**Overview**

The algorithm involves simulation of a system of particles. The system comprises of population of particles (belonging to various types – type A, type B etc.) that can diffuse and react in the three-dimensional space. The reactions between the particles are pre-specified.

For example

1) A+B->C

2) A->2A

3) B->[]

Thus I have three reactions in my system (there can be only unimolecular or bimolecular reactions in the system). A can react with B and produce C, A form 2A molecules and B can degrade to nothing. In **bimolecular reactions like 1**, **A and B** have **to be within each others “capture radii/neighbors”** i.e. molecules of type A and molecules of type B have to be within a distance of each other to react. The species formed, C is either at the former position of A or at the former position of B or somewhere within the capture radii of A and B (this can be randomly specified).

In addition to reacting, the particles can diffuse within the system in any direction based on diffusive constants. Thus we simulate this reaction diffusion system wherein we observe the states of the system at t=0 and t=T.

**Simulating the system**

To simulate the above system we developed an accelerated stochastic simulation algorithm also know as COPS. This is based on modification of another algorithm called Stochastic Simulation Algorithm (SSA), which is explained below.

Initialize the system of N particles with M reactions. Choose two random numbers from a uniform distribution r1 and r2. Calculate **propensities** of the reactions.

**Propensity of a unimolecular reaction like A->2B is product of rate constant (pre-specified) of the reaction and number of molecules of A. Propensity of a bimolecular reaction like A+B->C is product of number of pairs of A and B that are within the capture radius of each other. Thus to calculate propensity of a bimolecular reaction we need to know all possible pairs of particles of type A and particles of type B that are neighbors/within capture radius of each other. Thus propensity of a unimolecular reaction is proportional to number of particles of reactant and that of bimolecular reaction is proportional to number of pairs of the reactants that are within capture radii of each other.**

After calculating the propensities a(i), we calculate a(i)/Σa(i) for each reaction and find within which interval r1 lies. We choose the lower bound to pick the specific reaction to be executed. Thereafter we fire the reaction. **For example if we are firing reaction A+B->C we randomly choose a pair of A and B, fire the reaction i.e. reduce the count of A and B and generate a C somewhere within the capture radii of A and B.**

In COPS apart from reaction events there are diffusion events as well. Total diffusion events will be equal to number of unique species (A, B, C etc).

Propensity of diffusion events will be product of diffusion constant (pre-specified) and number of particles of the specific species. Thus in COPS we have both reaction and diffusion events and we calculate propensities of reaction and diffusion events.

**Firing a diffusion event involves choosing a random particle of the specific type and moving it by a constant distance h.**

After firing the event we calculate Δt=(1/Σa(i))\*ln(1/r2). We increment the time from t to t+Δt. Subsequently we continue this process till maximum time T is reached. In each step system has a new configuration and requires calculation of propensities.

In accelerated COPS we calculate a parameter called ‘tau’. We fire multiple events rather than a single event in the time interval tau**. Calculation of tau is the most expensive computational step of the algorithm. This calculation depends on the change in an event propensity due to firing of other events.** Thus we have change in reaction propensity due to execution of other reaction events and diffusion events, change in diffusion propensity due to execution of diffusion events and reaction events.

**Calculation of tau**

All the mathematics behind calculation of tau is well defined. The calculation is split into four parts – a) Change in propensity of a reaction due to firing other reaction events b) Change in propensity of a reaction due to firing other diffusion events c) Change in propensity of diffusion event due to other reaction events d) Change in propensity of diffusion event due to other diffusion events – this last effect is currently neglected since we have point sized particles.

a) Change in reaction propensity due to other reactions

Consider two reactions *S* 1 + *S* 2 → *S* 4 ,   *S* 2 + *S* 3 → *S* 5 .  Firing reaction 1 will decrease amount of S2 available for reaction 2 since they have a common reactant. This will happen only if the **same S2** is within the capture radius of both S1 and S3. Similarly consider these two reactions

*S* 1 + *S* 2 → *S* 3 , *S* 4 + *S* 5 → *S* 2 Firing reaction 2 will increase amount of S2 available for S1. Thus propensity of 1 will change. However we need to keep in mind that only that S2 will matter that will be within the capture radius of S1. The change in propensity of a reaction due to other reaction events is given by the following equation

∆*aiR*(*t*) = *ci*(*pijKj*(τ)+*qijKj*(τ)). Change in propensity of the concerned reaction i is given by the delta term, *Kj*(τ) number of instances of reaction j fired. *ci* is the rate constant of reaction i.

*pij* is the common reactant impact factor – this is the number of change in occurrences in reaction i due to occurrence of reaction j which causes a **decrease** in reactants of i. For a better discussion please refer page 15 in the paper.

*qij* is the common product impact factor – this is an increase in the number of occurrences of reaction i due to occurrence of reaction j which causes an **increase** in the reactants of i. For a better discussion please refer to page 15-16 in the paper

Similarly due to diffusion events there is change in propensity. Since diffusion causes particles to come in and out of the capture radius of reactants, propensities will change. The change in reaction propensity due to diffusion is given as follows.

∆*aiD* (*t*) = *ci* (*rij K* j(τ)) where rij is average increase in occurrences of reaction i due to movement of species j. Please refer to pages 15 -20 for a better discussion.

**Algorithm**

Input: System with N particles and their positions with K types and M reactions.

Output: System with N’ particles and their positions

1. Initialize the system with N particles and M reactions. Assign positions to each of the particles randomly.
2. **Calculate propensities of each event**
3. **Choose tau**
4. Consider if we need to execute COPS or SSA
5. Fire K(tau) number of events
6. Update the time from t=t+tau
7. Check if algorithm needs to end