Evolution of the microstructure during the process of consolidation and bonding in soft granular solids

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Abstract

The evolution of microstructure during powder compaction process was investigated using a discrete particle modeling, which accounts for particle size distribution and material properties, such as plasticity, elasticity, and inter-particle bonding. The material properties were calibrated based on powder compaction experiments and validated based on tensile strength test experiments for lactose monohydrate and microcrystalline cellulose, which are commonly used excipient in pharmaceutical industry. The probability distribution function and the orientation of contact forces were used to study the evolution of the microstructure during the application of compaction pressure, unloading, and ejection of the compact from the die. The probability distribution function reveals that the compression contact forces increase as the compaction force increases (or the relative density increases), while the

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maximum value of the tensile contact forces remains the same. During unloading of the compaction pressure, the distribution approaches a normal distribution with a mean value of zero. As the contact forces evolve, the anisotropy of the powder bed also changes. Particularly, during loading, the compression contact forces are aligned along the direction of the compaction pressure, whereas the tensile contact forces are oriented perpendicular to direction of the compaction pressure. After ejection, the contact force becomes isotropic.

Keywords: powder compaction; discrete particle modeling; microstructure anisotropy; tablets; tensile strength; force distribution;

1. Introduction

Powder compaction is widely used in manufacturing, such as pharmaceutical industries, to produce tablets of high relative density and strength. To get high quality design and product, understanding the mechanics of the compaction process is essential. During compaction, the particles deform significantly and usually develop bonding at contact surfaces. The amount of deformation of each particle and the bond strength created between contacting particles depends on the properties of the particles and the applied compaction pressure.

A lot has been learned from prior experimental studies on tablet compaction, including the effects of particle size on powder compaction (Adolfsson et al., 1997; Almaya and Aburub, 2008; Eichie and Kudehinbu, 2009; Fichtner et al., 2005; Herting and Kleinebudde, 2007; Khomane and Bansal, 2013; Mckenna and Mccafferty, 1982; Patel et al., 2007; Sun and Himmelspace,

15 2006; Sun, 2008; Yohannes et al., 2015), the role of lubricants on com-
 16 paction and tensile strength of tablets (Almaya and Aburub, 2008; Sun and
 17 Himmelsbach, 2006), relationship between porosity and compaction pressure
 18 (Heckel, 1961) to mention a few. However, experiments alone cannot provide
 19 full description of the characteristics in the bulk of the compacted powders.
 20 To understand and investigate the compaction process in detail, particu-
 21 larly the interactions between individual particles and the heterogeneity in
 22 the bulk, computational modeling of the compaction process is required.
 23 Various methods have been used to model powder compaction in the past.
 24 These methods are based on Finite Element Method (FEM) (Klinzing et al.,
 25 2010), Discrete Element Method (DEM) (Cundall and Strack, 1979; Koynov
 26 et al., 2011; Martin and Bouvard, 2004; Olsson and Larsson, 2013; Sheng
 27 et al., 2004; Skrinjar and Larsson, 2004), or combined Discrete-Finite Ele-
 28 ment Method (DFEM) (Zavaliangos, 2002; Zhang, 2009; Zhang and Zavalian-
 29 gos, 2011; Zheng and Cuitiño, 2002). In FEM, usually, only the global values
 30 of the physical properties are assumed, while in DEM the interaction be-
 31 tween individual particles are accounted for, which enables modeling the
 32 heterogeneity of powders at the microscopic/particle scale. Hence, DEM
 33 gives more accurate results than continuum methods, which consider only
 34 the global physical properties of the material. In DEM, the inter-particle
 35 forces are computed based on the physical properties of the particles. Orig-
 36 inally, DEM was developed for application pertaining to very small elastic
 37 deformations (Cundall and Strack, 1979). In recent years, DEM has been
 38 used to model plastic deformation (Martin and Bouvard, 2004; Olsson and
 39 Larsson, 2013; Sheng et al., 2004) and bonding between particles (Potyondy

40 and Cundall, 2004).

41 In DEM, an explicit integration method is usually used to track the dis-
42 placement and deformation of individual particles at every time step. Since
43 DEM accounts for the interaction of individual particles directly, it requires
44 a significantly large computational resources, especially for large number of
45 particles. To reduce the computational time requirement, Sheng et al. (2004)
46 increased the time step in the numerical integration by increasing the mass
47 of individual particles by a factor of 10,000. Using this approach, the same
48 authors showed that for a given compaction pressure, the strain decreases
49 as the coefficient of friction between the particles is increased. In addition,
50 they showed that lower coefficient of friction of particle results in higher co-
51 ordination number (number of contact between particles). Similarly, Olsson
52 and Larsson (2013), using DEM simulations of binary mixtures, showed that
53 the particle size distribution has a very small influence on the compaction
54 pressure and elastic unloading for narrow particle size distribution (Martin
55 and Bouvard, 2004).

56 At larger deformations, the shape of particles deviates significantly from
57 a spherical shape and the inter-particle contact forces depend on each other,
58 in addition to the material property, effectively exhibiting a non-local ef-
59 fect (Gonzalez and Cuitiño, 2012). Further, Mesarovic and Johnson (2000)
60 used FEM models to study details of deformation mechanisms of particles.
61 To account for these complicated particle deformation and contact forces,
62 Zavaliangos (2002) has used DFEM, which can be considered as an advanced
63 DEM, because in addition to computing the contact force between two parti-
64 cles, the deformation of the particles is further modeled using a finite element

method. Specially, for compaction of powder bed to a very large relative densities, the particles deform significantly and only considering the assumptions of the DEM will not be sufficient. However, DFEM requires huge computational resource compared to DEM and is mostly applied to 2D simulations with limited number of particles, though it can be applied to 3D simulations as well (Güner et al., 2015).

In this paper, a 3D numerical compaction of granular materials was used (Gonzalez and Cuitiño, 2012, 2015; Martin and Bouvard, 2004; Mesarovic and Johnson, 2000; Storåkers et al., 1997, 1999). This method has a reduced computational time compared to DEM, while accounting for the interaction of particles directly as in the case of DEM. Based on this method and a compaction experiment, the material properties of two commonly used pharmaceutical powders were calibrated. The simulations were validated by compacting the powders at various compaction pressures and measuring the diametrical tensile strength. Then, the evolution of the microstructure during compaction, unloading, and ejection of the compacts were analyzed. Specifically, the evolution of the probability distribution of the contact forces, the anisotropy, and the inter-particle bond strength during the compaction process were investigated.

2. Numerical Simulation

The first step in all kinds of discrete particle modeling schemes is forming a packing of particles with the target particle size distribution. For this study, the particle size distribution of two pharmaceutical powders, lactose monohydrate (Foremost Farms, Baraboo, WI) and microcrystalline cellulose (MCC-

89 Avicel PH102, FMC Biopolymer, Newark, DE) were used. Since discrete
90 particle modeling methods require the representation of individual particles
91 in the material, the computational efficiency is constrained by the number of
92 particles in the system. State-of-the-art discrete particle models are capable
93 of modeling about a million particles. However, even a very small volume of
94 powder bed consists of a vast number of particles. For example, a 500 mg of
95 MCC-Avicel PH-102 (MCC) powder consists of about 9 billion particles. In
96 terms of number of particles, the majority of these particles (about 91%, cal-
97 culated based on measured particle size distribution (Yohannes et al., 2015)
98 and assuming all particles are spherical) are fine particles of less than 1 μm
99 size. In terms of volume, these fine particles account for about only 3% of the
100 total volume. On the other hand, if the particle sizes less than 100 μm are re-
101 moved, a 500 mg of MCC powder will have only about 500,000 particles. Our
102 previous experiments (Yohannes et al., 2015) have indicated that removing
103 the fine particles does not affect the compaction profile and tensile strength
104 of the compacts. Fig. 1 shows the compaction profiles, during unloading
105 and loading of the compaction pressure, for four samples of lactose powder
106 with differing amount of fine particles. The four samples were compacted
107 to in-die maximum relative densities of 0.90 and 0.97, which correspond to
108 maximum compaction pressures of 150 MPa and 230 MPa, respectively. The
109 four samples have very similar compaction profiles indicating that the fine
110 particles have little or no effect on the compaction of the samples. Based
111 on these results, it is possible to use particle sizes greater than 100 μm to
112 model the powder compaction, which will significantly reduce the number of
113 particles used in the simulations. (These compaction profiles are later used

114 to calibrate the mechanical properties of the powders). Fig. 2 shows the
 115 particle size distribution used in the simulations and experiments in terms of
 116 number of particles ($f_o(d)$). The procedures for the preparation of the sieved
 117 powder samples are discussed in detail in Yohannes et al. (2015). The sizes
 118 of particles range between 100 and 240 μm for lactose and between 100 and
 119 750 μm for MCC.

120 These particles were deposited in a cylindrical die using a ballistic gravita-
 121 tional deposition method (Bratberg et al., 2002; Jullient et al., 1992; Koynov
 122 et al., 2011; Mueller, 1997). In this ballistic deposition method only the
 123 static equilibrium of individual particles is used as a criteria, while the oth-
 124 ers factors that may affect packing of granular materials, such as the dynamic
 125 forces, friction, and cohesion are ignored. A particle is allowed to roll down
 126 on other particles freely until it locks into a stable configuration. To be in
 127 stable configuration (or static equilibrium) in 3-D systems, a frictionless par-
 128 ticle should be in contact with at least three other particles/walls such that
 129 motion or rolling in any direction is prohibited due to the contacts with the
 130 neighboring particles. A particle can also be in equilibrium if it lies on a hor-
 131 izontal plane wall. This ballistic deposition method is much faster than other
 132 gravitation deposition methods that consider the dynamic contact forces and
 133 integration time steps. Fig. 3.a shows deposited lactose particles. The par-
 134 ticles were deposited in a 3mm-diameter die and the total number particle is
 135 about 3000 and 2500 for lactose and MCC, respectively.

136 In the experiments, the initial relative densities for lactose and MCC
 137 powders were 0.47 and 0.34, respectively (Yohannes et al., 2015). These
 138 values are very small compared to theoretical possible relative densities for

139 pack of spherical particles. The lower initial density in the experiment can be
140 attributed to the irregular shape of the particles (Yohannes et al., 2015; Zou
141 and Yu, 1996) and inter-particle attractive force developed in the presence
142 of small particles (Castellanos, 2005). In the simulations, only spherical
143 particles were used and the inter-particle attractive force was ignored. The
144 initial relative density in the simulations for both lactose and MCC was about
145 0.51. The initial relative density using this deposition method is closer to
146 that of the experiments, compared to other particle deposition methods.

147 After the particles are deposited, a compaction pressure is gradually ap-
148 plied through upper and lower punches. The compaction simulation is a
149 strain controlled simulation, where a small displacement is applied to the
150 two punches. The pressure on the punches is then measured based on the
151 contact forces from the particles. The contact forces are discussed in detail
152 in the next section. After the powder bed was compacted to the target rel-
153 ative density (also referred to as solids fraction), the punches are gradually
154 removed. Finally, the compacted powder is ejected from the die by gradually
155 pushing the compact using the lower punch. Fig. 3.b shows lactose powder
156 after compaction.

157 During the compaction, unloading, and ejection simulation, the contact
158 force between the particles is computed based on the deformation and me-
159 chanical properties of the particles. The deformation is computed as the
160 overlap between pair of contacting particles. The plastic properties, elastic
161 properties, and bonding parameters of the particles are also used to compute
162 the force. A pair of contacting particles can be in a loading mode (where
163 the particles are in contact for the first time), or unloading mode (where the

164 contact force on a pair of contacting particles is decreasing), or reloading
 165 mode (where a previously contacting particles are overlapping again). Dur-
 166 ing loading mode, the particles are restricted to follow a power-law plasticity
 167 model (Martin and Bouvard, 2004; Mesarovic and Johnson, 2000; Storåkers
 168 et al., 1997, 1999),

$$\sigma = k\epsilon^{1/m}, \quad (1)$$

169 where k and m are particle plastic parameters, ϵ and σ are strain and stress
 170 of the particles, respectively. The contact force (P) between two particles is
 171 computed as

$$P = k_p a^{2+1/m}, \quad (2)$$

172 where a is the radius of the contact area between the pair of contacting
 173 particles $a = \sqrt{2c_2 \frac{\gamma}{\frac{1}{R_1} + \frac{1}{R_2}}}$, γ is the overlap between two contacting particles,
 174 and m is the average plastic parameter, $m = (m_1 + m_2)/2$ (the subscripts
 175 refer to the pair of contacting particles). The parameter k_p is given as

$$k_p = K\pi \left(\frac{1}{k_1^m} + \frac{1}{k_2^m} \right)^{-\frac{1}{m}} \left(\frac{1}{R_1} + \frac{1}{R_2} \right)^{\frac{1}{2m}-1} (2c_2)^{1+\frac{1}{2m}}, \quad (3)$$

176 where R is the radius of the particles, $K = 3 \times 6^{-\frac{1}{m}}$, $c_2 = 1.43 \exp(-\frac{0.97}{m})$.

177 During the unloading of the contact force, P is computed as,

$$P = \frac{2k_p}{\pi} a_p^{2+1/m} \left[\arcsin \left(\frac{a}{a_p} \right) - \frac{a}{a_p} \sqrt{1 - \left(\frac{a}{a_p} \right)^2} \right] - \sqrt{8\pi\omega E_m} a_p^{3/2} \left(\frac{a}{a_p} \right)^{3/2}, \quad (4)$$

178 where a_p is the radius of the contact area at the maximum P during the
 179 loading phase, ω is the bonding energy per area, and E_m is the effective

180 Young's modulus,

$$E_m = \left(\frac{1 - \nu_1^2}{E_1} + \frac{1 - \nu_2^2}{E_2} \right)^{-1}, \quad (5)$$

181 where E is the Young's modulus, ν is the Poisson Ratio.

182 The material properties of the particles in the simulation were calibrated
183 by comparing the compressibility of the powders (compaction pressure vs.
184 relative density curve) of the simulations to that of experiments. In the ex-
185 periments, a Presster machine (The Metropolitan Computing Corporation of
186 East Hanover, NJ) equipped with a 10mm flat face round tooling was used to
187 compact the powders (Yohannes et al., 2015). During the application of the
188 compaction pressure, the plastic parameters play a significant role compared
189 to the elastic and bonding parameters. Therefore, the plastic parameters
190 k and m are calibrated using the compaction pressure vs. relative density
191 curve during the application of the compaction pressure. Fig. 4 shows the
192 comparison of several simulation results with an experimental result. Ini-
193 tially (up to relative density of 0.55), only the position of the particles is
194 rearranged without pressure increase on the punches and die wall. Beyond
195 relative density of 0.55, the pressure on the punches increases steadily. To
196 select the appropriate values of the plastic parameters, several combination
197 of the plastic parameters k and m were tested. The tested values range from
198 0.15 - 3.75 GPa for k and from 1.0 - 4.0 for m . As shown in the figure,
199 increasing k and m increases the compaction pressure for a given relative
200 density. The best fitting combination of k and m was chosen by comparing
201 the least mean square values. Table 1 shows the material properties selected
202 for lactose and MCC powders based on the lowest least mean square value.
203 The difference between the simulation and experimental results are more no-

204 ticeable at the early stage of compaction. This difference is associated with
 205 the difference of the initial relative densities in the simulations and experi-
 206 ments during deposition of the powder in the die, as mentioned earlier. As
 207 the compaction pressure is increased the difference between simulation and
 208 experimental results decrease, with an error of 1-10% above relative density
 209 of 0.80.

210 Once the parameters k and m were selected, the effective Young's modulus
 211 (E_m) and the bonding energy (ω) can be calibrated using the compaction vs.
 212 relative density curve during the unloading of the compaction pressure. Fig.
 213 5 shows comparison of several simulation results with experimental results
 214 for lactose. Several combinations of E_m and ω were tested. As E_m and ω
 215 increase, the elastic recovery (amount of strain recovered during unloading)
 216 decreases. The same calibration procedure was followed for MCC. Figure 6
 217 shows comparison between experimental and simulation results for various
 218 values of the plastic, elastic, and bonding parameters. The difference between
 219 the simulation and experimental results are less for the unloading phase than
 220 that of the loading phase. Table 1 shows the best fitting E_m and ω values
 221 for lactose and MCC.

222 One additional reason, among several possible reasons, for not getting
 223 perfectly matching curves may be the shape of particles. Only spherical
 224 particles are considered in the simulations, while the actual powders are
 225 composed of irregular particle shapes (Yohannes et al., 2015). Johansson
 226 and Alderborn (2001) have shown that the irregular shape of particles cause
 227 complex compression behavior, attrition of the particles, and increased bed
 228 void, which ultimately change the compaction profile. However, it is assumed

229 that the differences between the simulations and experiments do not have a
 230 significant influence on the microstructure of the materials, especially for
 231 spherical particles that are used in this research.

232 Additional compaction simulations were done in order to analyze the ef-
 233 fect of the ballistic deposition and particle size distribution on the compaction
 234 profile. Fig. 5.b shows comparison of compaction profiles for three samples.
 235 Sample 1 is the same as the results shown in Fig. 5.a. Sample 2 has the
 236 same particle size distribution and material properties as that of Sample 1,
 237 but different initial particles arrangement. Sample 3 has the same material
 238 properties as Sample 1, but different particle size distribution (particle size
 239 distribution shown in Fig. 2.b). The compaction profiles for all the sam-
 240 ples are almost identical. These results are consistent with the experimental
 241 results (Fig. 1): the effects of the particle size distribution and the initial
 242 deposition of the powders on the compaction profile are negligible.

243 To validate the simulations, the tensile strength (σ_t) of the tablets was
 244 measured and compared to that of the experiments. Using a diametrical
 245 tensile strength test (also known as indirect tensile strength test), in which
 246 a compression force is applied along the radial direction, the breaking force
 247 (F_{max}) for the tablets was measured. The tensile strength σ_t can be computed
 248 from F_{max} as

$$\sigma_t = \frac{2F_{max}}{\pi Dt}, \quad (6)$$

249 where D and t are the diameter and thickness of the tablet, respectively. Fig.
 250 7 shows the simulation set up and the measured diametrical force and strain
 251 for lactose tablets with out-of-die relative density (relative density after ejection)
 252 of about 0.94. In the experiments, F_{max} for the tablets was measured

253 using a hardness tester (Dr. Schleuniger Hardness Tablet Tester, Pharma-
254 tron) (Yohannes et al., 2015). Fig. 7 shows comparison of experimental mea-
255 surements and simulation results of σ_t at different levels of compaction. The
256 simulation results are in good agreement with the experimental results. Since
257 there was no material property calibration for the tensile strength simulation,
258 these results indicate the calibrated material properties and the simulation
259 procedure were appropriate. These simulations were run on Xeon(R) X5650
260 @ 2.67GHz processor with 12 cores and a simulation for one tablet (including
261 deposition, compaction, ejection, and tensile strength test) takes about 72
262 hours wall time.

263 So far, a framework built upon clear physical theories based on the inter-
264 particle interactions was provided. It was demonstrated that the simulations
265 can reproduce experimental results, such as compaction profiles and diamet-
266 rical tensile strength, at various relative densities. These macroscopic pre-
267 dictions are dependent on the evolution of the microstructure which exhibits
268 anisotropy patterns consistent with the experimental data. In the following
269 section, the microstructure of Sample 1 is discussed in detail in terms con-
270 tact area, magnitude and orientation of contact forces, and bonding between
271 particles, along with some observations based on the other samples.

272 **3. Evolution of Microstructure**

273 As the relative density increases during the application of compaction
274 pressure, the microstructure of the powder bed evolves. For example, coor-
275 dination number has been shown to directly correlate with the compaction
276 pressure (Olsson and Larsson, 2013; Sheng et al., 2004). Another measure

277 of the microstructure during powder compaction is the inter-particle contact
 278 area. For tablet compaction applications, where the particles can bond with
 279 each other, the contact area between particles can be used as a partial mea-
 280 sure of the strength of the compacts (Adolfsson et al., 1997) (Eq. 4). Fig. 8
 281 shows the summation of all inter-particle contact areas between particles (to-
 282 tal contact area) during loading and unloading of the compaction pressure for
 283 both lactose and MCC. For both materials, the total contact area increases
 284 with relative density during loading phase, and decreases slightly as the com-
 285 paction pressure is gradually removed. The total contact areas for lactose
 286 and MCC are similar during the initial stages of compaction, up to relative
 287 density of about 0.6. A relative density of 0.60 is slightly less than random
 288 close packing (RCP) of cohesionless, spherical particles, which is about 0.64
 289 (Scott and Kilgour, 1969). For relative densities below the RCP value, the
 290 compaction is dominated by particle position rearrangements rather than
 291 particle deformation. This could be one of the reasons for the similarity of
 292 contact areas of the lactose and MCC particles. Beyond relative density of
 293 0.6, the contact area for MCC is larger than that of lactose. The contact
 294 area for MCC is larger because MCC has lower plastic, elastic, and bond-
 295 ing parameters than that of lactose (Table 1). Larger contact area does not
 296 necessarily indicate higher tensile strength, particularly when comparing two
 297 different materials.

298 To understand the bond strength between particles, it is important to
 299 track the history/evolution of the magnitude of the contact forces between the
 300 particles during compaction and ejection. The evolution of the magnitude of
 301 all contact forces is best represented by plotting the probability distribution

302 function (pdf), $f(P)$, of the contact forces. Fig. 9 and 10 show the pdf of the
 303 contact forces during the compaction, unloading, and ejection stages of the
 304 tablet compaction for lactose and MCC, respectively. Since the particles can
 305 form bonds between each other, some of the contact forces are in tension.
 306 (The tensile forces are represented by a negative sign in the Figures). The
 307 shape of the pdf and the magnitude of contact forces for lactose and MCC are
 308 similar. It is also noted that the distribution of forces for the samples with the
 309 same particle distribution (Sample 1 and Sample 2 in Fig. 5.b) are similar.
 310 However, for Sample 3, which contains more large particles, larger contact
 311 forces were observed. As the powder bed is compacted to higher relative
 312 densities, the pdf gets more positively skewed. The skewness indicates that
 313 the heterogeneity in the microstructure increases as the compaction force
 314 is increased. Since the bonding between particles is directly related to the
 315 contact forces between the particles, the heterogeneity will continue to exist
 316 even after the tablet is ejected from the die (Ragnar et al., 1995).

317 About 78% of all the contact forces are in compression at relative density
 318 of 1.0 and tensile contacts exist even during the application of the com-
 319 paction pressure. The magnitude of the compression forces decreases as the
 320 compaction pressure is unloaded, while the limit for the tensile forces (about
 321 -2 N) remains the same during loading, unloading, and ejection. The distri-
 322 bution at the end of the unloading stage resembles a Gaussian distribution
 323 with a mean value of about zero. At the end of the unloading stage, the
 324 percentage of contact forces in compression reduces to about 55%, for both
 325 lactose and MCC. The pdf during and after ejection is very similar to the
 326 pdf at the end of unloading, only getting slightly narrower, indicating a very

327 small change in the contact forces during ejection of the tablet.

328 Though the contact force distribution after ejection is dominated by near
329 zero forces, it does not mean that there is no contact or bonding between
330 the particles. Actually, the inter-particle bond generated by the compaction
331 pressure can support a larger tensile force. The bond force $\mathcal{B}$ for each inter-
332 particle contact, which is the tensile force required to break the bond between
333 the particles, depends on the material properties and the deformation of the
334 particles. $\mathcal{B}$ can be computed by taking the derivative of Eq. 4 with respect
335 to the contact radius (a). Fig. 11 shows the bond force generated due to
336 contact force between two 100 μm of MCC and two 100 μm lactose particles.
337 For both materials, $\mathcal{B}$ increases rapidly at lower compressive contact forces
338 and it approaches a limiting value as the contact force is increased further.
339 As shown in Fig. 9 and 10, the limit to the tensile contact forces is about
340 -2 N, which is very close to the computed $\mathcal{B}$ for a pair of 100 μm particles.
341 It can be concluded that at tensile forces of beyond -2 N, almost all bonds
342 between a pair of particles break.

343 Moreover, Fig. 12 shows the distribution of $\mathcal{B}$ ($f(\mathcal{B})$) for relative densities
344 of between 0.65 to 0.95. At these levels of compaction the value of $\mathcal{B}$ ranges
345 between 0 and -2.5 N. As the compaction level (relative density) increases,
346 $f(\mathcal{B})$ shifts to the left indicating an increase in the mean value of $\mathcal{B}$. Increase
347 in $\mathcal{B}$ directly contributes to higher tablet tensile strength. In addition, the
348 width of the distribution of $\mathcal{B}$ increases as the relative density increases, since
349 at higher relative density some larger compression contact forces are created.
350 The increase in the width of $f(\mathcal{B})$ also indicates increase in heterogeneity of
351 the microstructure. It is also important to notice that the change in $f(\mathcal{B})$

diminishes as the relative density increases, especially at relative densities above 0.85. The converging $f(\mathcal{B})$ corresponds to a plateau region of the tensile strength at high compaction pressures (Fichtner et al., 2008; Adolfsson et al., 1997; Ragnar et al., 1995)

For each contact between particles, the bond persists only if the actual tensile force is smaller than the maximum tensile force that can be supported. Therefore, during tablet compaction and ejection, bonds between particles may form, break, and/or reform. Discrete particle simulations provide complete information of inter-particle contacts, and the evolution of bond formation and breakage can be tracked. For lactose, for example, about 12% of the contact forces at relative density of 1.0 vanish when the tablet is ejected. On the other hand, only about 0.5% new contacts are formed/reformed during unloading and ejection.

Besides the evolution and heterogeneity of contact forces and bond strength, application of external forces may induce anisotropy in granular systems (Majumdar and Haines-Nutt, 2005; Mehrabadi et al., 1982; Ragnar et al., 1995; Mattsson and Nyström, 2001). The amount of anisotropy in granular systems is usually quantified by the fabric tensor. The fabric tensor is a second order tensor computed from the unit vector along the line connecting the centers of two contacting particles (Dubujet and Dedecker, 1998). Hence, the fabric tensor can be represented by plotting the orientation of the inter-particle contact forces. For convenience, the orientation of the contact forces is presented in two viewpoints in polar coordinate. First, the projection of the orientation of contact forces on XY-Z plane is shown (Fig. 13 and 14). (The compaction pressure is applied along the Z-axis). Second, the projection of

the orientation on X-Y plane is shown (Fig. 15 and 16). The orientation of the tensile and compression contact forces are shown separately. The radial direction indicates the magnitude of the projected force in units of Newton and the angular direction represents the angle the contact force makes with XY-plane or X-axis.

Fig. 13 (a) and (b) show the orientation of the compressive contact forces and the tensile contact forces, respectively, on XY-Z plane for lactose at relative density of 1.0 (porosity of 0.0). The large compressive contact forces (with magnitudes reaching up to 10 N) are mostly oriented along the direction of compaction pressure (along Z-axis), but only the small compressive forces (maximum magnitude of about 2N) are oriented along the XY-plane. On the other hand, the tensile forces are mostly oriented perpendicular to the direction of compaction. Almost all the tensile contact forces lie within $\pm 30^\circ$ from the XY-plane. This is also true for the other samples, Sample 2 and Sample 3, but slightly larger contact forces develop during compaction in Sample 3. This anisotropy in the contact forces could be one of the reasons for the difference between the axial and diametrical tensile strengths observed in prior experiments (Ragnar et al., 1995; Mattsson and Nyström, 2001).

When the compaction pressure is removed, the orientation of the contact forces also changes. Fig. 14 shows the orientation of contact forces on the XY-Z plane after ejection of a tablet. In general, the orientation of the compressive contact forces (Fig. 14(a)) and the tensile contact forces (Fig. 14(b)) after ejection of the tablet is more isotropic than during the maximum loading. The magnitude of compressive forces decrease after ejection, where as the increase in the tensile forces after ejection is negligible in all directions.

402 The anisotropy of contact forces generated during the loading phase vanishes
 403 after the ejection of the tablet from the die. However, it is important to note
 404 that large bonding forces (maximum tensile force) are created due to the large
 405 compressive contact forces. The isotropic contact forces after ejection by no
 406 means indicate an isotropic bonding force between particles. The orientation
 407 of contact forces, during compaction and after ejection, on the X-Y plane is
 408 isotropic for both the compression and tensile contact forces (Fig. 15 and
 409 Fig. 16). The diametrical tensile strength of a tablet would be the same
 410 independent the direction of breaking force on the X-Y plane.

411 **4. Conclusion**

412 Discrete particle modeling is an ideal tool to investigate the microstruc-
 413 ture evolution in powder compaction applications. In this study, a discrete
 414 particle model that accounts for plastic, elastic, and bonding properties of
 415 the particles, in addition to representing the exact particle size distribution of
 416 lactose and MCC powders, was used. During compaction the initial contact
 417 force between particle is compressive. However as the particle rearrange and
 418 deform some of the contact forces develop to a tensile forces, and eventually
 419 very few of these contacts break. As the compaction pressure is increased,
 420 the positive skewness of the probability distribution function of the contact
 421 forces increases, dominated by compressive contact forces. Whereas, the
 422 maximum value of the tensile contact forces remains within the limits of the
 423 bond force $\mathcal{B}$. During unloading of the compaction pressure, the distribution
 424 approaches a normal distribution with a mean value of zero. This evolution
 425 of contact forces is accompanied by evolution of the anisotropy in the pow-

426 der bed. Particularly, during application of compaction pressure, the largest
427 compressive contact forces are aligned along the direction of the compaction
428 pressure, whereas the tensile contact forces are oriented perpendicular to the
429 compaction pressure. After ejection, the contact forces becomes isotropic.

430 The simulations clearly show the evolution of the microstructure during
431 tablet compaction. Anisotropy, and hence inhomogeneity, is generated in
432 tablets due to the compaction process itself. The anisotropy will cause direc-
433 tional preference of breakage and cracks, and capping tendencies in tablets.
434 Understanding the evolution and nature of the contact forces due to the
435 compaction pressure is essential to mitigate these problems caused by the
436 heterogeneity and anisotropy in tablets. One possible way is to design shape
437 of the tooling that reduces the anisotropy in the particle-particle contact
438 forces. The numerical models introduced in this manuscript can play a sig-
439 nificant role towards selecting appropriate tooling for powder compaction.

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TABLE

Table 1: Material physical properties

Powder	k (MPa)	m	E (GPa)	ω (J/m ²)
Lactose	3750.0	1.0	10.0	1100.0
MCC	150.0	4.0	4.0	500.0

FIGURES

Figure 1: Compaction pressure vs. Relative density for lactose samples with different particle size distribution.

Figure 2: Particle size distribution based on the number of particles for (a) lactose and (b) MCC. The horizontal axis is in logarithmic scale.

Figure 3: a) Powder bed of lactose particles after ballistic deposition. b) compacted lactose powder (relative density ≈ 0.9).

Figure 4: Calibration of plastic parameter for lactose. (The units of k is Pa). The best fitting values are $k=3.75$ GPa and $m=1.0$.

Figure 5: a) Calibration of Elastic (E) and Bonding (ω) parameters for lactose. The best fitting simulation is for $E=10$ GPa and $\omega=1100$ J/m². b) Comparison of compaction profile results from simulations for three different lactose samples.

Figure 6: Comparison of experimental and simulation results for MCC. k and E , are given in Pa and ω is in J/m^2 . The best fitting values are $k=150$ MPa, $m=4$, $E=4.0$ GPa, and $\omega=500$ J/m^2 .

Figure 7: a) Force vs. strain measured during a diametrical tensile strength test for lactose. The test set up is shown in the inset. b) Tensile strength (σ_t) vs. out-of-die relative density (relative density of a tablet after ejection) plot from experiments and simulations for lactose.

Figure 8: Sum of all contact areas vs. relative density, during compaction, unloading, and ejection. The contact areas is normalized by the projected area of the smallest particle in the sample.

Figure 9: Probability distribution for contact forces during different stages of tablet compaction for lactose.

Figure 10: Probability distribution for contact forces during different stages of tablet compaction for MCC.

Figure 11: The maximum tensile strength generated due to a contact force between two $100\text{ }\mu\text{m}$ particles.

Figure 12: Probability distribution of maximum tensile force that can be supported by each particle-particle contact for lactose at different levels of compaction.

Figure 13: Orientation of contact forces on the XY-Z plane during compaction at relative density of 1.0 . (a) Orientation of compressive contact forces (b) Orientation of tensile contact forces. The compaction force is applied along the Z-axis.

Figure 14: Orientation of contact forces on the XY-Z plane after ejection (a) Orientation of compressive contact forces (b) Orientation of tensile contact forces. The compaction force is applied along the Z-axis.

Figure 15: Orientation of contact forces on the X-Y plane during compaction at relative density of 1.0 (a) Orientation of compressive contact forces (b) Orientation of tensile contact forces. The compaction force is applied along the Z-axis.

Figure 16: Orientation of contact forces on the X-Y plane after ejection (a) Orientation of compressive contact forces (b) Orientation of tensile contact forces. The compaction force is applied along the Z-axis.

Maximum compaction