Haptic communication tools for collaborative deformation of molecules

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Abstract. Several previous studies have investigated collaborative approaches for processing complex environments. Beyond the improvement of performance and working efficiency, these studies highlighted two important constraints, which limit the efficiency of these approaches. First, social loafing which is linked to the redundancy of roles in the same group. Second, coordination conflicts which are linked to the limits of communication in standard collaborative environments. This paper addresses these issues by providing an efficient group structure to overcome the social loafing, which is then coupled with haptic metaphors to improve communication between partners. The experimental study, conducted in the context of molecular docking, shows an improvement for group efficiency as well as communication between partners.

Keywords: collaboration, coordination, haptic, molecular docking

1 Introduction

In the field of molecular modeling, docking is a search process which aims to bind two or more molecules to predict the best complex of molecules. This study of molecular conformations and interactions allows biologists to understand the functions of the manipulated molecules. During the docking process, the biologists analyze and identify the best structural and chemical complementarity between two molecules [8] in order to find the best assembly solution. Moreover, they must consider the flexibility of the molecule [13] by deforming the geometric structure at different scales (intermolecular, intramolecular level, atomic level).

Today, several solutions based on Virtual Environments (VE) are proposed to process these complex problems. The objective is to introduce the experience and skills of biologists during the different steps of the docking process. However, docking relevant molecules of large size is beyond the capability of a single biologist working alone. Collaborative Virtual Environments (CVE) provide new approaches to deal with these complex problems [15,16]. HUTCHINS [6] showed that collaboration between several users improved global efficiency for the realization of a given task. The experimental study conducted on the collaborative

control of an airplane cockpit showed that group efficiency is more important than the sum of individual work. This phenomenon, called "workload distribution", was defined by HOLLAN et al. [4] as follows:

> *Unlike traditional theories, however, [the theory of distributed cognition] extends the reach of what is considered cognitive beyond the individual to encompass interactions between people and with resources and materials in the environment.*

Based on a "workload distribution" approach, SIMARD et al. [16] performed several experiments to study the contribution of CVE, in particular closely coupled collaboration, for the processes of complex docking. The results highlighted two important constraints: (1) social loafing and (2) coordination conflicts.

(1) **Social loafing** is defined by SCHERMERHORN et al. [14] as

> *The tendency of group members to do less that they are capable of as individuals.*

Social loafing has negative consequences on the group efficiency. In fact, the inaction of some members of the group induces a misbalanced workload. KRAUT [9] proposed an efficient solution for this issue. It consists of assigning different roles for each member. Each user is in charge of a part of the task process which acts as an incentive for better group performance.

(2) **Coordination conflicts** are due to imprecise or incomplete communication. This leads to poor coordination of actions during closely coupled collaborations (e.g. manipulation of the same structure, selection of the same artefact) [7,16].

Several solutions were investigated to improve communication during closely coupled manipulations. The use of haptic feedback to support different levels of communication was widely investigated. BASDOGAN et al. [1] studied the role of this channel for implicit communication (i.e. haptic feedthrough) during collaborative manipulation tasks. The experimental results showed that collaboration through the haptic channel significantly improved group efficiency and sense of togetherness in CVE. Based on this study, OAKLEY et al. [11] proposed to improve haptic communication for tasks of 2D UML diagram creation. The components of the proposed approach were, to: (1) push, (2) pull, (3) attract, (4) be attracted by, or (5) reduce the speed of the partner's cursor (damping), when the two cursors approach each other. These haptic functions significantly improved group efficiency. Moreover, users found these tools useful even if they caused some fatigue and frustration. MOLL et al. [10] proposed similar tools for 3D environments. The experimental results showed that the haptic communication tool significantly improved the communication of objectives and spatial information.

In this paper, we propose to improve the collaborative manipulation of molecules during a docking process. The proposed approach combines an efficient group

structure to overcome social loafing, with haptic metaphors to improve communication between partners. The paper is structured as follows. In section 2, we present the employed group structure and the proposed haptic communication metaphors. Section 3 describes the experimental protocol for the evaluation. Section 4 presents the results. Finally, we will conclude and present some perspectives in section 5.

2 Proposed approach

To identify the best group structure and the required communication tools, it is necessary to know the different tasks involved. Biologists identify two main tasks during the docking process [2]:

- The relative movement and rotation of the overall molecules: involves moving and rotating one molecule with regard to the second molecule to enable the assembly of the two structures.
- The deformation of the geometric structures: involves manipulating the molecule at the level of atoms and residues (i.e. group of atoms) to change the general shape of the structure. The objective is to find the most suitable configuration in order to assemble the manipulated molecule with the second structure.

To enable a relevant assembly of the two molecules, these different tasks must be managed simultaneously.

2.1 Proposed collaborative configuration of work

Previous studies [15] show that collaborations, where partners have similar roles lead to an increase in social loafing. To deal with this situation, we propose a new configuration of collaborative work where each member of the group has an identified role. Based on the analysis of the activity of the docking process [16], we propose the two following roles: the *coordinator* and the *operator*.

- The *coordinator* is the global leader of the docking process. The role consists of analysing and exploring the overall structures of the molecules, and then testing the relevant assembly solutions by moving and orienting one molecule relative to the second structure. If the two conformations (i.e. overall shape) are not adapted for the assembly, the coordinator will first identify the required deformations and corresponding points of manipulation, and then entrust the corresponding tasks to the *operator* by designating the residues to manipulate and the corresponding spatial targets. Based on these two tasks, we provide two tools to the *coordinator*. The first tool enables the control of the overall position of one molecule. It links the molecule to a haptic arm (i.e.

Desktop PHANToM) through a spring-damper force model. The second tool enables the designation of the targets to manipulate. Given the numerous structures that are to be simultaneously manipulated, we propose to use two *operators*for monomanual configuration of work. In fact, the bimanual mode shows some limits for the manipulation of complex structures GUIARD [3].
– The *operator* manipulates and deforms the molecule by grabbing designated atoms or residues[1]. We provide the *operator* with a tool that enables the selection and grasping of the designated targets [15].

2.2 Proposed haptic communication metaphors

Based on the proposed collaborative working configuration (*coordinator* and *operators*), we propose a designation metaphor to improve communication between the *operators* and the *coordinator*. This metaphor, inspired by the works of MOLL et al. [10], enables the indication of a region of interest (ROI) on the 3D structure of the molecule. It includes two components: (1) a visual component and (2) a haptic component. The visual component highlights, through the involved target, the 3D structure of the molecule. The haptic component enables active notification of new designated targets. Moreover, it provides an active guidance tool to facilitate reaching the designated targets on the 3D structure.

We summarize the working of the designation metaphor as follows:

1. the *coordinator* $\mathcal{A}$ identifies the required target.
2. the *coordinator* $\mathcal{A}$ designates the target.
3. a visual feedback highlights the target with a neutral color (gray atoms ar residues). All users ($\mathcal{A}$, $\mathcal{B}$ and $\mathcal{C}$) are notified about the new designation through a haptic vibration.
4. the *operator* $\mathcal{B}$ or $\mathcal{C}$ (for the example, the *operator* $\mathcal{B}$) accepts the target. The target is now highlighted with the same color as the cursor of the *operator* $\mathcal{B}$. The vibrations are stopped.
5. the *operator* $\mathcal{B}$ is attracted to the target through the following spring-damper force model:

$$F(\mathbf{x}) = \begin{cases} k\,(t - t_0)\,(\mathbf{x} - \mathbf{x_t}) - b\dfrac{\partial \mathbf{x}}{\partial t} & \text{if } t \geq t_0 \\ 0 & \text{if } t < t_0 \end{cases}$$

   where $\mathbf{x}$ is the cursor's position, $\mathbf{x_t}$ is the target's position, t_0 the time of acceptation of the target and k and b respectively the spring and damping constants. The force is saturated when over 4 N.
6. the process ends when user $\mathcal{B}$ selects the target.

[1] Internal structures of the molecule composed by 10 to 50 atoms.

3 Experiment

This section presents the experimental evaluation of the proposed metaphors in the context of molecular docking.

Hypothesis Based on the identified constraints of collaborative work and corresponding performance factors [15], we propose to investigate the following hypothesis.

$\mathcal{H}_1$ **Better efficiency** The proposed working configuration and the haptic communication metaphor will improve the global efficiency of the group.

$\mathcal{H}_2$ **Better coordination** The haptic communication metaphor will improve communication between users and therefore, improve coordination.

Hardware setup Experiments were conducted on a collaborative platform, coupling standard desktop workstations with a large screen display, for a public and global view (see fig. 1). This platform is integrating biologist's solutions with virtual reality softwares: VMD [5] is used for the molecular visualization, NAMD [12] for the molecular simulation and IMD [17] to create an interactive molecular simulation. One haptic interface is plugged on each desktop workstation with a VRPN server [18] which communicates with NAMD through VMD and IMD: 2 Omni PHANToM for deformation tools, 1 Omni PHANToM for designation tool and 1 Desktop PHANToM for the molecule's manipulation tool.

All participants are sitting in front of the large screen and can verbally communicate without restriction. The *coordinator* is placed in the center and the two *operators* are placed on each side of the *coordinator*.

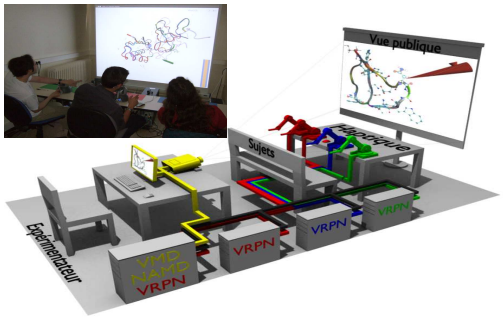


Fig. 1: Collaborative platform for molecular deformations

Molecular deformation task The proposed experiment consists of presenting a molecule with an *initial conformation* (i.e. a given shape and position) (see fig. 2). Participants are then asked to move and deform the molecule to reach a *target conformation* (see fig. 2). The *target conformation* provides the best geometrical complementarity with the second molecule. The participants evaluate the similarity between the *current conformation* and the *target conformation* with the RMSD score. This score, used by biologists, is defined by the following formula:

$$\mathrm{RMSD}\left(\mathbf{d},\mathbf{g}\right) = \sqrt{\frac{1}{N}\sum_{i=1}^{N}\left\|d_i - g_i\right\|^2} \tag{1}$$

where N is the total number of atoms and c_i, g_i are respectively atoms i from the *current conformation* $\mathbf{d}$ and the *target conformation* $\mathbf{g}$. The RMSD score is displayed on the right of the screen in a blue bar. The smallest reached RMSD score is displayed with an orange bar inside the blue one.

As developed above, the *coordinator* is in charge of the control of the overall position of the molecule as well as the designation of residues and atoms to manipulate. The *operators* select the designated residues (*current residue* on fig. 2) and pull them to a given position (*target residue* on fig. 2). Finally, some parts of the molecule are fixed (*fixed residue* on fig. 2) to avoid the displacement of the molecule outside of the working space.

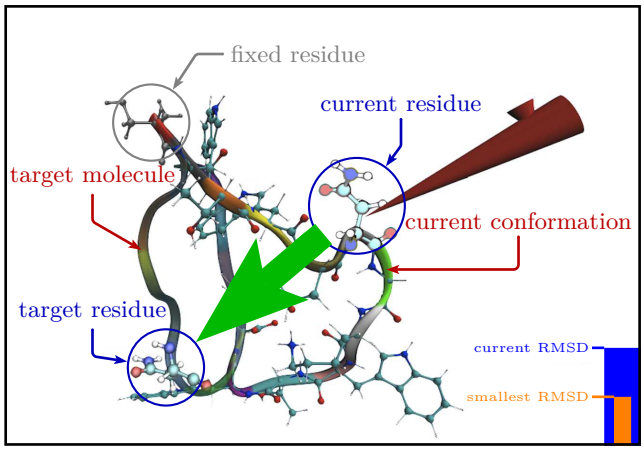


Fig. 2: Visual display to carry out the deformation process

Procedure The experiment presents three successive steps:

1. The experimenter presents the objectives of the experiment, the tasks, the roles (one *coordinator* and two *operators*)to the group. The group then deliberates and assigns each member a role.

2. In the second step we successively present the various tools to the participants through elementary experiments without effective evaluation. First, we present the platform and the manipulation tools (without the haptic communication metaphor) to the *operators*. A second training scenario is proposed to introduce the haptic metaphor (to the *operator* and *coordinator*). Finally, the tool to move the molecule is presented to the *coordinator* during a third training scenario.
3. The third step consists of presenting the effective experiential scenario. Participants are evaluated for both molecules (Ubiquitin then NusE:NusG) with and without haptic communication metaphor. The conditions are counterbalanced across the groups (see below the description of this condition). This step begins with a short period of exploration (1 mn) during which the groups elaborate an overall strategy. Then the participants begin the manipulation of the molecules in order to reach the smallest RMSD score (8 mn).

Subjects 1 woman and 23 men ($\mu = 27.4, \sigma = 3.8$) participated in the experiment. They were all students, researchers or researcher assistants in bioinformatics, linguistic, virtual reality or acoustic. They were all French speakers and had no visual or audio deficiency. No remuneration was given to the participants. To reduce learning effects during the experiment, we chose participants who already had experience with molecular deformation in virtual reality platforms.

Experimented conditions Two main factors were investigated in this experiment: the presence of communication metaphor and the complexity of the experimented molecules.

[$\mathcal{V}_{i1}$] **Haptic communication metaphor** , This within subject counter-balanced variable has 2 modalities: "without metaphor" or "with metaphor". The "without metaphor" condition provides the designation tools with visual feedback only; the "with metaphor" condition provides the designation tools with visuo-haptic feedback.

[$\mathcal{V}_{i2}$] **Complexity of the molecules** , This within subject variable has 2 modalities: "Ubiquitin" and "NusE:NusG". The complexity of both molecules is defined by the size of the molecules (number of atoms and of residues) and the nature of the task. The molecule Ubiquitin presents 1,231 atoms (76 residues); the corresponding task concerns the deformation of internal structures of the molecule. The complex of molecules NusE:NusG (a set of two molecules) is composed of NusE with 1,294 atoms (80 residues) and NusG with 929 atoms (59 residues); the corresponding task concerns the deformation and the movement of the molecule NusG (the backbone[2] of the NusG is entirely fixed in the virtual environment).

[2]Main internal structure of a molecule mainly composed of carbon atoms.

Objective measurements The analysis is based on the following objective measures:

- [$\mathcal{V}_{d1}$] **Smallest RMSD score** , Smallest RMSD score reached during the task fulfilment.
- [$\mathcal{V}_{d2}$] **Time of the smallest RMSD score** , Completion time to reach the smallest RMSD score during the realization of the task.
- [$\mathcal{V}_{d3}$] **Frequency of selections** , Number of selections realized by the *operators* during the deformation divided by the total duration of the task.
- [$\mathcal{V}_{d4}$] **Mean time of acceptation of targets** , Duration between a new designation (by the *coordinator*) and the acceptation of this designation (by an *operator*).
- [$\mathcal{V}_{d5}$] **Mean time to reach targets** , Duration between the acceptation (by the *operator*) and the selection of the target (by the *operator*).
- [$\mathcal{V}_{d6}$] **Number of accepted selections** , Number of fulfilled designations done by the *coordinator* that have been accepted by an *operator*.
- [$\mathcal{V}_{d7}$] **Mean speed of the *coordinator*** , Mean speed of the *coordinator*'s end-effector during the whole task.

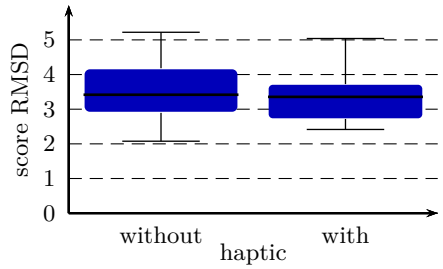
4 Results and discussion

All the results were analyzed using an analysis of variance with the WILCOXON signed-rank test.

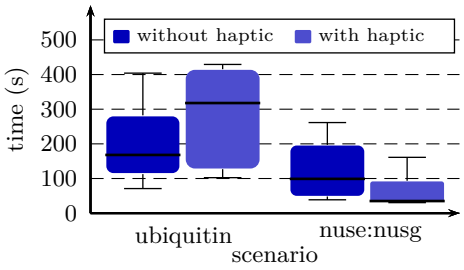
4.1 Improvement of efficiency

The fig. 3a shows that there is not a significant effect of the haptic communication metaphor [$\mathcal{V}_{i1}$] on the smallest RMSD score [$\mathcal{V}_{d1}$] ($W = 87$, $p = 0.348$). However, the fig. 3b shows a significant effect of the haptic communication metaphor [$\mathcal{V}_{i1}$] on the completion time to reach the smallest RMSD score [$\mathcal{V}_{d1}$] for the complex NusE:NusG ($W = 36$, $p = 0.008$) with a decrease of $-48.3\,\%$. However, there is no significant effect of the haptic communication metaphor [$\mathcal{V}_{i1}$] for the molecule Ubiquitin ($W = 13$, $p = 0.547$). The complex NusE:NusG presents the most difficult scenario due to the important number of residues to deform. On a simple scenario (Ubiquitin), there is no gain and no loss of working efficiency with the haptic communication metaphor. In fact, simple tasks involve less designations which limits the effect of the metaphor on the performance results of the overall process.

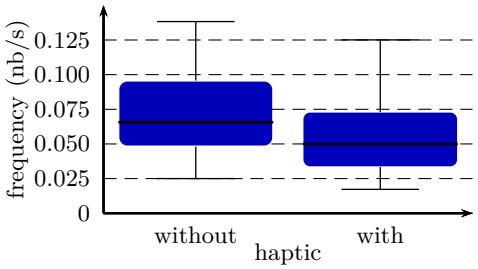
We observe on fig. 3c that *operators* significantly decreased the frequency of selection [$\mathcal{V}_{d3}$] by $-12.8\,\%$ with the haptic communication metaphor [$\mathcal{V}_{i1}$] ($W = 401$, $p = 0.009$). The completion time performance of the groups was better ($-48.3\,\%$ for the complex NusE:NusG) or at least the same (for the molecule Ubiquitin) with haptic, even if the frequency of selection iwas reduced: the efficiency of the groups was always better.



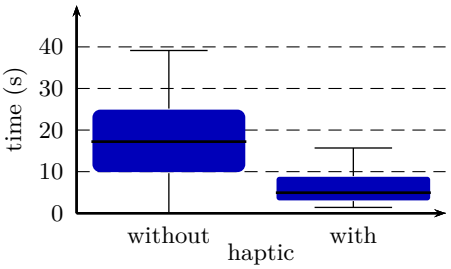
(a) Smallest RMSD score [$\mathcal{V}_{d1}$] reached during the realization of the task according to the two investigated conditions in haptic [$\mathcal{V}_{i1}$]



(b) Completion time to reach the smallest RMSD score [$\mathcal{V}_{d2}$] according to the two investigated molecules [$\mathcal{V}_{i2}$]



(c) Frequency of selections [$\mathcal{V}_{d3}$] for the *operators* according to the two investigated conditions in haptic [$\mathcal{V}_{i1}$]

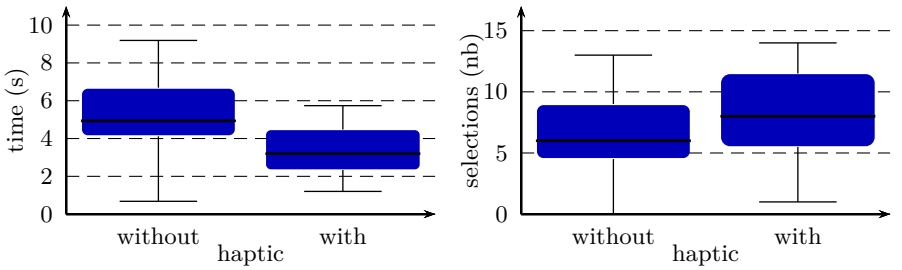


(d) Time between the acceptation and the selection for the *operators* [$\mathcal{V}_{d5}$] according to the two investigated conditions in haptic [$\mathcal{V}_{i1}$]

Fig. 3: Results related to the working efficiency

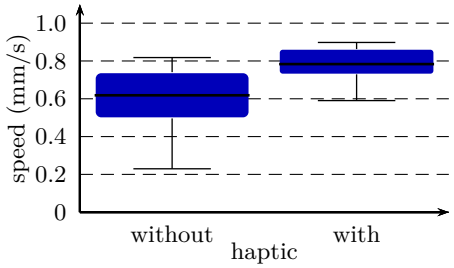
Finally, fig. 3d shows that the haptic communication metaphor [$\mathcal{V}_{i1}$] presented a significant improvement in the time between the acceptation and the selection steps [$\mathcal{V}_{d5}$] ($W = 473$, $p \ll 0.05$). The time was decreased by $-64.3\,\%$. Based on these results, the $\mathcal{H}_1$ hypothesis is validated.

4.2 Improvement of coordination



(a) Time between a designation by the *coordinator* and the acceptation by an *operator* [$\mathcal{V}_{d4}$] according to the two investigated conditions in haptic [$\mathcal{V}_{i1}$]

(b) Number of designations accepted by the *operators* [$\mathcal{V}_{d6}$] according to the two investigated conditions in haptic [$\mathcal{V}_{i1}$]



(c) Mean speed of the *coordinator*'s end-effector [$\mathcal{V}_{d7}$] according to the two investigated conditions in haptic [$\mathcal{V}_{i1}$]

Fig. 4: Results related to the improvement of the coordination

Fig. 4a shows that the haptic communication metaphor [$\mathcal{V}_{i1}$] introduced a significant decrease ($-51.5\,\%$) on the mean time of targets acceptation [$\mathcal{V}_{d4}$] ($W = 404$, $p = 0.008$). Moreover, fig. 4b shows that the haptic communication metaphor [$\mathcal{V}_{i1}$] significantly reduced the rate of acceptation [$\mathcal{V}_{d6}$] by $25.7\,\%$ ($W = 93.5$, $p = 0.004$). Finally, the haptic communication metaphor [$\mathcal{V}_{i1}$] had a significant effect of $25.7\,\%$ on the mean speed of the *coordinator* [$\mathcal{V}_{d7}$] as shown on the fig. 4c ($W = 15$, $p = 0.004$).

The mean time to reach the target [$\mathcal{V}_{d5}$] was directly linked tothe communication between the members of the group. During the deformation process, the

operator needs to be aware of the new designations in order to perform the corresponding manipulations. Two strategies of communication can be adopted. First, the *operator* detects the new designations based on the visual feedback. However, this strategy is constrained by the complexity of the molecule. In fact, the designation targets may be hidden by the structures of the molecule. In the second strategy, the *coordinator* verbally indicates the new designations to the *operators*. However, verbal communication is not precise enough to indicate 3D positions in the 3D virtual space. The haptic communication metaphor addresses these two constraints. The haptic tool provides an active notification of all new designations through a vibration feedback even if the *operators* are working on other regions. Moreover, the haptic metaphor enables the active guidance of the *operator* to efficiently reach the target on the molecular structure.

The fig. 4b shows that the rate of unaccepted designations was significantly reduced. Moreover, fig. 4c shows that the *coordinator* worked significantly faster. Indeed, the *coordinator* must wait until the *operators* accept the new designations. Since the *operators* are more effective at identifying and selecting the designated targets (i.e. active notification and gestural guidance), the *coordinator* can designate more targets with better acceptation rate. These results show that the communication with the haptic metaphor is faster and provides congruent spatial information. Based on these results, the $\mathcal{H}_2$ hypothesis is validated.

5 Conclusion

This paper presents a new strategy to address the two important constraints of closely coupled collaboration: social loafing and coordination conflicts. The proposed approach is based on a suitable group structure presenting two identified roles, and an efficient communication metaphor for the active notification and designation of targets in 3D complex environments. The experimental results, obtained in the context of complex docking process, show that the haptic metaphor significantly improves the performance and efficiency of the group working on complex tasks. In fact, simple tasks involve fewer designations which limit the contribution of the metaphor. Moreover, the results show that the metaphor improves communication through an active notification procedure coupled with an efficient gestural guidance strategy to reach effectively the designated targets. Based on these encouraging results, we will, in future works, investigate other steps of the collaborative docking process, for instance, the simultaneous deformation of the same molecular structure which requires a strong coordination of actions. Furthermore, to support some spatial information, we propose to study and integrate an audio component into the collaborative metaphor.

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