MODELING OF TWO-DIMENSION SOLID DISSOLUTION BASED ON GRANULAR PARTICLE INTERACTION: A SIMPLE APPROACH FOR TABLET DISSOLUTION SIMULATION IN 2-D

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Abstract. Simulation of 2-d rectangular tablet dissolution is constructed based on short range granular interaction through repulsive and attractive force. The former is based on linear spring-dashpot model, while the later is gravitation-like force. Fluid particles around the tablet is obeying Maxwell speed distribution, which can be tuned through temperature. Dissolution process seems to be influenced by the temperature.

Keywords: solid dissolution, granular particles, molecular dynamics, uniform distribution.

Introduction

Dissolution of solid body in liquid is interesting phenomenon to investigate since it emerges in our daily life such as in eroding strands, digesting food, and dissolving tablets/capsules. The last phenomenon plays important role in drug release process. Experiment setup must be carefully design to mimic the real process in human body [1], even though influence of fluid flow conditions around the solid body still a puzzle [2]. Several aspects must be considered in observing the dissolution, such as structure of the

solid [3], form of composing particles [4], and distribution of density and shear [5]. Simulation of tablet dissolution can be divided into two groups. The former tries to solve dissolution model described by the Nernst-Brunner equation using computational fluid dynamics [6, 7], while the later uses molecular dynamics method through the interactions between tablet molecular parts [8]. In this work, another approach is proposed, where tablet is assumed to be constructed from cluster of particles. The process will be a reverse from deposition process [9], which is based on molecular dynamics method.

Materials and Methods

Cluster of particles

Cluster of particles i is modeled with a spherical form with mass M_i and diameter D_i. At time t it can be at position $\vec{r}_i(t)$ and has velocity $\vec{v}_i(t)$. Composing particles are identical as point mass with mass m. Then, mass of cluster i is

$$M_i = N_i m \,, \tag{1}$$

where N_i is number of point mass particles in the cluster.

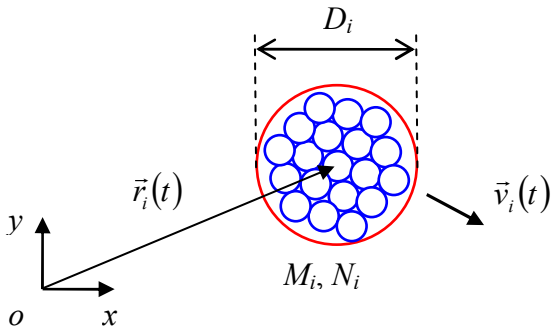

Figure 1. Cluster of particles i at position $\vec{r}_i(t)$ and has velocity $\vec{v}_i(t)$ consists of N_i identical particles.

Cluster i and j interact to each other through two interaction forces: repulsive and attractive forces. The first force is common in granular particle interaction, where the simplest form is known as linear spring-dashpot model [10], which describes force acting upon cluster i due to presence of cluster j

$$\vec{N}_{ij} = k_N \xi_{ij} \hat{r}_{ij} - \gamma_N \frac{d\xi_{ij}}{dt} \hat{v}_{ij} \,, \tag{2}$$

with k_N is spring constant and γ_N is dissipation constant. Each cluster has position and velocity $\vec{r}_i(t)$, $\vec{v}_i(t)$ and $\vec{r}_j(t)$, $\vec{v}_j(t)$, respectively. There are a new variable named overlap ξ_{ij} and its time derivation $d\xi_{ij}/dt$. The overlap is defined as

$$\xi_{ij} = \max\left(0, l_{ij}\right) \tag{3}$$

with

$$l_{ij} = \frac{1}{2}\left(D_i + D_j\right) - r_{ij}\,. \tag{4}$$

Position of cluster *i* relatively from cluster *j* and related motion variables are

$$\vec{r}_{ij} = \vec{r}_i - \vec{r}_j\,, \tag{5}$$

$$r_{ij} = \left|\vec{r}_{ij}\right| = \sqrt{\vec{r}_{ij}\cdot\vec{r}_{ij}}\,, \tag{6}$$

$$\hat{r}_{ij} = \frac{\vec{r}_{ij}}{r_{ij}}\,. \tag{7}$$

The variables $\hat{v}_{ij}$ in Equation (2) can be derived in similar way to obtain Equation (7).

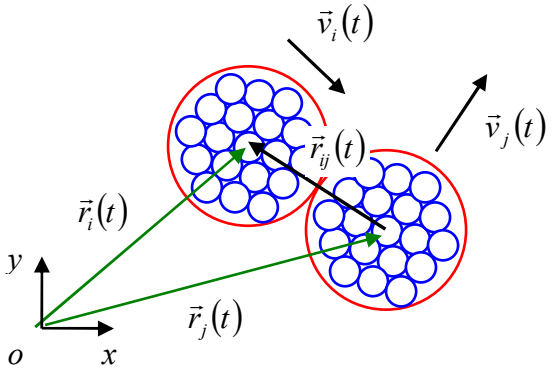

Figure 2. Interaction between cluster *i* at position $\vec{r}_i(t)$ and has velocity $\vec{v}_i(t)$ with cluster *j* at position $\vec{r}_j(t)$ and has velocity $\vec{v}_j(t)$.

For overlap with form in Equation (3) its time derivative will be

$$\frac{d\xi_{ij}}{dt} = -\text{sign}\left(\xi_{ij}\right)\vec{v}_{ij}\,, \tag{8}$$

with

$$\text{sign}(x) = \begin{cases} 1, & x > 0, \\ 0, & x = 0, \\ -1, & x < 0. \end{cases} \tag{9}$$

Since velocity and position of cluster *i* and *j* depend on time *t*, then the repulsive force $\vec{N}_{ij}$ in Equation (2) also depends on time *t*. This force works only when two clusters are in contact. It can be addressed as a short range force.

The second force, which is attractive, can be formulated as gravitation-like force but with limited working range. It will be different that gravitation force since it is a long range force. This attractive force may be defined as

$$\vec{G}_{ij} = \begin{cases} -k_G \dfrac{m_i m_j}{r_{ij}^{\,2}} \hat{r}_{ij}, & r_{ij} \le R_G, \\ 0, & r_{ij} > R_G, \end{cases} \tag{10}$$

with R_G is interaction radius. The parameters r_{ij} and $\hat{r}_{ij}$ are the same as in Equations (6) and (7).

From Equations (2) and (10) total force acting upon a cluster can be obtained through Newton's second law of motion, which gives cluster acceleration

$$\vec{a}_i(t) = \frac{1}{M_i} \sum_{j \ne i} \left(\vec{N}_{ij} + \vec{G}_{ij} \right). \tag{11}$$

Using molecular dynamics method implementing improved Euler algorithm, position and velocity of cluster i at time $t + \Delta t$ can be found through

$$\vec{v}_i(t + \Delta t) = \vec{v}_i(t) + \vec{a}_i(t)\Delta t\,, \tag{12}$$

$$\vec{r}_i(t + \Delta t) = \vec{r}_i(t) + \vec{v}_i(t + \Delta t)\Delta t\,. \tag{13}$$

With this new position and velocity, new value of repulsive force $\vec{N}_{ij}$ and attractive force $\vec{G}_{ij}$ can be calculated.

For simplicity from this part to the rest of this article cluster i will be addressed as particle i with mass M_i that can be reduced each time with m as it is hit by liquid molecules surrounding the particle. The size of particle i is considered to remain constant D_i.

Surrounding liquid particles

Liquid in surrounding of a cluster of particle is assumed to have Maxwell speed distribution at temperature T

$$f_M(v) = T^{-3/2} v^2 e^{-v^2/T}\,. \tag{14}$$

The most probable speed is

$$v_p = \sqrt{T} \tag{15}$$

which gives

$$f_M\left(v_p\right)=T^{-1/2}e^{-1}. \tag{16}$$

Equation (14) is simplified into uniform distribution using

$$f_U(v)=\begin{cases}0, & 0<v<v_{\min},\\ A, & v_{\min}\le v\le v_{\max},\\ 0, & v_{\max}<v.\end{cases} \tag{17}$$

Values of $v_{\min}$ and $v_{\max}$ are roots of

$$f_M(v)-bf_M\left(v_p\right)=0 \tag{18}$$

with b is a certain value, and then

$$A=\frac{1}{v_{\max}-v_{\min}}. \tag{19}$$

Equation (19) guarantees that

$$\int_0^{\infty} f_U(v)dv=1. \tag{20}$$

Figure 3 show the Maxwell speed distribution from Equation (14) and its simplified form from Equation (17).

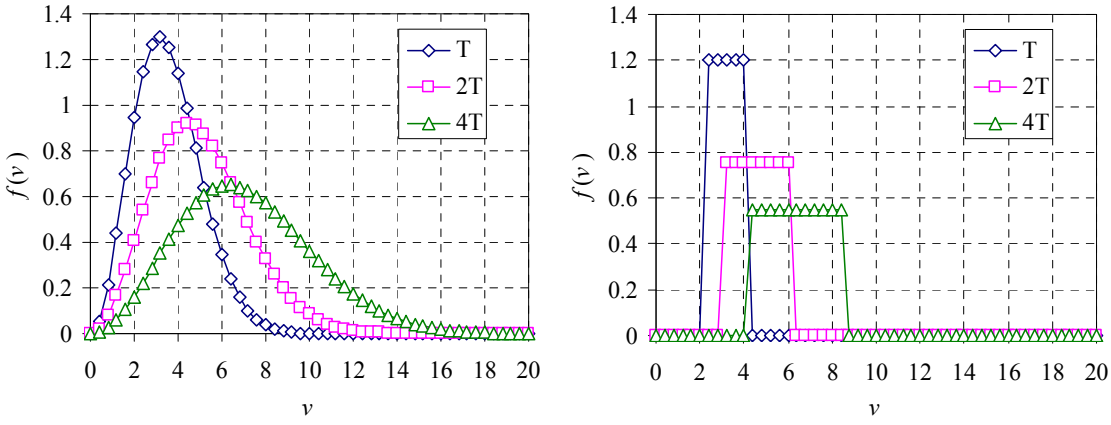

Figure 3. Illustration of typical Maxwell velocity distribution with different temperature (left) and its simplification (right).

Tablet is aggregate of cluster of particles

In this work tablet is an aggregate of cluster of particles, the simplest arrangement is a rectangular form with two-dimension simple cubic (2-D SC), while a more complex

arrangement but with the same form is two-dimension hexagonal close-packed (2D HCP). These two arrangements are shown in Figure 4.

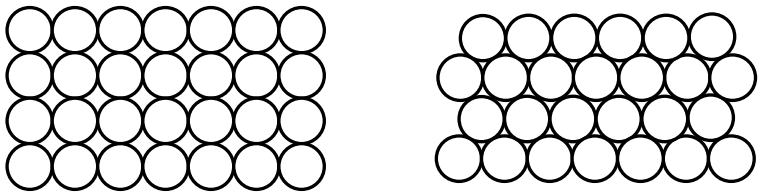

Figure 4. A simple rectangular form can be formed using arrangement of 2-D SC (left) or 2-D HCP (right).

The 2-D SC arrangement can be simply obtained using

$$\vec{r}_i = \left\{\left[(i-1)\bmod N_x\right]+\frac{1}{2}\right\}D\hat{e}_x + \left(\left\lfloor\frac{i-1}{N_x}\right\rfloor+\frac{1}{2}\right)D\hat{e}_y, \tag{22}$$

with $i = 1 \,..\, N$ and $N = N_x N_y$, while the 2-D HCP is a little bit complicated through

$$\begin{aligned}\vec{r}_i = &\left\{\left[(i-1)\bmod\left(N_x-\left\lfloor\frac{i-1}{N_x}\right\rfloor\bmod 2\right)\right]+\frac{1}{2}+\left\lfloor\frac{i-1}{N_x}\right\rfloor\bmod 2\right\}D\hat{e}_x \\ &+\left(\left\lfloor\frac{i-1}{N_x-\left\lfloor\frac{i-1}{N_x}\right\rfloor\bmod 2}\right\rfloor+\frac{1}{2}\right)\frac{1}{2}\sqrt{3}D\hat{e}_y.\end{aligned} \tag{23}$$

The complexity in Equation (23) is that in each event row from bottom number of particles is N_x while in event on is N_x–1. This can be obtained through the $N_x-\left\lfloor\frac{i-1}{N_x}\right\rfloor\bmod 2$ term.

The mechanism how a cluster of particle can be separated from the aggregate is by bombarding the cluster with fluid particles. Each time a cluster of particles hit by fluid particles, if the velocity of liquid particle v_k surpasses a threshold value v_{th} then the cluster of particle i release a mass m from the cluster or simply

$$M_i(t+\Delta t) = M_i(t) - g_i(v_k)m, \tag{24}$$

where $g_i(v_k)$ is a function that determines whether cluster of particle i should release the mass m or not, due to the hit of fluid particle with speed v_k

$$g_i(v) = \begin{cases}0, & v < v_{th}^i, \\ 1, & v_{th}^i \le v.\end{cases} \tag{25}$$

Threshold velocity v^{i}_{th} can be different for each cluster of particle i or the same for all clusters. Beside releasing part of mass the cluster of particle i should also receive velocity from the liquid, which can release the cluster from its aggregate. From this scenario a cluster can leave the aggregate if it has mass zero after hit multiple times by liquid particle with velocity surpassing the threshold velocity or due to the transferred velocity from the liquid. The first way is clear from Equation (10), while the second is competition between Equation (10) and cluster velocity. Transferred velocity can be obtained from particle speed

$$\vec{v}_i(t+\Delta t) = g_i(v)\left[\hat{i}\cos\theta + \hat{j}\sin\theta\right]v \tag{26}$$

with

$$\theta = 2\pi U(0,1). \tag{27}$$

Function $U(0, 1)$ is uniform distribution function similar to Equation (17), which is

$$U(x) = \begin{cases} 1, & 0 \le x \le 1, \\ 0, & 1 < x. \end{cases} \tag{28}$$

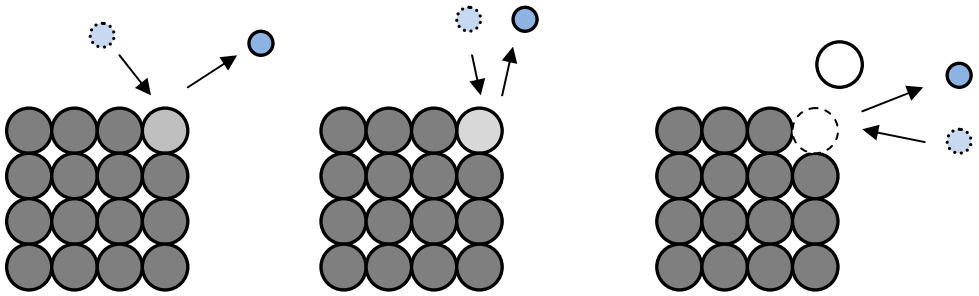

Figure 5. Cluster of particles release mechanism from the aggregate: first hit reduces mass of the cluster (left), successive hits continue (center), last hit releases the cluster (right). Mass of the cluster is presented in color (darker color means heavier mass).

Results | Discussion | Results and Discussion

Values of simulation parameters are given in Table 1.

Table 1. Simulation parameters.

Parameter	Value
cluster arrangement	2-D SC
tablet form	rectangular
L/D	10
H/D	4
b	0.8

γ_N	0
k_N	10^4
D	0.1
R_G	0.3
m	0.1
$N_i(0)$	5
Δt	1
t_{beg}, t_{end}	0, 1000
T	2, 4, 8
$v_i(0)$	0
v^i_{th}	4

As a preliminary following results are obtained from Gedankensimulation where steps in molecular dynamics method are skipped.

Table 2. Velocity values of fluid particles.

T	v_{min}	v_{max}
2	2.4	4.0
4	3.2	6.0
8	4.4	8.4

Table 2 shows the simplification proposed through Equations (17)-(20). Since from Table 1 $v^i_{th} = 4$, it can be assumed that $T = 2$ will not perform dissolution, while the other temperature will.

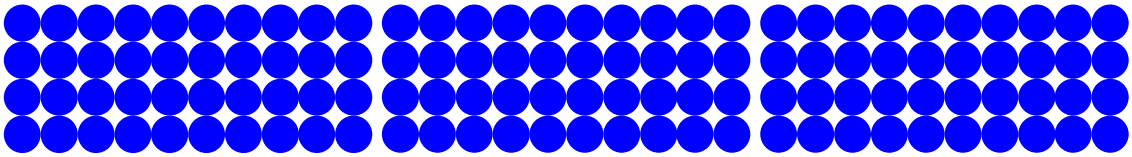

Figure 6. Clusters of particles in an aggregate for $T = 2$ at $t = 0, 1, 2$.

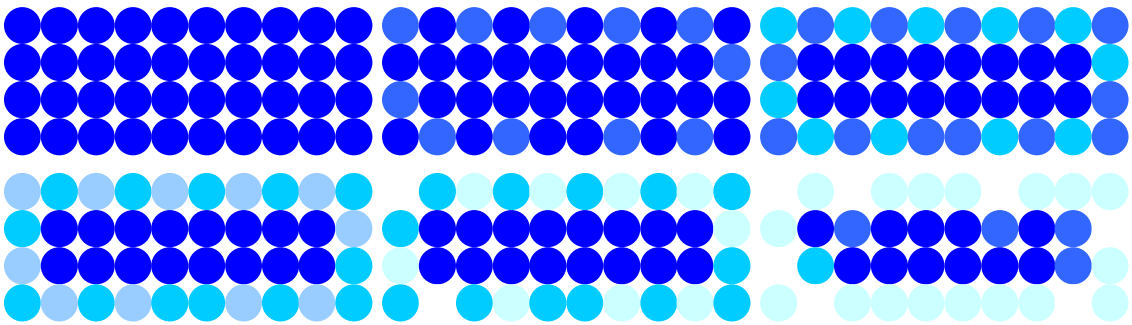

Figure 6. Clusters of particles in an aggregate for $T = 4$ at $t = 0, 1, 2, 3, 4, 5$.

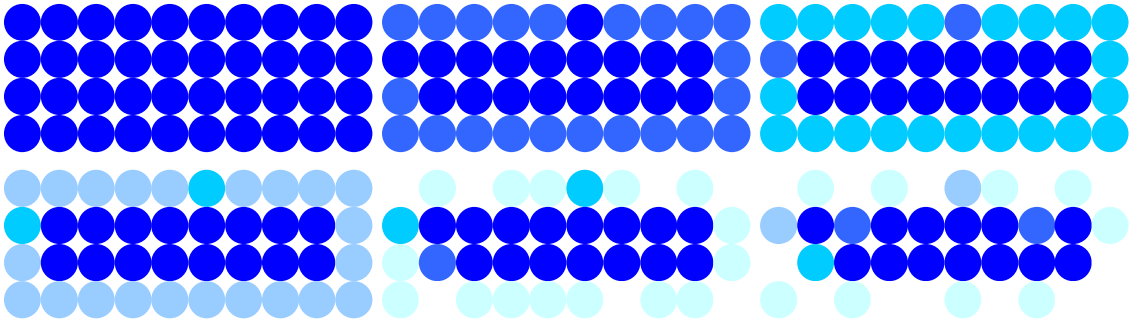

Figure 7. Clusters of particles in an aggregate for $T = 8$ at $t = 0, 1, 2, 3, 4, 5$.

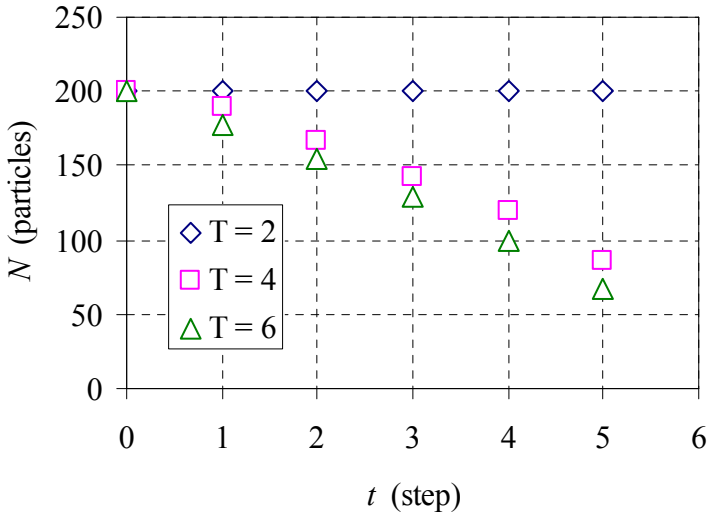

Figure 8. Number of remaining particles in the aggregate N as time step t increasing.

Influence of fluid temperature can be seen in Figure 8, where warmer fluid will dissolve the aggregate better than the cooler one.

Summary

A simple model for tablet dissolution in 2-d based on granular interaction has been constructed. It can show dissolving process which is temperature-dependent.

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