

# ***In silico* Analysis of Human Erythrocyte using E-CELL System**

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## **ABSTRACT**

We previously reported the computer model of the human erythrocyte using E-CELL simulation system. The model has three major metabolic pathways including glycolysis, the pentose phosphate pathway, nucleotide metabolism, and ion transport systems. In this work, we modified this simple model, and the second version was used for simulation experiments as follows:

### **(i) Pathological Analyses of Enzyme Deficiency**

The simulation experiments of glucose-6-phosphate dehydrogenase (G6PD) deficiency were carried out. G6PD is a key enzyme that produces NADPH in the pentose phosphate pathway, and G6PD deficiency is the most common hereditary enzyme deficiency of erythrocyte causes hemolytic anemia. As a result, in this simulation, sequential changes in the quantity of NADPH, GSH, and ATP were observed. However, the depletion of ATP occurred very rapidly compared with that of the real erythrocyte with G6PD deficiency. This difference was presumably due to the lack of pathways producing GSH and the export system of GSSG. We implemented these pathways and several pathways in the proximity of GSH to the model. After the modification, the longevity, predicted from ATP level, of the cell was longer and the ratio of GSH/GSSG was higher. This result indicates that these pathways compensate the reduction of GSH partially, and have a role to ease anemia, a condition of G6PD deficiency. This result can be a good explanation for the fact that G6PD deficiency is the most common cause of anemia. From the standpoint of evolution, if the deficiency has no severe disadvantage for surviving because of these compensation pathways, it would spread.

### **ii) Analyses of the effect of osmotic pressure that changes the cell volume.**

The second model is capable of simulating osmotic balance and the variable volume. The cell volume is made to increase or decrease until both intracellular and extracellular osmotic pressures became equal.

After this improvement, we analyzed the effect of this variable volume on metabolism. We could show the differences between the fixed volume model and the variable volume model. In variable volume model, the change was absorbed more quickly in all ten substances that we tried. Furthermore, the reaction rates, which were oscillating in the fixed volume, were stabilized in the variable volume model. These differences indicated a possibility that the volume, which changes with osmotic pressure, is stabilizing the metabolism. The osmotic balance presumably acts as a sort of feedback system.

## **REFERENCES**

**E-CELL project :** <http://www.e-cell.org/>

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