Simulation of biochemical reactions using a Particle System

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This dissertation proposes a novel approach to simulate biochemical reactions. We describe the algorithm and show its basic characteristics.

The fields of bioinformatics and genetics are not only concerned with the analysis of data, but also with the verification of result using simulation. This is because the huge amount of data that is constantly collected makes it impractical at best to rely on purely manual techniques. The motivation behind simulating biochemical reactions is the hypothesis that the complex mechanism of life is fully determined by the combination of simple chemical reactions. But, according to the general opinion of experts in artificial life and complex systems, an object does not necessarily consists of the sum of its parts. In some cases, the very essence of the object is an emergence from the combination of the parts. Clearly, this viewpoint must also be seriously considered when studying the mechanisms of life. The particule system presented here uses algorithms that aim at reconciling the viewpoints both viewpoints (i.e., life science vs. artificial life).

- Bottom-up simulation; chemical reactions are determined only by local information.
- Chemical compounds are represented as "particles", and each particle has its positional information on a virtual plane.

- Particle repeatedly perform thermal motion and chemical reactions.
- Chemical reactions are determined by a "reaction radius" and a "reaction probability," where the reaction radius determines the range up to which particules can react, and the reaction probability is the likeliness that such a reaction actually takes place.

As a result, our particule system exhibits the following characteristics.

- can handle positional information
- can simulate fluctuations
- can manipulate chemical compounds that are too scarce to be handled uniformly

Biochemical reactions can involve in the order of several thousands different chemical compounds, and hence cannot be handled uniformly. This is for instance the case with the intra-cellular signaling system. In such a case it is important to simulate fluctuations. This can be easily simulated with our particule system, but not with differential equations.

To validate our approach we show that, on average, results obtained with our particule system closely match those obtained with differential equations. More specifically, we use our particule system to simulate of a chemical reaction described by a system of differential equations. The contant P, which denotes the reaction velocity in the differential equations, becomes the reaction probability for the particule system. The value of P is determined by the following formula.

$$P = \frac{\Delta t S'}{\pi d} \quad (S' = \frac{S}{0.5921} \quad \text{when } d \text{ is "big enough"})$$

Here, S' is the area (estimated by Monte Carlo; see below), Δt is the duration in seconds of a single time step in the particule system, and d represents the number of particules par mole in the system of differential equations. The value of S' is determined by the following algorithm.

1. Take S/d for the area of 1 particle and determine the reaction radius,
2. Calculate the total coverage of d particles over the plane, with the Monte Carlo method,

3. Define S' as the value of S divided by the coverage. We observe that S' converges to $S' = \frac{S}{0.5921}$ as d increases.

Now, let us consider the fluctuation.

The particule system shows fluctuations admirably well when there are only few particules. As a result, we observe that the steady-state fluctuation obeys the law of great numbers, that is, the fluctuation is inversely proportional to $\sqrt{N}$, where N is the number of particles. Also, we observe that the fluctuation increases as $\log r'$; the ratio of the reaction radius to the area of the virtual plane.

So far, the particule system can simulate biochemical reactions involving less than a thousand compounds, such as intra-cellular signaling. However, we must demonstrate the approach on more complex biochemical reaction systems before we can convince biologists and geneticians to use it.