Alvarez (eds.) *Mechanisms, symbols and models underlying cognition*. Lecture Notes in Computer Science, 3561 (2005), 268-278.
- A.N dos Reis, J.C.M. Mombach, M, Walter, L.F. de Avila: The interplay between cell adhesion and environment rigidity in the morphology of tumors. *Physica A*, 322 (2003), 546–554.
- R. Sedivy, S. Thumer, A.C. Budinsky, W.J. Köstler, C.C Zielinski: Short-term rythmic proliferation of human breast cancer cell lines: Surface effects and fractal growth patterns. *Journal of Pathology*, 197 (2002), 163–169.
- R.F. Voss: Fractals in nature: From characterization to simulation. In *The Science of Fractal Images* (H.-O. Peitgen, D. Saupe, eds.), 1988, 21–70
- 24. P systems web page: http://psystems.disco.unimib.it/