Smoothing haptic interaction using molecular force calculations

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Abstract

This paper presents a new method for smoothing haptic interaction with molecular force calculations that uses Lennard-Jones forcefield. The gradient of the forcefield is used unaltered when the distance between two atoms is greater than the sum of their van der Waals radii. However, when they are smaller, a hard-surface wall implemented using a spring model is used to repel two atoms. This eliminates the instability when two atoms are in contact in the presence of forcefields that have strong gradients. This method is tested on rigid hydrocarbon molecules with no bond creation or breaking.

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1. Introduction

The fundamental problem we are addressing is the stability of haptics in the presence of molecular forcefields that have strong gradients. Our solution is to reduce the force felt by the user when molecules penetrate. We use simple spring model to render this penetration. This is not the only solution to this problem, other way would be possible by the use of viscosity or inertia. With stability, the simulation of the molecular interaction motions becomes more natural.

The computer simulation of assembling molecules has been studied intensively in the field of computer-aided drug design. On the basis of the 3D structure of the target protein, the interaction between the designed drug molecule and the protein can be simulated [1–3]. The process of a drug molecule finding the energy-minimized configuration in the protein is called ‘docking.’ These approaches are based on molecular mechanics [4,5] and assumed the molecules to be rigid and non-reacting to reduce the computing time. There are, however, computing methods that allow intermolecular chemical bonding [6]. Furthermore, quantum mechanics [7] can be used. But considering the extreme computing resources required to solve even a simple problem, molecular mechanics is more practical.

There are also works that extend simulations through the use of Virtual Reality (VR) technologies. Brooks et al. [8] developed a system that presented haptic and graphics output while interacting virtually with protein molecules. They designed and built a robot arm that presented the user with force and torque feedback. Levine et al. [9] used parallel computing and genetic algorithms to develop a VR system that allowed a user to input approximate docking configuration and the system then computed the optimized configuration. Stone et al. [10] developed a system that could steer selected atoms by moving a restraint point attached via linear spring. Users were also able to feel the reaction forces. Harvey and Gingold [11] developed a system that lets the user feel the probability density function for the electron at any point, given by the square of the wavefunction describing a particular atomic orbital through a haptic device.

Haptic displays are typically positioning devices with force feedback. The history goes back to late 1950s at General Electric when Ralph Mosher developed several tactile simulation projects [12]. His work focused on the amplification of human motions in tele-operation. Additionally, the user was provided with a scaled version of the forces the teleoperator was encountering. Haptic technology found its way into VE (Virtual Environment) as the technology grew more mature [13]. Convincingly hard
walls and free space that feels free are the two key ingredients for an effective experience. Massie [14] used integration of velocity in time interval to achieve more realistic virtual haptic wall. Another important factor is high force refresh rate. The refresh rate for smooth tactile experience has been shown to be approximately 1 kHz. The key to achieve this quick refresh rate relies on the efficiency of the collision detection algorithm. Most moving parts in the literature are point probes. If the probe is more complex, the general scheme is to simplify the moving part or the environment such that fast collision detection can be achieved. The following two works use complex moving parts. Balasubramaniam et al. [15] developed a program for generating 5-axis tool paths. A five degree-of-freedom force feedback haptic device is used to generate collision-free paths. With a virtual impenetrable 3D part, a user teaches the collision free paths to the system and further post-processing is applied to refine the given paths. To present real-time haptic display, the tool is modeled by implicit solids and the environment is modeled by point clouds [16]. To increase the efficiency of the collision detection, the point clouds are then sorted into k-Discrete Oriented Polytope (k-DOP). k-DOP is an axis-aligned method that uses several axes (k) to achieve a bounding volume. Mcneely et al. [17] also demonstrated a teapot flying inside an aircraft. Complex pipes and walls were present as the environment. The environment is modeled with single surface points, each corresponding with surface normal vectors. Another solution to achieve fast refresh rate is to use some sort of an in between force approximation. If the simulation program cannot send force vectors fast enough to the haptic device control program, some sort of simplified force-estimating program that is directly linked to the haptic device control program generates in-between force vectors to give the user a more continuous feel thus enhancing the perceived realism [18,19].

Previous docking works have not addressed sufficiently the problem of dealing with the repulsive force that rapidly increases as two atoms approach each other. Our experiments showed that this occurs frequently during assembly and without proper handling of this problem the quality of the system degrades. To address this problem, a spatial constraint was introduced that resisted atoms from being closer than the sum of their van der Waals (VDW) radii. Including a spatial constraint in a spatial force vector field is a new approach in the haptic research and this algorithm has a potential to be used in other applications that need to impose a constraint while experiencing the vector field.

2. Approach

We first introduce molecular mechanics as the physics behind the interaction between molecules. Then, we describe a special technique to achieve real time computations regarding forces and collisions between molecules. Lastly, we present the application of spatial constraints to atoms.

2.1. Molecular mechanics

Molecular mechanics uses the laws of classical mechanics to treat the diverse interactions occurring in a real molecule according to a model that is empirically parameterized. The model, often called force field, is composed of several terms to describe the energy cost of deviating from ideal geometry. We can perform minimization to the potential energy to move the structure toward the optimum geometry. We can then take the spatial derivative of the potential energy to get the force acting on each atom. The parameters can be obtained from experiments or through quantum chemistry computation [20].

For this work, we used a parameter and equation set called Consistent Valence Forcefield (CVFF\textsuperscript{2}), originally developed to simulate small organic crystals and gas phase structures. The CVFF\textsuperscript{2} forcefield representation is used in the commercial energy minimization program called Discover\textsuperscript{2} and the interactive molecule design tool called Insight II\textsuperscript{2} (http://www.accelrys.com/). Recall that first computing the energy and then differentiating it spatially compute the force. Thus energy is the key element in computing the force vectors. There are many kinds of forcefields but most use similar equation forms. For example, the Morse bond stretching term in CVFF\textsuperscript{2} is given in Eq. (1). In this equation, \( r_0 \) is the current bond length; \( r_{0ij} \) the reference bond length; \( D_{ij} \) the bond dissociation energy; \( \alpha_{ij} \) the Morse anharmonicity parameter.

\[
D_{ij}(1 - e^{-\alpha_{ij}(r_ij - r_0^{ij})})
\]

CVFF\textsuperscript{2} also has angle-bending term given in Eq. (2). In this equation, \( \theta_{ij} \) is the current bond angle; \( \theta_0^{ij} \) the reference bond angle; \( H_{ij} \) the quadratic force constant.

\[
H_{ij}(\theta_{ij} - \theta_0^{ij})
\]

In addition to Eqs. (1) and (2), CVFF\textsuperscript{2} uses seven more energy terms to describe the bond energy and two more terms to describe the non-bond energy. This paper does not consider the bond energy terms for computing the forces and torques between molecules.

There are two fundamental assumptions of forcefields. First, the potential energy of a molecule can be represented as a sum of terms associated, respectively, with the various types of molecular deformations or atom–atom interactions. And the correctness of the additional energy associated with
the deviations of the structure with respect to an ideal situation where all geometrical elements would be in a reference state is assured. Secondly, the parameters needed to calculate the potential energy can be derived from information gained on small set of experimental observations can be transferred to larger systems. These assumptions are justified by the countless successes of the method.

Our primary interest is in the non-bond terms, which represent the energy formed by atoms that are not bonded or indirectly bonded by a third or fourth atom. They are the VDW and electrostatic terms. The non-bond energy between two atoms is defined as in Eq. (3).

\[ E_{ij} = \frac{A_{ij}}{r_{ij}^6} - \frac{B_{ij}}{r_{ij}^{12}} + 1389.1 \frac{q_i q_j}{D_{ij}} \]  \( (3) \)

Eq. (3) is called Lennard–Jones potential [21]. In Eq. (3), \( E_{ij} \) is the energy between two atoms \( i \) and \( j; A_{ij} \) and \( B_{ij} \) are VVD repulsion and attraction parameters; \( r_{ij} \) is the distance between atoms \( i \) and \( j; q_i \) and \( q_j \) are the point charges on atoms \( i \) and \( j; D \) is the dielectric function (we used unity for our tests); 1389.1 is a factor that converts the electrostatic energy into kilojoules per mole.

Although there are other equation sets for similar purposes, Eq. (3) is widely used since polynomials can be handled efficiently in computer programs. Jensen [5] showed that this equation exhibits much deviation from experiments at close distances and even goes to infinity as two atoms approach each other. Jensen stresses that it is less meaningful to use this equation when the energy between the two atoms is in excess of certain large energy value since large energy is sufficient to break most bonds, and should never be sampled in actual calculations. He states that energy value over 400 kJ/mol will break most bonds.

In the computational chemistry literature, it is common to refer to the stationary molecule as the receptor and the moving dynamic molecule as the ligand. We will also adhere to this terminology and call the two components in the assembly process as ligand and receptor. For the energy between two molecules Eq. (3) becomes

\[ E = \sum_{i=1}^{\text{ligand}} \sum_{j=1}^{\text{receptor}} \left[ \frac{A_{ij}}{r_{ij}^6} - \frac{B_{ij}}{r_{ij}^{12}} + 1389.1 \frac{q_i q_j}{D_{ij}} \right] \]  \( (4) \)

To understand the characteristics of the non-bonded energy terms, we investigated the force directions and magnitudes. Since it is difficult to view the forcefields in three-dimensions, we lowered the dimensions to two-dimensions. In Fig. 1, at each grid point, we show the force vectors of a hydrogen atom having \(-0.1\) charge (in units of electronic charges) induced by two carbon atoms having \(+0.1\) charges (in units of electronic charges). The carbon atoms are represented by two dots symmetrically located along the horizontal axis. The distance between two carbon atoms was set to 1.5260 \( \text{Å} \). This is the reference bond length between two carbon atoms when no other forces are applied. This value is obtained from the \( r_{ij}^0 \) in Eq. (1). Here we show only the direction of the force vectors with unit sized arrows, and the magnitudes are not shown. Fig. 1(a) shows force vector plot of a hydrogen atom placed on grid points when only the attractive and repulsive VDW potential terms (first and second term in Eq. (4)) are used. Fig. 1(b) shows force vectors when only the electrostatic potential term (last term in Eq. (4)) is considered. Finally, Fig. 1(c) shows the combined effect of VDW and electrostatic potential terms. The elliptic loop in Fig. 1(c) is obtained by rolling a probe sphere with the hydrogen VDW radius on top of two spheres with carbon VDW radius and collecting the locus of its centre. This boundary is known as the Lee and Richard’s solvent accessible surface [22]. This boundary can also be obtained by offsetting the receptor surface with the VDW radius of the probe atom type. We will subsequently call this boundary as the ‘wall.’

The force vectors inside the wall is numerically problematic as Eq. (3) goes to infinity as two atoms approach. If one does not pay special attention to atoms crossing through this threshold, the resulting solutions will not be technically sound.

2.2. Real-time computation

Typical molecules have large number of atoms and often Eq. (4) cannot be evaluated in real time. To achieve real-time computation, we pre-compute the force vectors on finite number of grid points. The method is called ‘grid-based energy’ and is widely used in molecular docking simulation [1–3]. Grid-based energy computation can be accomplished efficiently when the ligand and receptor terms in the evaluation function are separable. This is generally true for the electrostatic part of a potential function. For the VDW terms, it is necessary to use a geometric mean approximation

\[ A_{ij} \approx \sqrt{A_{i}A_{j}} \text{ and } B_{ij} \approx \sqrt{B_{i}B_{j}}. \]

Using this approximation, Eq. (4) can be rewritten as

\[ E \approx \sum_{i=1}^{\text{ligand}} \sum_{j=1}^{\text{receptor}} \left[ \sqrt{A_{ij}} \frac{q_i}{r_{ij}^{3}} - \sqrt{B_{ij}} \frac{q_j}{r_{ij}^{3}} + 1389.1 \frac{q_i q_j}{D_{ij}} \right] \]  \( (5) \)

Three values are stored for every grid point \( k \), each a sum over receptor atoms. \( r_{jk} \) is the distance from atom \( j \) to the grid point \( k \).

\[ a_{val} = \sum_{j=1}^{\text{receptor}} \frac{\sqrt{A_{ij}}}{r_{jk}^3} \quad b_{val} = \sum_{j=1}^{\text{receptor}} \frac{\sqrt{B_{ij}}}{r_{jk}^3} \quad c_{val} = \sum_{j=1}^{\text{receptor}} \frac{q_j}{D_{ij}} \]  \( (6) \)

\[ = 1389.1 \sum_{j=1}^{\text{receptor}} \frac{q_j}{D_{ij}} \]
These values, with or without interpolation, may sub-
sequently be multiplied by the appropriate ligand values to
give the interaction energy. Our method is a slight variation
of above Eq. (6) and resembles the work of Tomioka [3].
Instead of $a_{val}$ and $b_{val}$ in Eq. (6), we compute $c_{val}$ in Eq. (7)
for every atom type in the ligand.

$$c_{val} = \sum_{j=1}^{\text{receptor}} \frac{A_{ij}}{r_{jk}^2} - \frac{B_{ij}}{r_{jk}^6}$$  \hspace{1cm} (7)

The overall procedure is as follows. An enclosing box of the
receptor (base part) is computed and its interior is divided
into regular grid points. User supplied number is used as the
divisor. Increasing the number would allow finer molecular
force experience. This is restricted by the memory size of
the computer. For each atom type in the ligand (assembled
part), that atom is positioned at the grid point and the
resulting force vector exerted by the receptor is computed
and saved. This process is done at every grid point for each

Fig. 1. Force vectors experienced by hydrogen atom. (a) Due to VDW force. (b) Due to electrostatic force. (c) Due to VDW and electrostatic force.
atom type in the ligand. For example, when we have a methyl (CH₃) as our ligand, we would compute three volumetric data sets (carbon, oxygen and electrostatic) of force vectors. This is displayed with a two-dimensional drawing in Fig. 2. The receptor (left) is composed of four atoms and the ligand (right) composed of two atoms. The hatch patterns in the circles represent different atom types. Now for each atom type in the ligand, it is put at grid points and the force vector acted on the atom by the receptor is computed. In Fig. 2, since the ligand has two atom types we have two grid data sets of force vectors. One set is for the white atom type and the other set is for the crosshatched atom type. The arrow at each grid point shows the computed force vector when an atom of specific type is placed at the grid point. Similarly, we compute one more grid data set for es. Note that only one set is required since these grid values do not depend on the atom types present in the ligand.

2.3. Spatial constraint

This paper presents a haptic presentation that differs from others in that it repels two atoms when they are closer than the sum of their VDW radii. This is accomplished with the introduction of a virtual wall that resists atoms from penetrating beyond the wall boundary. Most of the sophisticated haptic devices are constructed with electrical motors yet they do not have a physical brake system. The common tactic to give the illusion of a wall is through the use of the force model based on a spring-damper system. This technique is widely used after the introduction by Zilles et al. [23]. They used god-object, a virtual location of the haptic tip that is constrained to move along the surface of the target object. The god-object is computed by minimizing a penalty function that is composed of the distance between the god-object and the haptic tip and the distance between the god-object and the constraining surfaces of the object. Simple impedance control techniques were used to calculate a force to be displayed. This scheme is shown in Fig. 3. Note that to achieve the illusion of wall force, the object is actually allowed to penetrate inside the wall. The illustration shows this situation. The lower solid sphere represents the object that the haptic device is associated with. The upper solid sphere is the projection of the lower sphere onto the surface of the wall. The mechanism that attaches the lower solid sphere to the upper solid sphere symbolizes the damper and the spring that constitutes the force model. The force applied is represented by Eq. (8). In this equation, \( m \) denotes the mass of the object, \( c \) denotes the damping coefficient, \( k \) denotes the spring constant and \( \tilde{p} \) represents the projection point of object \( \tilde{x} \) to the wall. Eq. (8) is only used when the probe is touching or penetrating inside the wall and zero otherwise.

\[
\tilde{F} = m \frac{d^2 \tilde{x}}{dt^2} + c \frac{d \tilde{x}}{dt} + k(\tilde{x} - \tilde{p})
\]

For simplicity, our method does not consider the effect of mass and damping. In other words, it is a purely position based force model. Our situation requires modification from the above model since the space that our ligand resides has a spatial force vector distribution. In other words, we do not have an empty space. Our force model is defined as the spatial force vectors in the empty space and through Eq. (9) when the probe is touching or penetrating inside the wall. \( \tilde{F}_{\text{wall}}(\tilde{p}) \) is the spatial force vector at the point \( \tilde{p} \). Introducing this vector to the force model makes it smooth through out as the object travels from the space to the wall and penetrates it (for the purpose of giving the illusion of wall). Note since \( \tilde{p} \) is the projection point of object \( \tilde{x} \) to the wall, it is determined by \( \tilde{x} \) and thus \( \tilde{F} \) is a function solely of \( \tilde{x} \).

\[
\tilde{F} = \tilde{F}_{\text{wall}}(\tilde{p}) + k(\tilde{x} - \tilde{p})
\]

Noting that because of the first term in Eq. (9), implementation is not as simple as adding the haptic wall that commercial haptic library provides to the spatial...
forcefield. If the spatial forcefield is all zero we could do this way. However when it is not zero, there is a discontinuity at the wall. Fig. 4(a) shows the situation when commercial haptic wall is used. It is discontinuous at the wall. Notice our method shown in Fig. 4(b) is continuous at the wall. That is why we use slightly modified spring-damper model by adding the force at the spatial forcefield.

The complexity of finding the projection point on the wall is proportional to the number of atoms present in the receptor. To reduce the computation time, another pre-computed volumetric data structure is used. First, the space is partitioned into unit-sized cells. For each cell, every receptor atom that would intersect a ligand atom centered inside the cell are pre-computed and saved. Note that pre-computation is possible since we have a finite number of atom types in the ligand. This way, a quick intersection test between a ligand atom and the wall can be accomplished. And from the small collection of intersecting receptor atoms, the projection point can be further computed.

Our definition of the projection point is different from common usage. It is defined as the intersection point between a ray originating from the probe and the wall. The direction of the ray is selected such that it maximizes the distances to the intersecting receptor atoms. The projection point is obtained by finding the closest point along a direction that moves the probe out of collision with all receptor atoms. The direction is computed by averaging the vectors pointing from the colliding atoms to the probe. The most time consuming part in this calculation is the collision detection. To reduce the time in searching the colliding atoms, grid cells that list the potential colliding atoms are used. These procedures are described here with an example. In Fig. 5, a probe atom collides with a receptor composed of six atoms. The outer offset curve of the receptor is the wall. The wall can be obtained by offsetting the receptor by the probe atom radius. If the probe center is moved outside the wall, the collision can be avoided. The collision area is emphasized with a hatch pattern. The probe center is contained within a square that represents a grid cell. For given probe atom type, the grid cell maintains a list of receptor atoms that could collide with the probe centered within it. The part of the receptor that is drawn with solid line shows the subset pertaining to this list. Within this subset, actual collision test is performed. Only two atoms actually collide. Vectors from these two atoms are then added and the resulting vector is intersected with the wall. Notice we are doing exact collisions between the atoms in the ligand and receptor using lists of atoms near each grid cell. After computing the projection point \( \mathbf{p} \), \( \mathbf{F}_{\text{wall}}(\mathbf{p}) \) is computed.

Eq. (9) can be easily understood with an example. If we plot the magnitude of force vectors that a charged hydrogen atom experiences along an axis passing through two carbon atoms given in Fig. 1(c), we get a plot as given in Fig. 6(a). The horizontal line represents zero force magnitude. The height from this horizontal line denotes the magnitude of the force vector. Noting that there are two distinct curves in the force plot. The left and right exterior curves are the attractive region and the middle interior curves are the repulsive region. The two atoms are shown with two dots. Note that the force at the midpoint of two atoms is zero due to symmetry. This is shown with the vertical line. The solid squares represent the wall. Fig. 6(b) is the plot of the magnitude of force vectors along an axis that bisects the two atoms at the midpoint. This is the vertical axis in Fig. 1(c). Note only one atom is shown since the other is hidden behind this atom. Notice the slope of the force magnitude is very stiff and diverges to infinity very quickly. Previous research has not paid special attention to this problem and used a simple threshold value to limit the force magnitude. We tested this simple approach and two problems were
encountered. First, there was a very abrupt increase in the force response that resulted in unstable oscillation of the haptic device drive motors and an alarming buzzing sound. Secondly, it was very difficult to find a stable contact position or do a sliding motion. The latter is important because assembly operations often require two mating surfaces to slide along each other in the process of assembling. Our proposed distribution of the magnitude of force vectors is given in Fig. 7. The coordinate systems of Fig. 7(a) and (b) correspond to those of Fig. 6(a) and (b). By introducing a slanted slope, we were able to get rid of the buzzing and enable sliding motion. The slanted line represents the virtual wall and once it reaches a certain limit it is kept constant. The limit exists since a haptic device has a limit in the output force magnitude.

Fig. 6. VDW force magnitude plot. (a) Along the receptor axis. (b) Perpendicular to the receptor axis.

Fig. 7. Modified VDW force magnitude plot. (a) Along the receptor axis. (b) Perpendicular to the receptor axis.
3. Results

We designed two parts for the assembly. The receptor has a couch-like appearance (Fig. 8) and the ligand (Fig. 9) resembles a L-shaped bracket. A test was conducted to check whether the two parts would assemble using the haptic device. Each shape was designed with carbon and hydrogen atoms and subsequently went under structural energy minimization. There are two sphere sizes and the bigger one is the carbon atom and the smaller one is the hydrogen atom. The design and energy minimization was done in a commercial software called Insight II and Discover. Also, the electrical charge distribution was done automatically by Insight II. To test the effect of the hole size of the receptor to the ease of assembly, three receptors of varying hole sizes were built as in Fig. 10(a)–(c). The color is used to represent the electric charge. Red is used for +0.1 (units of atomic charge), green is used for −0.1, and the gray is used for neutral charges. Fig. 10(d) shows the charge distribution of the ligand.

The grid-based force and unit cell collision lookup table was computed before the simulation. The number of grid points on each axis was set to 64 giving 64³ number of force vectors for $c_{val}$ and $e_{val}$ in Eqs. (6) and (7). The number of unit cells was also set to 64 on each axis giving 64³ number of cells. The CPU times, in seconds, required to compute the table on an SGI Onyx with 4 processors and 1GB of RAM for the three models are given in Table 1. Memory locking and parallel processing were used to achieve faster computing. The third column pertains to single processor computation and can be compared with other columns that used various combinations of the two techniques. Unix systems typically swap out part of the program’s data area to the hard disk to save the use of the main memory. This can affect the performance since data retrieval tasks are increased. The fourth column forced this not to happen and always had the table in the main memory area. The fifth column, the result of utilizing four processors was found to be the most effective way to reduce the computing time. Finally, the sixth column uses both features, memory locking and parallel computing.

We now investigate how the magnitudes of these force vectors are distributed spatially. The line (shown by red in color image) shown in Fig. 11 is where the force vectors were sampled. First we plot the magnitudes of the force vectors without using the wall. A neutral carbon atom is used as the probe. All the force vectors are purely the result of the VDW forces. The electrostatic terms are neglected for this example due to their small magnitude relative to the VDW terms. The plot is given in Fig. 12(a). This is a computer-generated image and only a finite number of points were sampled and shown as dots and then connected with line segments for visual clarity. The horizontal width is about 30 Å and the vertical height is about 120 kJ/mol/Å. Notice there are three valleys and two ridges. The shift from the valley to the ridge is when two opposing atoms get close. Also note that only the three intervals at the valleys on the drawing are meaningful because the other intervals denote situations when the ligand atom overlaps the receptor atoms. This is physically impossible during assembly operation. This plot shows the variation in the force magnitude and not the direction. To see the change in the direction, Fig. 12(b) plots only the force component in the direction of the line. The horizontal axis shows where the magnitude is zero. The curves above the axis are where the force is in the direction from bottom left to top right in Fig. 11. Again, the maximum force magnitude is 120 kJ/mol/Å and the minimum force magnitude is −120 kJ/mol/Å. Notice the repulsive force increases rapidly as atoms approach and the experience was very rough when displayed haptically. Note the two ranges marked with both sided arrows denote intervals deep inside the molecule and are not accessible to the ligand. Fig. 12(c) is the result of using the wall. The numbers denote the atom IDs used when computing the projection point. All sample points to the right of the number shown and before a new number is shown correspond to those that used the same atom when computing the projection point. One exception is ID 1 and it is used when the probe is outside.
the wall. The evidence of the strength of the wall method can be found in Fig. 12(d). Again the axes correspond to that of Fig. 12(b). Notice we have good areas that show the non-bond forces and these immediately accompanied by matching sloped curves for the purpose of restricting further penetration. This means the users would feel the important non-bond forces outside the wall and if they penetrate the wall, the system would render a virtual wall resisting further intrusions. Notice there are two regions marked with both sided arrows in Fig. 12(c) and (d) that are sandwiched between two opposing walls. These are typically deep inside the boundary walls. When the probe goes deep inside the boundary walls it would eventually reach the other side of the wall reaching a point where going further would make it jump to the next wall. Before the jump, there is a transition area and Fig. 12(c) and (d) shows that very large fluctuations will occur. Though this would cause undesirable reactions of the haptic display if this transition area would be actually used, in real practice it is very difficult to go into this area since the repulsion force given by the virtual wall is perceived as impenetrable.

Table 1
CPU times for various computations

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>Number of atoms</th>
<th>Normal</th>
<th>Memory lock</th>
<th>Parallel</th>
<th>Memory lock and parallel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor A</td>
<td>325</td>
<td>5307.92</td>
<td>5297.88</td>
<td>1557.14</td>
<td>1543.86</td>
</tr>
<tr>
<td>Receptor B</td>
<td>428</td>
<td>7024.90</td>
<td>6996.52</td>
<td>1991.98</td>
<td>1957.92</td>
</tr>
<tr>
<td>Receptor C</td>
<td>532</td>
<td>8704.30</td>
<td>8704.41</td>
<td>2423.60</td>
<td>2371.24</td>
</tr>
</tbody>
</table>

Fig. 10. Electrostatic charge distribution. (a) Receptor A. (b) Receptor B. (c) Receptor C. (d) Ligand.
Since the range of force magnitude that a haptic device can give is limited, it is important to know the maximum molecular force of the probe so that scaled force spreads out most of the haptic force range. We cannot use the full haptic force range since we need some portion to render the wall. Current implementation uses one half to render the molecular force and the other half to render the wall. A scale factor is chosen such that when multiplied by the maximum molecular force, the resulting force value is half of the haptic force limit. This way we can experience rich force variation when we are outside the wall and also have some force range remaining to render the wall. We describe this in Fig. 13. The molecular force calculated on the left is mapped to the haptic force on the right. The maximum molecular force can be obtained by looking at the grid points outside the wall and also on the surface of the wall. In Fig. 14(a), those grid points marked with dots are the grid points exterior to the wall. We search the maximum force at

![Fig. 12. VDW force plot. (a) Magnitude. (b) Component along the axis. (c) Magnitude with the wall used. (d) Component along the axis with the wall used.](image-url)
these grid points. We also search on the wall surface. Together, we can calculate the maximum molecular force that a given probe atom type would experience. Since the wall can be computed analytically, we can precisely compute the maximum molecular force on the wall. However, for implementation convenience, we chose to utilize the facet representation of the wall that is easily obtainable from off-the-shelf software. In case of the facet representation, we looked at the vertices to find the maximum molecular force. This is shown in Fig. 14(b).

Table 2 shows the number of facets to represent the wall for each receptor. MSMS\(^2\) [24] was used to obtain the facet representation of the wall. Table 2 also shows the maximum non-bond forces computed for each receptor. The current spring constant value \(k\) used in the implementation is 40 kJ/mol/Å\(^2\). The spring constant was chosen such that when the penetration depth of the probe atom inside the receptor atom is half the minimum VDW radius of the atoms in the receptor, the resulting force sent to the haptic device would hit the device limit.

We now see how all the presented algorithms work in the simulation. In subsequent drawings, spheres of corresponding VDW radii draw the atoms. The purple (darker color in gray image) and yellow (lighter color in gray image) arrows show the resultant force vector and the resultant torque vector that the ligand experiences. The vectors are positioned at its mass center. Fig. 15(a) shows the ligand being pulled by the receptor in close proximity. This is due to the attractive VDW force and is known to be the driving force in molecular docking. Fig. 15(b) shows the ligand being pushed away as being too close to the receptor. This means the repulsive VDW force outweighs that of the attractive VDW force. Fig. 15(c) shows the interesting characteristic of the molecular assembly. Notice as we get in the close proximity to the hole, the ligand is actually pulled into the hole by the receptor. This greatly helps the assembly process since the receptor actually takes the role of guiding the ligand into the base part. Fig. 15(d) shows the final assembly configuration. In Fig. 16, we try a larger hole. Fig. 16(a)–(c) show the left, right and diagonal free space extent that the ligand can move inside the hole, respectively. Though the hole is big, still the head (Fig. 16(d)) does not fit in. In Fig. 17, we try even larger hole. The hole is large and the attractive force pulls the ligand and it is difficult to stay in the center. Fig. 17(b),(c) are typical positions inside the hole and it is almost impossible to stay in the center due to the strong attractive forces on the side walls. Fig. 17(d) shows the hole is big enough to pass the ligand from the initial position in Fig. 17(a).

The implementation uses the SGI Onyx\(^2\) for the graphics display and Windows NT PC\(^2\) for the haptic rendering. PHANTOM\(^2\) was used for the haptic display. The haptics loop and the graphics loop are independent. They only communicate to share the peripheral device states such as the position of the stylus endpoint. We don’t need to communicate computed values because each loop has its own copy of the data and the methods to process the data. The software that we use to drive the PHANTOM\(^2\) is

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Maximum non-bond forces</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probe atom type</td>
<td>Receptor A</td>
</tr>
<tr>
<td></td>
<td>Carbon</td>
</tr>
<tr>
<td>Number of triangles to represent the wall</td>
<td>11264</td>
</tr>
<tr>
<td>Maximum non-bond force (kJ/mol/Å)</td>
<td>49.73776</td>
</tr>
</tbody>
</table>
custom software. The examples in this paper performed interactive graphics refresh rate and more than 1 KHz for the haptic display.

4. Discussion

As the number of the ligand atoms in contact with the receptor increases, the resultant force that is the summation of all forces contributed by each atom, increases proportionally. Since there is a limit on the output force magnitude of the haptic device, it seems logical to scale down the haptic force according to the number of atoms present in the ligand. However, this poses some problem. Suppose we have calculated the maximum force for an atom as in Fig. 18(a). Since there is only one atom, the orientation has no effect on the calculated molecular forces. However, orientation plays an important role when we have multiple atoms touching the receptor. For example, we would experience similar magnitude of force (Fig. 18(b)) when there is one contact point or three times larger force (Fig. 18(c)) when there
are three contact points. If we scale the molecular force such that the molecular force in Fig. 18(c) is scaled to the haptic device limit, we would feel lesser sensitivity for situations as in Fig. 18(b). However, if we use the molecular force in Fig. 18(b) as the scale factor, stronger forces such as Fig. 18(c) would be thershed out at the limit value. It is not possible to be sensitive to Fig. 18(b), (c) at the same time. In the current implementation, the sensitivity is targeted to single probe atom touching the receptor. In other words, we try to be sensitive to situations illustrated as in Fig. 18(b) while thershed out large force values as in Fig. 18(c).

The current work assumes that the designed atomic structures are rigid. When we build structures with atoms, the design space is restricted with only a finite number of design solutions. In other words, a design of a receptor with physical dimensions in between receptor A in Fig. 10(a) and receptor B in Fig. 10(b) is physically

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Fig. 16. Receptor B assembly. (a) Left extent of the ligand position. (b) Right extent of the ligand position. (c) Diagonal orientation of the ligand. (d) Ligand head blocked by the hole size.
inadmissible. Let’s assume that we have a ligand that is slightly thicker than the ligand in Fig. 9. This thicker ligand would not fit in the receptor A since the hole would be too tight. If we consider the fact that bonds are flexible we could assume that the hole in the receptor A would stretch against the thicker ligand and the thicker ligand would contract meeting a new equilibrium (e.g. detent mechanism). Receptor B is not a possible solution because in order for the hole to contract, the attractive non-bond forces in the ligand should outweigh the forces between the bond forces in the receptor and bond forces are typically much stronger than non-bond forces.

We were able to find that there is one convenient aspect in molecular assembly. In our experiment with the ligand and the receptors, we found that exact positioning of the ligand was not required for the assembly fit to

Fig. 17. Receptor C assembly. (a) Initial position. (b) Ligand being forced to the left wall. (c) Ligand being forced to the right wall. (d) Ligand completely passing the hole.
**5. Conclusion**

We presented a new method to solve the stability problem in molecular interactions that use Lennard–Jones forcefield. The proposed wall method presents one way to solve the stability problem when ligand and receptor make contact. Noting that, however, we do not strictly prohibit the penetration. It is anticipated that the stable motion between molecules when they touch or slide would make the molecular simulation more usable.

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