

## **A Cellular Automaton Model Examining the Effects of Oxygen, Hydrogen Ions, and Lactate on Early Tumour Growth**

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**Abstract :** Some tumors are known to exhibit an extracellular pH that is more acidic than the intracellular, creating a 'reversed pH gradient' across the cell membrane and this has been shown to affect their invasive and metastatic potential. Tumour hypoxia also plays an important role in tumour development and has been directly linked to both tumour morphology and aggressiveness. In this paper, we present a hybrid mathematical model of intracellular pH regulation that examines the effect of oxygen and pH on tumour growth and morphology. In particular, we investigate the impact of pH regulatory mechanisms on the cellular pH gradient and tumour morphology. Analysis of the model shows that: low activity of the Na<sup>+</sup>/H<sup>+</sup> exchanger or a high rate of anaerobic glycolysis can give rise to a 'fingering' tumour morphology; and a high activity of the lactate/H<sup>+</sup> symporter can result in a reversed transmembrane pH gradient across a large portion of the tumour mass. Also, the reversed pH gradient is spatially heterogenous within the tumour, with a normal pH gradient observed within an intermediate growth layer, that is the layer between the proliferative inner and outermost layer of the tumour.

**Keywords :** acidic pH, cellular automaton, ebola, tumour growth

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