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Designing and Evaluating a Haptic System for Biomolecular Education

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ABSTRACT

In this paper we present an *in situ* evaluation of a haptic system, with a representative test population, we aim to determine what, if any, benefit haptics can have in a biomolecular education context.

We have developed a haptic application for conveying concepts of molecular interactions, specifically in protein-ligand docking. Utilizing a semi-immersive environment with stereo graphics, users are able to manipulate the ligand and feel its interactions in the docking process.

The evaluation used cognitive knowledge tests and interviews focused on learning gains. Compared with using time efficiency as the single quality measure this gives a better indication of a system's applicability in an educational environment. Surveys were used to gather opinions and suggestions for improvements.

Students do gain from using the application in the learning process but the learning appears to be independent of the addition of haptic feedback. However the addition of force feedback did decrease time requirements and improved the students understanding of the docking process in terms of the forces involved, as is apparent from the students' descriptions of the experience. The students also indicated a number of features which could be improved in future development.

Keywords: Haptics, Haptic Interaction, Life Science Education, Visualization, Protein Interactions.

Index Terms: H.5.1 [Multimedia Information Systems]: Artificial, augmented, and virtual realities— [H5.2]: User Interfaces— Haptic I/O K3.1 [Computer Uses in Education]: Computer-assisted instruction— [H.3.4]: Systems and Software—Performance evaluation (efficiency and effectiveness) J.3 [LIFE AND MEDICAL SCIENCES]: Biology and genetics— [J.2]: PHYSICAL SCIENCES AND ENGINEERING—Chemistry

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1 INTRODUCTION

Haptics¹ is becoming common within the research community but often the technology is not applied in real work flows outside research, possibly because there is a lack of evaluation of its use. Intended end users are likely to be reluctant to incorporate new, and sometimes very expensive, equipment into their workplaces without clear indications of its benefits. In this work the aim is to perform an extensive evaluation *in situ*, with a test population that well represents the targeted end users, to determine what, if any, benefit haptics can have in this educational environment. The evaluation we have carried out provides insight into the usefulness of haptic interaction in this learning environment and indicates needed future developments of haptics for molecular interaction.

Ivan Sutherland, even as early as 1965, wrote a document [23] stating his vision of future VR interaction tools. Perhaps the most common citations are about the virtual world he described, which bears a close resemblance to that of *The Matrix* [25]. More important, however, are his more realistic visions about force feedback devices and their ability to directly represent physical phenomena like particles in electric fields. The biomolecular topic which is the focus of this work is protein-ligand docking, a fundamental biochemical process within all living organisms involving large molecules interacting with smaller molecules in docking events. Examples of such events are a receptor interacting with its ligand, or a substrate molecule entering an active site of an enzyme and interacting with it through a set of bonds.

Figure 1: (a) Screen dump from the Chemical Force Feedback software showing the protein, the ligand and a torque visualization, and (b) a student using the Chemical Force Feedback system.

¹Using our tactile/kinaesthetic senses to interact in a virtual environment.

Molecular biosciences make great use of visual representations, from sketches to advanced computer graphics, often to convey abstract knowledge. Within these sciences there is often a need to conceptualize multiple and complex three-dimensional relationships, in molecular structures as well as between molecules. However, instructors, as well as science education researchers, have repeatedly found that students often have great difficulty understanding these relationships and concepts which the visualization tools aim to make more comprehensible [27].

To improve the students' situation and to investigate the technical difficulties involved when utilizing haptics in life science we have developed a haptic application. The application, known as Chemical Force Feedback (CFF), combines a visual and haptic display, allowing the user of the system to manipulate the ligand and feel its interactions with the protein as the ligand is fitted into the docking site (figure 1). Similar techniques have previously been used by [17, 5, 15] and we, and [11], have extended this work to include more dynamic molecular models and force representations.

2 RELATED WORK

Real-time haptic docking systems have been developed previously and the most well known is probably that of the GROPE project, which began in 1967 [5, 17]. Some have focused on using haptics to interact with otherwise automated docking calculations [1] and others have aimed at a replacement for automated dockings [15]. Each system is based on some set of approximations due to the high refresh rates needed for force feedback (the tactile sense requires updates at speeds of the order of 1kHz, something that is hard to combine with the time consuming calculations required for docking). Some systems give five or six degrees of freedom (DOF) feedback but, like the work of [11], most of these use custom made hardware and are, thus, not commercially available. The high cost of commercial 6DOF devices restricts most systems to only 3DOF, especially if the aim is to incorporate the system into an educational setting. The haptic molecular models aimed at education generally use more simplified force calculations, which is acceptable as long as the most significant force behaviour is preserved.

2.1 Haptics and Visualizations in Learning Contexts

Haptics enables a learner to identify several different physical properties of an object, such as hardness, density, shape etc. [22, 12, 28], and while visuals are rapid and more encompassing, helping in the perception of macro structures, haptics is often superior when investigating micro-geometric properties [20, 24]. In many learning contexts the combination of the two senses can be superior to either alone [16, 8] and the ability to use kinaesthetics may help in grasping concepts concerning physical phenomena [3].

Too little is known about which types of representations ought to be used when conveying information about molecular life science and under which conditions haptic and visual immersive applications are beneficial for these educational purposes. However, in the research that has been carried out investigating the area of using haptics in educational settings, there seems to be a consensus that the use of force feedback can ease the understanding of a variety of complex processes. A gain is especially apparent when dealing with cases that include elements of forces we handle regularly (such as in mechanics) or when there exists an intuitive translation from the studied phenomenon into force for example, as stated in [10], concerning a model of a molecule: "...mapping certain quantities to force is fairly intuitive as far (sic) as we accept the traversal from the real microscopic world into virtual macroscopic one". The work of Reiner [18] is also very interesting where, after using a simple tactile interface to a computer program, students developed a concept of fields and constructed representations close to those of formal physics.

The impact of visualization has been strong in biology and chemistry education since the new ways of teaching offered by novel kinds of technology are expected to aid the understanding of the molecules' structures and their interactions. Haptics is one example as it can enable a user to feel intermolecular forces or even subatomic structures, such as the electron density function, through a force representation.

In [8, 10] an electron density function is used as basis for the generated force feedback. According to [8] the electron density function is hard for students to grasp and images trying to visualize it often lead to misconceptions since the function needs four dimensions to be represented. Haptics is found to be a good way to ease understanding by translating the fourth dimension to force, thereby also avoiding oversimplifications. In [10] a different approach is taken: the density function is utilized in the force calculations as a haptic cursor in the form of a virtual electron enabling a user to probe a molecule's effective shape.

There are several other examples of how haptics has proven useful: in [16] visual and haptic feedback is compared in a simple docking task, producing shorter docking times with haptics. Physical models, augmented reality and haptics was used in [19, 26], showing the system to be engaging and instructive, and when a molecular modelling program was evaluated in [21] there were time gains from the use of haptics. There is, however, a need for further evaluation in real teaching situations, investigating the ease of understanding of the molecular interaction forces potentially provided by haptics.

3 THE CHEMICAL FORCE FEEDBACK SYSTEM

The Chemical Force Feedback system has been developed with the purpose of investigating how haptics can be used to convey the process of protein-ligand docking and molecular interactions, as well as to develop and evaluate new kinds of haptic representations of molecular structures and events.

Most haptic molecular docking systems utilize force field techniques similar to those used in earlier systems, such as [17, 5], and all rely heavily on previous research within automated docking programming. Automated docking systems, however, do not have the same harsh time constraints as haptic systems and can thus perform more accurate calculations. Simplifications are, however, inevitable when creating representations of molecular structures and phenomena. Molecules and their interactions can not be seen but haptics enables us to increase the fidelity of the representation, at the same time as there are possibilities to use different levels of simplifications for students at different stages.

The Chemical Force Feedback application is written in C/C++, using OpenGL to render the molecular visualizations. The core of the system is designed to be a framework for general molecular visualization, with or without haptics, being easily adaptable to any haptics API. CFF has been developed using both the Reachin² and the SenseGraphics³ H3D APIs.

This API-independent design makes the CFF system functional with any hardware supported by the chosen haptics API and it is currently used with Phantom Desktop and Phantom Omni devices, both from SensAble Technologies, mounted in a Reachin display and a SenseGraphics 3D-MIW. Both systems provide the user with stereo graphics and a semi-immersive desktop workspace, giving you the sense of holding the ligand molecule at your fingertips, see figure 1.

²www.reachin.se

³www.sensegraphics.se

3.1 Preprocessing

The system can use any protein structure file from the Protein Data Bank [2] that has been preprocessed by the tools in the AutoDock⁴ suite [7, 14, 13], which assigns charges to the atoms in the molecules and generates volumetric potential grid maps, as well as specifying torsional bonds in the ligand. AutoDock is a system for automated protein-ligand docking, used, for example, to calculate how well a drug candidate molecule docks to a protein.

Multiple potential grid maps are generated: one common electrostatic potential map and one for each atom type (e.g. carbon, nitrogen, hydrogen) present in the ligands to be docked. These maps are the basis for the force calculations. Although calculating a single interaction force between a pair of atoms is a simple operation, the sheer number of calculations required for a normal protein renders the task impossible within the short time frame imposed by a haptic system. By reducing the effect of the entire protein to these volumetric grids, the time consumed for each force calculation depends only on the number of atoms in the ligand, which is a much more manageable calculation.

3.2 The Force Calculations

Using the potentials in the grid maps, the force on a particle at any point within its volume can be calculated through the gradient of the potential.

In calculating the resulting force on the ligand, the force on each atom in the ligand has to be determined, involving a few steps for each atom. First the gradients of the potential fields have to be calculated by an interpolation of the surrounding cell data values, both for the species-specific volume and the electrostatic potential volume. To determine the complete force contribution from the electrostatic field the atom's partial charge is used, as assigned during the preprocessing. This results in two force vectors which are summed, thus representing the force acting on the atom, and added to the sum of forces from all the ligand's atom, resulting in the complete translational force, see equation 1.

$$\mathbf{F}_{ligand} = \sum_{i=0}^n -\nabla\phi_i(\mathbf{x}_i) - q_i\nabla\phi_{esp}(\mathbf{x}_i) \quad (1)$$

Where n is the number of atoms in the ligand, ϕ_i is the potential field volume appropriate to the species of atom i , $\mathbf{x}_i$ is the position vector of atom i , and q_i is its partial charge, and ϕ_{esp} is the electrostatic potential field volume. The use of the complete set of potential grids increases the accuracy and brings the system closer to what is commonly accepted in automated docking programs.

Once the force is calculated a force transfer function is used to translate it into the final force that is fed back to the user. The transfer function can be edited to suit the working force range of different force feedback devices but also to select which forces should be emphasized, for example to emphasize only very weak and very strong forces.

Most affordable force feedback devices are 3DOF devices but, to enable full use of a 6DOF device, calculation of torques acting on the ligand has been included. The torque is calculated using the same atom forces as in equation 1 and is calculated around the haptic device's attachment point ($\mathbf{x}_{att}$) to the virtual molecule, normally the atom closest to the ligand's center of mass (see figure 2). The torque is given by equation 2.

$$\tau_{ligand} = \sum_{i=0}^n (\mathbf{x}_i - \mathbf{x}_{att}) \times (-\nabla\phi_i(\mathbf{x}_i) - q_i\nabla\phi_{esp}(\mathbf{x}_i)) \quad (2)$$

⁴AutoDock is free for non-commercial academic and educational use.

3.3 Flexible Ligand Model

Molecular structures are not as static as they often appear on the computer screen. To convey some of the dynamics in a molecular docking process we, and [11], have implemented a flexible ligand model. In both cases the dynamics of the ligand is based on a real-time energy minimization process, mimicking the likely behaviour of the real ligand.

Given that the project is currently aiming at an educational setting as the primary area for incorporation of the CFF system, the implemented energy minimization model is simplified. The evaluation performed indicates that the model is sufficient for the educational context, but, if we are to pursue a target population within the biomolecular research community the accuracy of the model must be increased.

Figure 2: Principle of the ligand representation.

In the preprocessing step the AutoDock suite [7, 14, 13] produces a modified pdb-file with definitions of torsional bonds within the ligand. In this file there is a tree structure, defining branches for every torsional bond, which is read together with the rest of the molecule's data and used in the ligand representation. The tree is restructured, setting the atom closest to the ligand's center of mass as the root (see figure 2), giving a natural point of attachment for the haptic 'pointer'. Each node atom of the tree also contains a list of atoms that are rigidly attached, either directly or forced to follow the node via other atoms, all connected through non-torsional bonds.

As the ligand is moved through the potential grids an energy minimization procedure is executed, trying to find a configuration of the ligand where it reaches a potential energy minimum for its current position. The current model is over-simplified but dockings made during the software development process that have been compared to automatically docked ligands show that results can be achieved that should be sufficiently good for the current purpose.

4 IN SITU EVALUATION

Our approach for the evaluation was to use a combined quantitative and qualitative assessment of the haptic tool in an *in situ* learning situation. The strategy of placing the tests in a real teaching situation shifts the focus from merely the speed of task completion to the quality of learning and understanding of the molecular interactions. Speed is, however, still a factor.

The aim was to evaluate the CFF system's features, its interface and usability, but specifically to explore the impact of haptics on students' performance and learning, investigating what the haptic

modality adds to a visual 3D protein structure representation. Our research questions fall into three main areas: learning, performance and usability.

Learning

- Does adding haptic representations improve learners understanding of molecular biosciences?
- Do tasks that vary in their complexity differentially benefit from haptic support?
- If haptics do improve learning, can we identify specific forms of knowledge that it helps to support?

Performance

- Do learners perform the task of ligand docking more accurately with haptic support?
- Do learners perform the task of ligand docking more efficiently (faster) with haptic support?

Usability

- Do learners find the system useable?
- What improvements do they suggest to help develop the system further?

4.1 Evaluation Setting

The study was performed with students at Linköping University and the subjects were life science and engineering students enrolled in a course at masters level called *Biomolecular interactions*, focusing on biomolecular structures and interactions, in particular between proteins and ligands. The course gives a thermodynamic background to factors determining structure recognition and the goal is to give the students an understanding of the dynamics of molecular exchange. In order to achieve this level of understanding they have to grasp concepts like *molecular structure, fit, interactions, forces, binding, molecular dynamics, affinity, specificity, energy levels, and transition state*, some more complex than others.

Data was collected as the students carried out computer based lab exercises using the CFF haptic environment. Performing the labs was a compulsory element in the course, participating in the research was voluntary. This approach, using students from a real course, hopefully lowers any positive bias towards the new technology, which might have been expected to reduce the validity of the evaluation if the tests had been performed using volunteers only.

4.2 Test Design

Being limited to only 23 subjects (13 women and 10 men) a partial cross-over was chosen as a suitable test design, see figure 3. The subjects, being undergraduates in Biological Chemistry and Biotechnological Engineering and some graduate students in Molecular Biotechnology, were divided into two groups (*O/H* and *H/O*) according to gender and score on the initial domain knowledge test, aiming at even gender and achievement level distribution between the groups. Unfortunately, due to scheduling constraints, the gender distribution ended up being somewhat unbalanced, giving a 7M/4F ratio in one group (*O/H*) and 3M/9F in the other (*H/O*).

Two tasks were designed for the computer lab; both required the students to attempt to find the best docking of ligands with the enzyme *human carbonic anhydrase II*, each ligand producing a different strength of the forces binding it to the enzyme. Both groups performed the exercises with the same CFF system (as described in section 3) but with different conditions for the force feedback element: one group (*H/O*) performed the first task, labelled *Task IS*, with force feedback enabled, whereas the other group (*O/H*)

Figure 3: Schematics of the partial cross-over test design.

had force feedback disabled. For the second task, labelled *Task TS*, the condition between the groups was reversed; the conditions have been named *O/H* and *H/O*, beginning without or with haptics respectively.

The students were given pre- and post-tests in connection to the tasks. These tests were designed to enable an estimate of the potential cognitive gain from the use of the haptic representation; estimated after applying statistical analysis. In addition to the pre- and post-tests the students' written answers to the tasks were available for qualitative analysis. After the labs were completed a subset of the students were chosen for semi-structured clinical interviews [4, 6, 9] centred on cognitive understanding, affective factors and opinions as well as on meaning making and the use of the haptic protein representation while solving a docking problem. The subset of students was chosen, based on their achievement level, to sample the spectrum of students in the course.

The audio-taped interviews focussed on the students' understanding of ligands' interactions with proteins, in particular on the concepts *specificity, affinity* and *recognition*, all related to the way a specific ligand 'connects' with a protein and how well it can dock. After an introductory phase, the interviewer initiated a discussion, in which the students were asked to elaborate on two of the questions from the pre- and post-tests. In the third phase of the interview (clinical) the students were asked to solve a docking task using the CFF system and encouraged to 'think aloud'. In the fourth phase, the students were asked about their experience from working with the CFF system, their opinions and proposals for its improvements.

More quantitative data comes from two surveys: one before the tasks, asking the students questions about their previous experiences of haptics, computer gaming and protein visualization, and a second survey querying their opinions about the system. Interaction and time logs and the saved results from the students' dockings also provide useful information, adding up to five different data sources:

- Pre- and post-tests scores
- Responses to the lab tasks
- Semi-structured clinical interviews
- Survey questionnaires
- User interaction/time logs and saved dockings

The data was collected according to the timeline described in figure 3.

In order to ensure reliability the assessment of the students' responses, to pre- and post tests and to the tasks, was performed independently by two teachers/scientists. The intersection of the equally assessed responses covered more than 95% of the total, indicating a strong consistency.

Reasoning in the task responses, as well as in the interviews, was qualitatively analyzed using the technique of analytical induction. This process involves repeated readings of the responses and interview transcripts, focusing on key terms of the subject. In the case of task responses, the number of occasions where “steric”, “chemistry”, “force”, and “dynamic” reasoning appear in each individual task response have been counted and the mean value for each task has been calculated (see table 3).

The students’ ligand dockings performed with the CFF system, in both conditions, were compared to docking results calculated by AutoDock (briefly described in section 3). The Root-Mean-Square (RMS, expressed in Ångström) was calculated between the corresponding student and AutoDock results. A zero value would indicate that the student managed to dock the ligand just as well as AutoDock, while the error increases with higher numbers.

Through the analysis of these data the aim is to isolate any effects from the use of haptics, to be able to use the students’ feedback to set the direction for further development, to map affective issues and to compare what students actually learned with what they think they learned.

5 RESULTS

In an educational context the students’ learning has to be in focus, thus effort has been put into evaluating how the system affects the way the students understand the content. A cognitive gain analysis of the pre- and post-tests reveals an indication of an effect on learning from the VR protein model, independently of whether the students used haptic force feedback or not.

5.1 Learning Results

To examine if the students learnt more about substrate and inhibitor binding (task *IS*) or about transition state analogues (task *TS*) and whether this was influenced by use of haptics, a mixed [2 by 2 by 2] ANOVA was performed. The design of the analysis was by pre-test/post-test by task (*IS/TS*) by condition (*O/H* or *H/O*), as presented in table 1.

A main effect of the test is revealed ($F(1,21) = 61.74, MSE = 82.55, p < 0.001$) with post-test scores being significantly higher than the pre-test scores (see figure 4), having means 7.15 and 5.23 respectively. It can also be seen in figure 4 that there is no significant difference between the students’ scores, either at pre- or post-test ($F(1,42) = 3.15$ and $F(1,42) = 2.80$). Performance on both tasks improved over time ($F(1,42) = 42.89, p < 0.0001$ and $F(1,42) = 7.04, p < 0.02$) and there is a significant interaction between task (*IS* or *TS*) and the test performed.

To further clarify, and because no significant difference is present between the students’ scores at the pre-test, the gains (the difference between the post-test score and the pre-test score) were computed and examined using a mixed [2 by 2] ANOVA by condition (*O/H* or *H/O*) and by use of haptics.

This analysis shows that the use of haptics was not associated with higher learning gains (see table 2), but there was, however, a significant interaction between condition and the use of haptics ($F(1,21) = 5.83, MSE = 29.50, p < 0.025$), thus exposing a task effect. Students learnt somewhat more from the *IS* task, producing a mean gain of 2.67 ($SD = 1.95$), as compared to the *TS* task with a mean gain of 1.07 ($SD = 2.02$), see figure 5.

It is also interesting to consider whether the availability of haptics influenced the way the students reasoned when giving their answers to the tasks. To examine the type of explanations presented and the possible impact of the haptics, a mixed [2 by 2] MANOVA was performed. A dependent variable was used, measuring the number of times that explanations appeared based on steric, forces, chemical or dynamic reasoning (see table 3 and section 4 for details about how the numbers were obtained).

Figure 4: Scores on pre- and post-tests.

Table 1: Scores at pre- and post-test by task and condition.

Task Condition	IS		TS	
	H/O N=12	O/H N=11	H/O N=12	O/H N=11
Pre-test	(SD) 5.29 (2.43)	(SD) 4.36 (2.06)	(SD) 5.56 (1.87)	(SD) 5.80 (3.02)
Post-test	(SD) 7.44 (2.60)	(SD) 7.61 (2.11)	(SD) 6.23 (2.38)	(SD) 7.32 (2.33)

Figure 5: Gain scores, by task and use of haptics.

Table 2: Gain scores.

Condition	H/O (N=12)	O/H (N=11)
Haptics	(SD) 2.14 (2.28)	(SD) 1.53 (1.38)
No Haptics	(SD) 0.67 (2.45)	(SD) 3.25 (1.38)

Analysis revealed a significant multivariate effect of haptics ($F(4,18) = 3.81, p < 0.021$) and a univariate effect on force based explanations ($F(1,21) = 11.17, MSE = 0.341, p < 0.003$); when participants used the haptics tool they generated more force ex-

planations in their answers than when they used the system without force feedback. This analysis also revealed an interaction between condition and use of haptics (which exposes a task effect) ($F(4, 18) = 3.35, p < 0.032$). Participants used more steric explanations ($F(1, 21) = 4.17, p < 0.055$) and more dynamic explanations ($F(1, 21) = 7.12, p < 0.014$) in the TS task.

Table 3: Type of explanation by task and condition.

Task Condition	Haptics			
	IS H/O		TS O/H	
		(SD)		(SD)
Steric	1.09	(0.70)	1.00	(0.73)
Forces	0.82	(0.87)	0.42	(0.67)
Chemical	1.27	(0.65)	1.50	(0.67)
Dynamic	0.09	(0.30)	0.17	(0.39)
Task Condition	No Haptics			
	IS H/O		TS O/H	
		(SD)		(SD)
Steric	0.73	(0.64)	1.50	(0.52)
Forces	0.00	(0.00)	0.08	(0.29)
Chemical	1.18	(0.75)	1.75	(0.62)
Dynamic	0.00	(0.00)	0.67	(0.89)

5.2 Students' Performance Results

The first measure of performance, the time required for each task, was extracted from the log files and the analysis shows a time gain for solving the tasks with haptic force feedback as compared to without, see figure 6 and table 4.

Figure 6: Time spent learning with the system, for both tasks, with and without the application of haptics.

Table 4: Time (in minutes) spent learning with the system.

Condition	H/O N=12	O/H N=11
	(SD)	(SD)
Haptics	15.83 (5.82)	23.52 (11.73)
No Haptics	24.73 (13.93)	27.09 (7.54)

A [2 by 2] ANOVA analysis of the time data reveals a single main effect of haptics that validates that participants spent less time learning with haptic force feedback ($F(1, 21) = 7.71, MSE = 446, p < 0.011$). The overall time with haptics was 19.50 ($SD = 9.74$) and 25.86 ($SD = 11.14$) without haptics, and, as can be seen in figure 6, the time difference between the tasks is not significant. Overall, we did not find any gender differences.

The second performance measure was the RMS value (see section 4), telling how well the students managed to dock the ligand, compared to a docking by an automated docking application, see figure 7. Analysis revealed no main effects of either haptics ($F(1, 21) = 0.7$) or condition ($F(1, 21) = 1.3$), but did show an a significant interaction between condition and use of haptics ($F(1, 21) = 6.65, MSE = 1.75, p < 0.02$), that is, participants performed better on the IS task irrespective of use of haptics ($IS = 5.28, SD = 1.30$ and $TS = 6.28, SD = 1.50$).

Figure 7: Docking accuracy (RMS) by haptics and task.

These results show no main effects because of the big spread of fit scores. The majority were moderately poor but there were a few accurate dockings as well as a few very poor ones, making it hard to tell whether the students perform poorly during the docking, or if the application is giving force feedback with too low fidelity, however survey results point to the latter.

5.3 Survey Results

In the first survey the students gave background information about themselves, such as their previous experience with protein visualization programs and their preferred ways of representing molecules, possibly giving some indication of how easily they would adapt to using the CFF system.

From the second survey there are a few points that stand out. The most common suggestion when it comes to future improvements of the system is addition of further options for visual representations of the protein, better matching that of common protein visualization software. Close behind are requests for other visual aids and options, like transparency, moveable clip planes and improved zooming.

These issues map well to the things the students specified as most difficult when using the system, like visual occlusion of the docking site and positioning of the ligand in the docking site. Positioning of the ligand depends on both visual and force feedback, and the students might experience some frustration as a lot of different forces are acting on the ligand during the docking. The results are, however, a bit contradictory as the top ranking statements about what haptics aided specifically included finding good positions and rotations of the ligand.

A very clear majority of the students stated that using the CFF system in the labs was a positive experience. They described the system as being novel and ‘cool’ as well as helpful in their understanding of the forces involved. In fact, 20 out of the 23 ranked the system as helpful (13) or even invaluable (7). Most students would have liked to use the system at an earlier stage of their education in order to gain even more.

5.4 Interviews

The interviews of selected students provide more in-depth information about the students’ understanding of molecular recognition and offer an opportunity to probe their feelings towards the use of the CFF system within this course as well as their opinions and suggestions about improvements (they are, after all, soon to be professionals in the biomolecular community). To date three students have been interviewed in semi-structured interviews, however more interviews are to be conducted before more elaborate conclusions can be drawn.

Comments about the system and improvements were in compliance with the results from the surveys. Students commented on difficulties in placing the ligand where they wanted it to be, as well as on the dynamics of the ligand and they suggested several improvements to the visuals. Suggestions were not significantly different from those given in the surveys but clarified their personal preferences.

All three interviewed students stated strong positive opinions about the use of the system in their education, once again pointing out the motivational effect of being given the opportunity to use VR technology.

The interviews also confirm some of the reasoning difficulties observed in pre- and post-tests and task responses, however the most striking result, so far, is that all three interviewees (one high and two intermediate performers) responded to the question “*What does haptics do?*” with approximately the same answer. Here exemplified with one of the responses (by the high performer): “*You already know the chemistry and the properties of different groups in a compound and the side chains of the amino acids. You also know about the different types of forces acting upon them and between them, electrostatic, hydrophobic, van der Waals and all that stuff. . . . and you know about the energy reasoning and the dynamics. But you know all of this as separate things. You think of it, one at the time. What haptics did was to couple this together to a coherent whole. They are there at the same time. All together. As different aspects of the same thing. I suddenly understood this in a ‘click’ when I used the haptic model.*”.

6 CONCLUSIONS AND FUTURE WORK

Analysis of the collected data has led to various conclusions, some very solid and some just indications, thus providing guidelines for the continued work to further solidify the conclusions.

Overall, analysis showed that providing students with the opportunity to practice protein-ligand docking with a VR application improved their understanding of molecular recognition processes and ligand docking. There was, however, no obvious advantage from the addition of the force feedback element to the system that could be isolated in the pre- and post-test analysis.

The most significant result is the fact that haptics did successfully convey the importance of forces in understanding the ligands’ interaction with the enzyme. In answers to the task where the students used the haptic tool, their explanations much more frequently included reasoning based upon forces. Understanding of forces, binding energy and strength of interactions are probably the concepts that could have been expected to benefit from haptics, but to see the support it provided in helping the students’ reasoning is a very positive indication and shows that the CFF system appears to help the students to link their knowledge together.

The results from the comparison of the students’ dockings with dockings calculated with AutoDock [7, 14, 13] indicate that further development of the force fidelity is required, especially when close to the docking site. This agrees well with the input coming from the students, both in surveys and interviews, asking for improved force feedback as well as further implementation of visual options. It appears that the students reach a task conclusion faster when using the haptic tool, however their docking accuracy does not seem to improve accordingly. A possible reason could be that they suffer from the illusion that they had docked successfully, lacking the required force fidelity close to the docking site. These are issues that have to be investigated further as the system evolves.

In our continued work we are not only focusing on improving the Chemical Force Feedback application, but the aim is to improve the design of the investigation as well. Improvements will be made in an attempt to further map the students’ reasoning around the protein-ligand docking concepts and how VR and haptics may aid their understanding. As a complement to the background survey there might be an implementation of a spatial ability test to estimate the students’ ability to navigate in a 3D environment. Formulations of both the survey and lab task questions will be sharpened to better fit the aims of the investigation, but it has to be done without leaving the true teaching context, there must still be a clear connection to the educational environment in which the system is intended to be put to use.

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