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Molecular modelling as the spark for active learning approaches for interdisciplinary biology teaching

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We present here an interdisciplinary workshop on the subject of biomolecules offered to undergraduate and high school students with the aim of boosting their interest toward all areas of science contributing to the study of life. The workshop involves mathematics, physics, chemistry, computer science and biology. Based on our own areas of research, molecular modelling is chosen as the central axis as it involves all disciplines. To provide a strong biological motivation for the study of the dynamics of biomolecules, the theme of the workshop is the origin of life. All sessions are built around active pedagogy, including games, and a final poster presentation.

1. The route toward new teaching strategies

As natural sciences professors in life science departments, we regularly see the struggle of our students with the perceived methodological rigour of the subjects we teach (mathematics, physics, chemistry) that seem to pose a much greater obstacle to the progression toward a degree than most other subjects. In our experiences, we have identified at least two issues contributing to the disappointing results we often face. The first issue comes from the fact that students who choose life sciences might have done so precisely because they already have had difficulties with the related disciplines in previous years and therefore arrive at the college level with a shaky background. The second issue comes from their difficulties in seeing the purpose of studying mathematics, physics and, to a lesser extent, chemistry, as a necessary and integral part of their curriculum. Interestingly, a very recent paper studied this issue, showing that whereas mathematics literacy is crucial for biology research, researchers in biology often realize this importance only after their studies [1]. From our perspective, the two issues are intertwined. We will not be successful in our teachings if we cannot clearly demonstrate the importance of our subjects to students and show them hands-on how concepts that might seem at first very abstract have a high practical use in biology. If we can get the students interested in our subjects, we then have the opportunity to address the first problem by reaching out to those who come to us with more difficulties from the start, and, by applying less conventional teaching methods, have the chance to help them fill the gaps in their knowledge.

Many previous experiences have taught us that traditional lectures do not constitute an appropriate and efficient solution to these issues, even when a lot of care is put into showing examples and applications from biology. The mere fact that our classes are named mathematics or physics may be enough to scare some students off. We then started experimenting with different alternative solutions stemming from our privileged position of researchers working at the interface between biological sciences, physics and chemistry. Inspired by active teaching methods [2], by our own personal experiences with the Montessori method [3], and after having had the chance to attempt different teaching strategies throughout the years, we developed a one-week workshop, named RIGOLE (a French acronym for group work around the origins of life, and that in French corresponds to a word that could be translated as laughter) aimed at first- and second-year life science bachelor students. The goal of the workshop was, and still is, to boost students' interest and motivation by showing them through unconventional teaching how all subjects matter and how the knowledge from very different disciplines is needed to be able to tackle interesting and fundamental biological (research) questions. For this purpose, biomolecular modelling constitutes an ideal playground for bringing together the various disciplines around a common challenge. Indeed, a recent study showed that bioinformatics is amenable to high school students being compatible with their knowledge and allowing students to interact with authentic research software [4]. To break the barriers and the fears that students may have with respect to subjects such as chemistry, physics and mathematics, all teachings of the RIGOLE workshop are as far as possible interactive, integrating scientific games, hands-on activities and group projects, together with short guiding lectures. Students therefore have the opportunity to see the importance of these disciplines in the context of a scientific challenge and to approach them from a new perspective, with less apprehension, thanks to the active pedagogy.

2. The specificity of French education

Before describing the details of the workshop implementation, it is useful to set the stage by providing a brief presentation of the French high school and college system, to put our work into context.

High school students choose an orientation in their junior and senior years. One of the options is science, which in the senior year differentiates further in the three options of mathematics, physics and chemistry, and life sciences. The science option is the choice made by students that have an interest in pursuing a career in science-related fields, spanning from hard sciences and engineering to more soft sciences and medicine, as it is the only orientation opening to college studies in these fields. The science orientation is often perceived as more challenging than other orientations and it is suggested to students with a solid school record in the previous years. Since in college we teach to students coming from this background, our high school workshop is offered only to junior students having chosen the science option, which implies that we touch a population with a bias of interest in science and generally a good performance in this field. About half of the high school students who attended the workshop had already in mind to study physics, chemistry or engineering in college, while another half was leaning toward medicine or biology. This second category is of the kind of students that we wish to motivate in particular.

The French university system is composed of two paths: regular universities, that all students with a degree opening to the specific curriculum can attend, and selective universities where students access via an exam. Top students generally choose this second option, while all others are directed to regular universities, which is where we teach mostly. This situation means that despite having a high school diploma with a science orientation, our college students do not necessarily have a solid background in the hard sciences, which are the main topics of the exam to enter selective universities for science-oriented studies.

In college, students choose one major that they pursue for 3 years, with a main imposed curriculum and a few classes that can be chosen more freely. There are generally no minors. After the 3 years, they obtain a bachelor degree and can then continue in a multitude of master programmes. In fields such as biology and medicine, hard sciences are taught in the first 2 years and account for a non-negligible portion of the curriculum. The specific topics treated depend on the major and can vary from one university to another, but they generally involve some basic calculus, statistics, differential equations, for mathematics; optics and acoustics, related to perceptions of living organisms, fluids and transport, related to circulatory systems and membrane equilibrium, electrostatics, for physics; and organic and inorganic chemistry.

Interdisciplinary teachings are rare both at high school and college level, even though this situation is slowly changing in the last few years. Subjects such as computer science and, more in general, topics where the use of computer programs is predominantly present, such as molecular visualization, bioinformatics and simulations, are completely absent from high schools and in college are offered only to specific computer science majors or as a complement to other disciplines, in the most advanced years.

3. Design of an interdisciplinary workshop

The workshop we present here was developed in 2015 and has run several times since 2016. Overall, about 180 university students have participated. The workshop is also offered to high school students, in an adapted version, with the aim of showing them early on in their curriculum the importance of each subject. This information gives them a first idea of the research carried out at university and ultimately offers them the chance to make a more educated choice for their future professional orientation. About 100 high school students have participated so far. Information on the logistics of the workshop organization can be found as electronic supplementary material.

3.1. Setting goals

The workshop has two main objectives:

— Discover what scientific research is and understand the importance of interdisciplinarity through a syllabus centred around the questions of the origins of life from a molecular standpoint. Understand the interconnections between disciplines showing how each one is necessary to study the behaviour of biomolecules through molecular dynamics simulation approaches.
— Motivate students for the study of scientific disciplines through an interactive and fun teaching where the student is the primary actor of the learning process.

More specifically, several sub-objectives have been identified to promote the effectiveness of the learning process. (i) Discover the context of university research, different possible orientations after the second year of college, the pleasure of learning without pressure. (ii) Understand the coherence of first- and second-year life science curricula, concepts studied in first- and second-year courses, applying them to a specific

	Monday	Tuesday	Wednesday	Thursday	Friday
9 h	welcome and general presentation				
9 h 30 min		introduction to molecular dynamics physics/maths	physics/maths RNA modelling	posters group work (research on assigned topic)	posters (finalizing presentation)
10 h	biology				
10 h					
10 h 15 min					
10 h 30 min					
10 h 45 min					
11 h					
11 h 15 min					
11 h 30 min	crowdsourcing Foldit				
12 h					
13 h 30 min		13 h 30 min–17 h programming	human folding	posters group work (first draft and pitching to other groups)	posters presentations and evaluations
14 h	chemistry molecular interactions		RNA folding lab (interactive simulations)		
14 h 30 min					
15 h					
15 h 30 min					
15 h 45 min					
16 h					
16 h 30 min	EteRNA				

Figure 1. Schedule of the typical week for the workshop. (Online version in colour.)

problem, scientific reasoning, how different disciplines are interdependent. (iii) Share with students coming from different backgrounds and interests, with teachers coming from various scientific disciplines working side-by-side with the students, with more advanced university students helping in the course as tutors. (iv) Enjoy learning without fears, learning through games and practical activities, group work, open discussions with students and teachers.

3.2. The pedagogical and organizational approach

The workshop adopts a large variety of teaching methods including group activities, practical activities and online games and demonstrations. Activities are always supervised and guided by professors and researchers from different disciplines (biology, chemistry, bioinformatics, physics and mathematics), as well as more advanced university students (from the bioinformatics curriculum, from the interdisciplinary curriculum frontiers of life science, and from the pharmaceutical science curriculum) acting as tutors for practical activities and group projects.

The workshop lasts a full week (5 days), for a total of 30 h and it is organized in half-day modules (see figure 1).

Each disciplinary module is composed of short 10–20 min lectures, with the professor introducing and developing concepts, mixed with short practical activities, while the longer-lasting activities (online scientific games) are presented to students at the end of the modules (biology and chemistry) in order to introduce the main ideas of the game and its relation to the workshop [5]. Students are then encouraged to continue playing in their free time. At the end of the disciplinary module of chemistry and physics, a quiz (available in electronic supplementary material) is proposed to the students to promote further reflection and possibly independent investigations. In the first workshop, the quiz was given as homework, while more recently, it has been integrated into the modules and is used as a basis for group discussions and debriefing. Students are divided into small groups to answer the questions of the quiz. Then, groups are paired to form larger groups where the answers are reviewed and discussed in case of disagreement. Finally, the whole class comes together and the answers are once more reviewed in the presence of the instructor who steps in to redirect the discussion correcting possible mistakes.

3.3. The message and learning objectives

The central theme of the workshop is evolution, from the standpoint of molecular biology, with the hypothesis of an RNA world and the later development of DNA and proteins. Students discover a very rich molecular world that goes well beyond the DNA double helix that they are used to when considering the basis of life. They discover the existence of RNA molecules of complex architectures that can act as a cell's machinery in the absence of proteins. Each discipline contributes complementary building blocks needed for developing the central theme focusing in particular on the topics presented in table 1.

4. The workshop in detail

In this section, we are going to present each teaching sequence, highlighting the main concepts discussed in class together with the activities proposed to the students as independent or group work. All teaching material, including slides, links to online activities, instruction booklet, computer programs, and more, can be found on the workshop website where it is used as support for the class: http://rigole.galaxy.ibpc.fr (the website and some of the material are in French).

4.1. Monday morning: biology

The goal of the biology module is to convey to the students that the most important properties of living organisms are

Table 1. List of topics discussed in each disciplinary module.

biology	concepts needed to address the question of the origin of life	from organisms to cells to molecules
		definition of a living organism
		Darwin, natural selection
		LUCA (Last Universal Common Ancestor) and the main constituents of eukaryotic and prokaryotic cells
		definition of a living organism
		different types of biomolecules (nucleic acids, proteins, lipids) and their functions
		the role of water
		RNA world hypothesis
chemistry	structural properties of biomolecules	from atoms to biomolecules
		atomic structures and properties
		intermolecular forces
		interactions and folding of proteins and nucleic acids
physics	concepts needed to build a molecular model and a molecular dynamics simulation	from classical mechanics to molecular dynamics
		Newton's equations of motion and trajectories
		building a molecular model force-field
		the role of temperature
mathematics	quantitative analysis of a force-field	how to sketch a function from calculus
		maxima and minima to find equilibrium points
		limits to understand long- and short-range behaviour of intermolecular interactions
computer science	basic programming concepts and use of a molecular dynamics software	how to provide instructions to a computer
		programming elements (variables, functions, loops)
		example of simple programming languages (SCRATCH and Python)
		visualization tools (VMD [6] and UnityMol [7])
		interactive simulations [8]

determined and can be explained by their molecular properties. The fact that the role of RNA cannot be captured by the central dogma is put forward. This observation allows us to point to other properties of RNAs that are related to their capability to fold in three dimensions. This property is both directly related to the RNA world hypothesis and the molecular structure preparing the students to understand the importance of the point of view of the other disciplines.

The basic concepts for biology are provided via a series of short videos [9] available to the students before the workshop. The session then starts with a reminder of the definition of life. Depending on the level of the students, they are either asked to build their own definition or are given one by the instructor. The students are then asked to consider a list of words and to decide whether a given word corresponds to a living organism or not. The following list has been constructed over time: bee, palm tree, bacteria, mitochondria, virus, lichen, fish, computer virus, three-dimensional printer, prion, fire. Many of these examples do not raise questions, but others do. For example, the bee is often considered problematic because only the queen reproduces in some cases, leaving the others apparently off evolution. Lichen, being a symbiont, might also be seen as an issue. These two cases force the reasoning to occur at the level of species, not individuals. Viruses are also frequently the matter of intense debates, reflecting the ones of the scientific literature. This case is used to prepare students to see the influence of the initial definition put forward, but also the need to change their point of view, which echoes the fact that later they will have to consider RNA for its potential role in the RNA world and not just in protein production.

To identify the main biological molecules of interest for a minimal origin of life scenario, the students are asked to build a portrait of Last Universal Common Ancestor (LUCA). They are advised to start from the observation of current living organisms and to look for their common points that might have been already present in LUCA. They usually easily arrive at a cell, surrounded by a lipid bilayer, with genetic material made of DNA and RNA, and proteins. The structure/function relationships of the molecules can be highlighted: e.g. the lipids are amphiphilic which allows them to form bilayers, which in turn allows them to separate cell interior and exterior. This property has important consequences for evolution by maintaining together DNA and proteins. The link between genotype and phenotype is also highlighted for RNA, which can both bear genetic information and act as a catalyst. It is underlined that both properties originate from RNA's ability to form hydrogen bonds, in replication and three-dimensional folding.

The citizen science game Foldit [10] is used as a tool to allow students to experience the physico-chemical properties

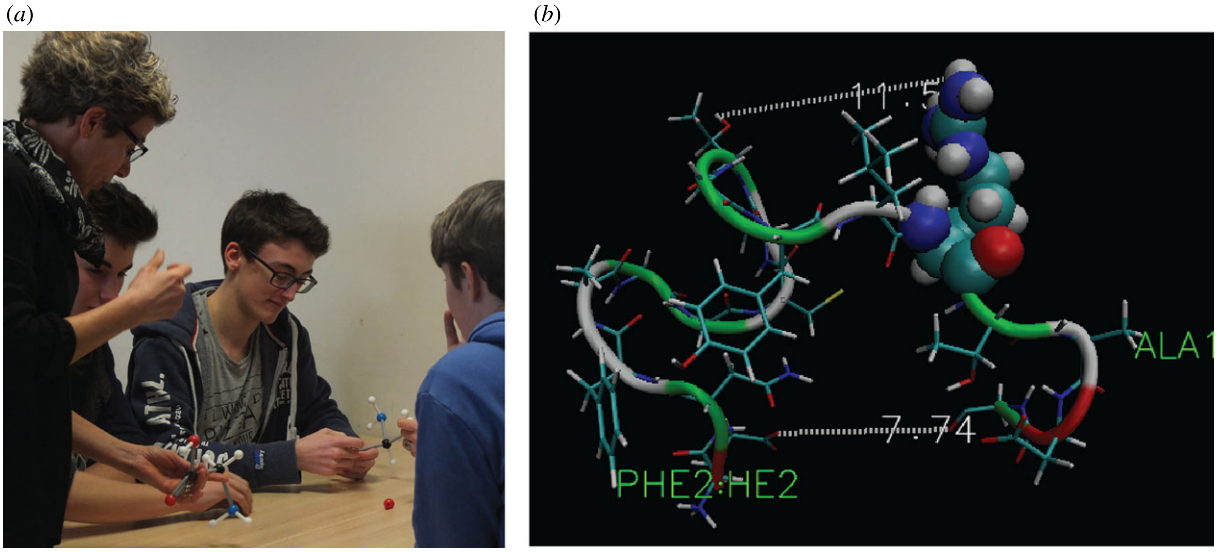

Figure 2. (*a*) Building amino acids using ball-and-stick chemistry kits and (*b*) analysis of the same amino acids inside a peptide using the VMD software. (Online version in colour.)

of proteins. The activity is inspired by the one described in [11].

4.2. Monday afternoon: chemistry

The main goal of the chemistry module is to provide students with the understanding that in order to study the behaviour of DNA, RNA and proteins, it is necessary to look at the physical interactions that govern these systems. We start by briefly reviewing the structure of atoms, focusing on the geometries of the orbitals and electronegativity properties, highlighting how these two factors determine the kinds of interactions forming between two atoms, ionic or covalent. For covalent bonds, we focus on the relationship between the shape of the orbitals and the geometry of the molecules that are formed when these orbitals are involved in the bond. This part is given as a short lecture that includes several schematic videos.[1] Students are then asked to turn to a practical activity where they first have to build simple molecules (water, methane, ammonia) using chemistry ball-and-stick kits. These same molecules are then studied *in silico* using the VMD software,[2] where the students can make measurements of bond lengths and angles.

We then resume the lecture and present the different kinds of non-bonded molecular interactions, namely the different electrostatic terms (Coulomb and dipolar), hydrogen bonds and van der Waals. These terms are presented in a qualitative fashion using movies and demonstrations (see endnote 1). As a practical activity, students are asked to use VMD to explore the structure of an ionic crystal of liquid water and of ice.

The last part of the chemistry module is devoted to presenting proteins and nucleic acids and how they form structured molecules through folding. We first discuss the peptide bond that constitutes the backbone for proteins and look at the different physico-chemical properties of amino acid side chains discussing how their interactions lead the molecule from an unfolded, unstructured conformation to a well defined folded state. As a practical activity, students are asked to build two amino acids with the chemistry kit and to then form an oriented dipeptide. The dipeptide can then be visualized in VMD for a further, more quantitative analysis. In VMD, the students can comparatively visualize the dipeptide as part of a full protein and start getting familiar with the fold of a protein as a whole (figure 2). At last, we introduce nucleic acids, focusing on the analysis of the interactions that nucleobases can form with each other. We discuss the double helix but put the accent on how, based on the chemistry of the bases, it is possible to form many other base pairs that are non-canonical, and on how these pairs are often important in the three-dimensional fold of single-stranded RNA. Examples are provided with the help of several videos [13,14]. A group quiz is given before the prolonged practical activity.

We conclude the module with the online citizen science game EteRNA [15], where the students can explore the secondary structures of single-stranded RNA molecules. In the game, students are asked to optimize an RNA sequence to obtain a given two-dimensional structure. After guiding them through the first levels of the game, students are introduced to a module specifically addressing the hypothesis of an RNA world. In the latest workshop, the activity has been replaced by Pangu, a game in augmented reality in which the player builds molecules with chemistry kits and take pictures of the molecules to make progress in the game [16].

4.3. Tuesday and Wednesday morning: physics and mathematics

The physics module focuses on explaining how to give a quantitative description of the molecular interactions described in the chemistry module. The goal is to show students that in order to study the interactions of molecules, they need to understand their physical behaviour in terms of equations, and therefore they need to be familiar with some basic principles of classical mechanics. In this module, we present the logical steps and explain the main physical concepts needed to build a molecular dynamics simulation: Newtonian dynamics, potential energies and force fields. To present the concepts underpinning equations of motion, the relationship between potential energies and forces, as well as the concept of bound and unbound states, we recall some mathematical concepts from calculus, in particular, limits and derivatives.

This module is at the heart of the workshop as it directly involves a discipline with which some students have difficulties. Here students have the chance to see first-hand the role of physics and mathematics in the interdisciplinary challenges posed by the biological problem and understand their role in the overall picture. It is therefore important to focus on a few central concepts, to allow enough time to treat the subject and to put to use different teaching tools. Thereby, we always combine the formal presentation in terms of equations and mathematical analysis with fun, practical exercises and hands-on examples to provide the opportunity to build an intuition. The module takes two half-days, Tuesday and Wednesday morning, with computer science done on Tuesday afternoon, to allow the students a break and focus on something more practical.

The module starts with a qualitative presentation of what molecular dynamics is, in order to clearly show that the goal of the module is to be able to understand the various steps of the simulation process. By presenting molecular dynamics first, teachers have a thread to which they can refer back during the module, refocusing the students on why the different physical concepts are needed.

The first concept presented is Newton's second law, $F = ma$, discussing what forces, accelerations, velocities and displacements are, and what an equation of motion is. At first, we give a discrete treatment in terms of finite variations of quantities over time. Next, we move to the continuum description using derivatives to define the velocity and the acceleration. We present the concept of derivative, highlighting its role as the slope of a function, and review simple rules to compute such derivatives. The students work in groups to determine the equations of motion for a free-falling object. We then continue to present the principles of the harmonic oscillator, which will later be used extensively to model covalent bonds. An online exercise is proposed to explore the properties of this simple system and to visualize the behaviour of the displacement as a function of time, from which students see first hand the arising of a sinusoidal function.[3] To conclude this part, we discuss Newton's third law of action and reaction to explain the behaviour of multi-body systems and we review vector sums to combine multiple forces acting on the same particle.

The second part is devoted to energy: potential energy, kinetic energy and energy conservation. We first introduce potential energy and its relation to work and force. Marble roller coasters are used to familiarize students with the concept of potential energy function and equilibrium points. Together with the instructor, students build the equivalent of a harmonic potential function and of a Lennard-Jones potential and discuss the role of maxima, minima and long-range behaviour. Next, we present kinetic energy, total energy and energy conservation in relation to the concepts of bound and unbound states based on the functional profile of the potential energy and the total energy provided to the system. Students further explore these concepts through an online application with examples of a roller coaster and a skateboard.[4]

The next section presents the functional forms commonly used to describe intermolecular potentials, that is harmonic functions for covalent bonds, inverse power laws for electrostatic interactions and Lennard-Jones potentials for van der Waals interactions. We review how to sketch the profile of a function, computing the existence domain, limits and determining maxima and minima through derivatives. For each of the functional forms analysed, we discuss the possible existence of bound and unbound states based on the presence of minima and on the limits at large distances and put this in relation to the molecular behaviour we want to capture with these models (figure 3). Students are asked to do some calculations to sketch these potentials themselves.

The last section is devoted to the role of temperature from a microscopic point of view in relation to bound and unbound states and the depth of potential wells. We present the roughness of a biomolecular energy landscape and the role of temperature in the ability of the system to explore it. To make this concept clearer, we ask students to shake a model of a roughed energy funnel printed in three dimensions with a small bead inside, representing a molecule exploring its energy landscape. To conclude the section, students are asked to explore the role of temperature in various forms of molecular interactions (charged particles, neutral particles, etc.) using online applets, guided by some questions.[5,6,7]

The module concludes with a group quiz in which the students are asked to critically review the main physical concepts presented in the module in relation to their application to molecular modelling (see electronic supplementary material).

4.4. Tuesday afternoon: computer science

Computer science is typically not a subject in the curriculum of first-year life science students. However, we considered it useful to introduce the basics of giving instructions to a computer, in order to provide students with some understanding of what a computer simulation is and to show them at least the existence of simple coding languages that can be used to perform data analysis. We approach the subject from a distance and first propose a practical activity seemingly unrelated to computers to make students understand the logic of giving unambiguous instructions to a computer. Students are spread out in the room and each one is given a small Lego abstract construction of a dozen pieces of different shapes and colours. They are given 15 min to write down instructions on paper on how to build the exact object they received, using only textual descriptions and no drawings. After that time, they are asked to take a picture of the object with their phone and to disassemble it, leaving it on the table together with the instructions. Students swap places and in another 15 min they have to rebuild the object following the instructions. Reconstructed objects are then compared with the pictures of the originals. This activity is used to start a discussion session in which the successful and unsuccessful instruction strategies are analysed and in which students are led to deduce what an effective way to give instruction to a machine would be. A short lecture is then given to describe the basic elements of a computer code: variables, loops and functions, presenting examples with the Python programming language. The rest of the module is dedicated to practical activities, first using Python and a series of exercises proposed by the Codeacademy website,[8] and then presenting an enzyme-docking code written using Scratch [17], a programming language developed by the Massachusetts Institute of Technology to teach the basics of programming to children. After working on some common predefined exercises, students are instructed to choose one of the two programming languages and to either extend the enzyme-docking code to make it perform new functions or to write a completely new code on a subject of their choice.

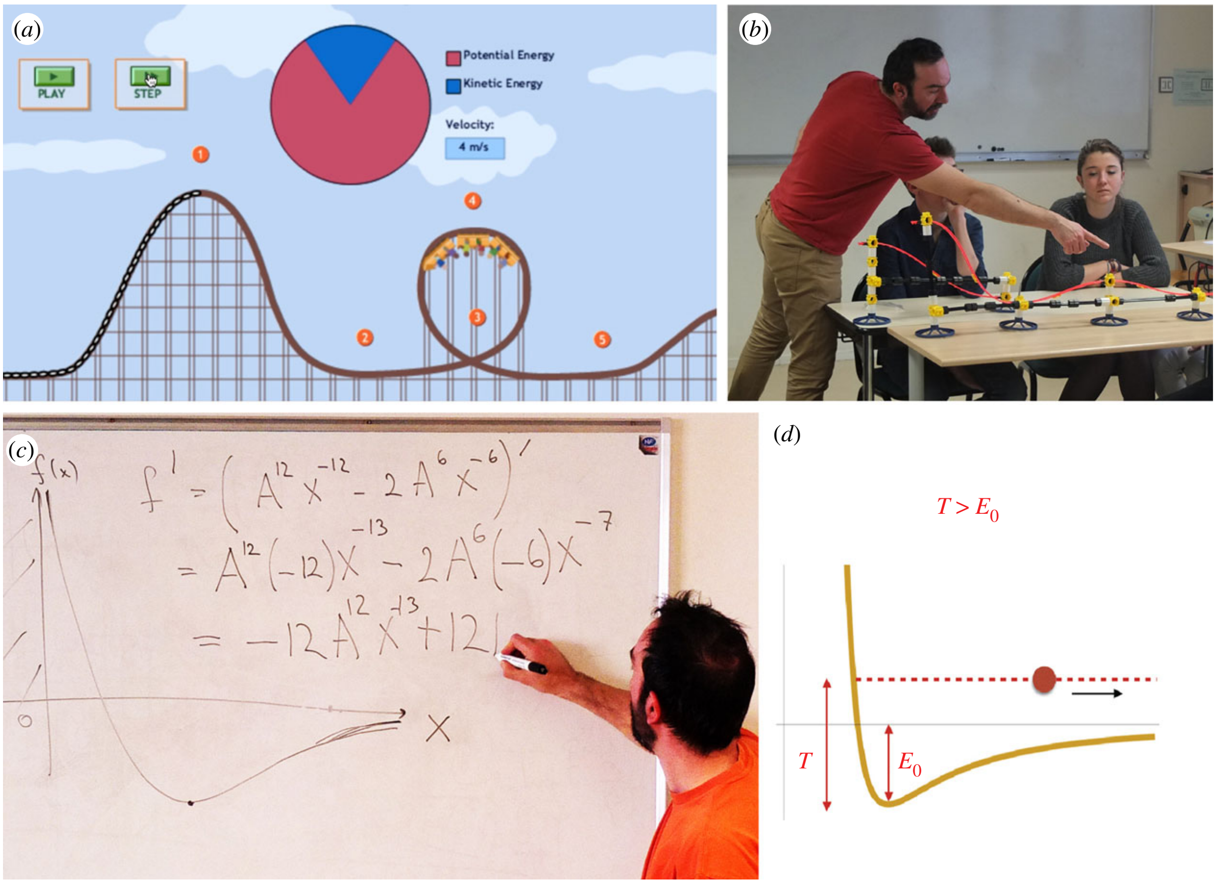

Figure 3. (*a*) Energy conservation presented with the roller coaster applet, (*b*) marbles roller coaster to explain the concept of potential energy function, (*c*) the equation for the Lennard-Jones potential is discussed at the board and (*d*) the concept of binding energy and its relation to temperature is presented in a lecture (T indicates the thermal energy due to a heat bath and E_0 indicates the depth of the energy well of the potential, defining bound states). (Online version in colour.)

4.5. Wednesday afternoon: molecular dynamics laboratory

Half of a day is fully dedicated to a computer laboratory where students use an interactive simulation software developed for our research activities [18,19] to explore DNA double-strand assembly and single-stranded RNA folding.

After the comparatively more abstract physics and chemistry modules, before the computer laboratory, we propose a physical activity in order to bring the students back to the central theme of the RNA world. In the human folding game, each student receives a T-shirt of one of four different colours, each colour representing one of the RNA bases. The class is then asked to form chains of a given sequence and attempt to form contacts to reproduce given RNA secondary structure motifs such as the double helix, hairpin and pseudoknots, as well as to optimize the sequence for a given structure, following up on what was done in the earlier EteRNA exercises.

After the game, lasting usually about 20 min, students start working at the computer laboratory using the UnityMol [20] software and entering the HiRE-RNA folding competition [21] (figure 4). The software performs a molecular dynamics simulation using a simplified, coarse-grained representation for nucleic acids, which is visualized in real time on the computer screen. By selecting a particle of the system, it is possible to apply an external pulling force, which is integrated into the Newtonian dynamics, allowing the user to pull the molecule toward a desired conformation.[9] Pop-up graphs monitor different energy terms from which one can deduce, for example, when a base pair is formed. Students first familiarize themselves with the software performing simple interactive simulation tasks on the DNA double helix, such as unwinding a preformed helix. Then they have to solve four RNA folding puzzles with increasing complexity, from hairpins, to a pseudoknot, to a triple helix, starting from a completely unfolded configuration. By observing the stability of the conformations they generate and by analysing the graphs of the energy terms, the students select plausible native-like folded candidates and submit them to the HiRE-RNA folding contest Web server to be automatically compared to the known experimental structures, receiving a score and a ranking in the class. As a side note, this student experiment brought up particularly interesting observations. We found that humans (e.g. students) explore phase space in a very different way compared to automated computational approaches, as discussed in more detail elsewhere [8].

In the 2018 workshop with junior high school students, a parallel session was added to the molecular dynamics laboratory to present ligand–biomolecule interaction through interactive simulations and virtual reality.[10] This hands-on demonstration allowed us to show yet another aspect of molecular modelling where the interplay between biology, chemistry and physics is essential for conducting an *in silico* experiment addressing biomolecules.

4.6. Thursday and Friday morning: posters group work and presentation

Students have 1.5 days to prepare a poster to be presented to the rest of the class on the last half day of the workshop.

A number of pre-selected topics ranging from more biological to more physical ones are proposed to groups of three

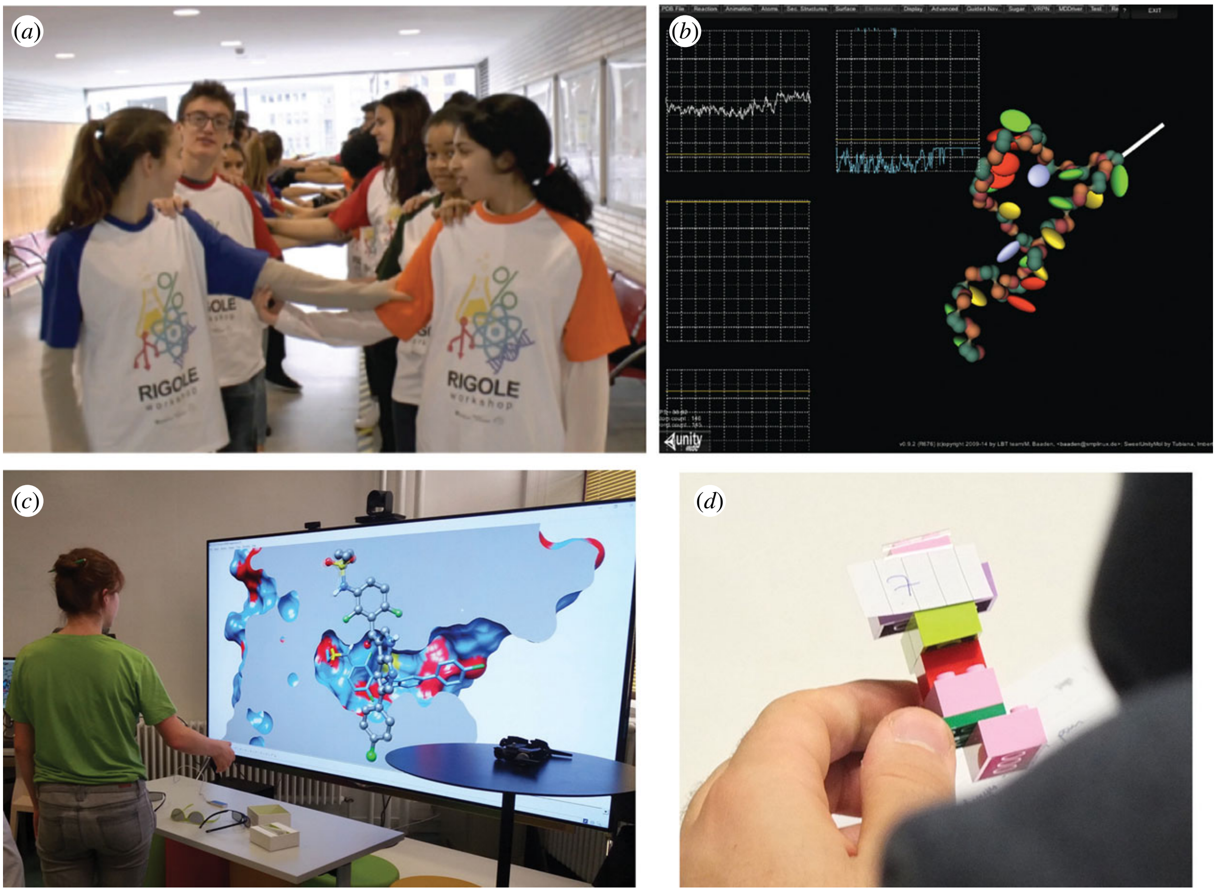

Figure 4. (*a*) Human folding activity, (*b*) interactive RNA folding simulation on the computer, (*c*) interactive docking (for high school students in 2018) and (*d*) example of Lego structure used in the computer science module. (Online version in colour.)

or four students. Groups are chosen to be as much as possible heterogeneous and complementary in the disciplinary strengths of their members. Topics include the role of clay in the formation of the first 'cellular' compartments, the Urey and Miller experiment for the creation of the first amino acids, the life cycles of phages comparing systems based only on RNA with those also using DNA, RNA thermometers, G-quadruplexes and ribozymes. Students are encouraged to use the knowledge and tools explored in the disciplinary modules to address the subject from different angles. On purpose, we do not provide more than the title of each subject, to allow each group to develop its study creatively and critically. A sample of posters produced by high school students in 2018 can be found in electronic supplementary material.

The poster presentation is organized as a rotation, so that each group member has the chance to present the work in front of a group of participants and a professor. For the workshops addressed to college students as a course, the poster session contributes to the students' grades. Through the rounds of presentations, each student is evaluated both by his/her peers and by a professor and acts themselves as an evaluator for other participants. More information on the organization of this kind of poster presentation can be found elsewhere [24].

5. Goals assessment

The workshop was offered so far to three high school groups of students, one of seniors and two of juniors (about 100 overall), two 45-student groups from the first- and second-year biology degree and three 30-student groups from the first year of the interdisciplinary degree of 'Frontiers of life science'.

Unfortunately, long-term follow-up of students has not been feasible for us neither for high school nor for college. Because of the articulation of the French education and its administration, we were not able to access students' records and track how they performed in their studies after the workshop. We have tried to contact students 1 or 2 years after the workshop, but we collected only a few replies. Therefore, we could only perform an assessment of our initial goals in the short term, by observing the evolution of the students' attitudes and performances during the week of the workshop.

We analysed several factors which included a survey at the end of each workshop, results of the quizzes when these were given as homework, results of the folding challenge, quality of the posters produced in the group work and the impressions of all instructors (11 all together) on the students' attitude, participation and reflection. Even though the overall number of participants is not large enough to perform a statistical analysis of the impact of the workshop and given that some appreciations could only be qualitative, we nonetheless are able to draw some overall conclusions. The full results of the survey are presented as electronic supplementary material.

Students of all categories showed great enthusiasm for the workshop. They very much appreciated the innovative teaching methods giving them a more active role than traditional teachings, as well as the learning environment in a more relaxed and fun setting. Their active participation grew over the days. While at first, they were relatively shy, not being acquainted with a system where they were asked to participate in open discussions with professors and with classmates, they rapidly found their place building constructive interactions. This more direct relationship with the teachers opened the grounds for facilitated communication, essential to address the harder topics among the proposed ones, thereby promoting a genuine and deep understanding of the subjects. The productivity of the students in the group work was satisfactory, with a good portion of posters reflecting the interdisciplinarity of the teachings of the week.

To further investigate the impact on high school students, in 2018, we proposed a new, additional, survey to gauge the initial interest of participants in the different subjects, their assessment of the importance of each subject to address biological problems, their perception about how easy or hard each subject is, and to what extent they would like to further study the subject in their future curriculum. The same questions were posed at the end of the workshop to see to what extent the programme changed the students' point of view. Questions and results are available in electronic supplementary material. Overall, what emerges from this inquiry is that the workshop helped giving participants a more realistic perception of the four disciplines, and, as was our initial goal, helped them in seeing the connections between them and the need for pursuing some knowledge of the hard sciences in order to make progress in biology. As discussed above, this is an important result given that students, and even researchers, in biology typically realize that they need other disciplinary knowledge, in particular, mathematics [1], only very late in their education. Interestingly, this insight seems to motivate students to pursue studies in biology even further than initially assessed.

Another criterion to assess the impact of the workshop was through the feedback received by colleagues and institutions. The workshop has been an opportunity to spread innovative teaching methods among university professors. At first, only three of the 11 teachers involved in the project were active users of unconventional teaching methods, and through the conception and the realization of the workshop, the other teachers enthusiastically discovered the new methods and some of them applied them in other contexts as well. The workshop was presented in various teaching councils and faculty meetings, gathering significant interest also at the institutional level. As a consequence, after the first year when funds to cover all expenses, including teaching hours, were provided by an outside source (Idex Paris Sorbonne Cité University), the various disciplinary departments took charge of the teaching load allowing the workshop to continue to be offered both as a college course and as an extracurricular activity for high school students.

The workshop also received important institutional recognition being selected for initial financial support by the Paris Sorbonne Cité University (USPC), and, more recently, from the joint Sao Paolo University—USPC grant to offer the workshop in Sao Paolo University in March of 2018.

6. Perspectives and conclusion

Convinced of the effectiveness of the teaching method that we have developed within this original workshop, in the 3 years since its first conception the workshop has evolved and parts of its content and teaching strategies have been used as blocks for other courses.

With the recent involvement of a pharmacy department supporting the project, we have developed an alternative high school workshop based on the theme of the interactions of biomolecules with drugs. With respect to the original theme of the origins of life, this extension involves changes in the biology module, in the practical laboratory, and in the subjects given for the poster group work. Instead of folding an RNA molecule, in the new laboratory, students analyse the results of a molecular dynamics simulation of a protein interacting with a small ligand in its native sequence and structure and of a protein where mutations have been introduced near the ligand binding site. The subject of the posters is now focused on the binding of small ligands to proteins. For example, students are asked to investigate how caffeine and nicotine work at the molecular level. As a further development, for the summer of 2018, an experimental wet laboratory was introduced in which students investigated the structure of biomolecules using biophysical techniques.

As an example of how the workshop can be easily adapted to a different context, we illustrate our experience with a course for second-year pharmacy students in an early elective research programme, Pharmascience. The one-week set-up of the workshop was proposed as a biophysics/modelling course adapting and changing certain modules to the higher level of these students and course requirements. The modules of chemistry and physics of RIGOLE were used as starting points to familiarize students with the structural analysis of biomolecules and modelling. For both subjects, additional, more in depth, concepts were introduced. For example, for physics, we devoted one half-day to normal mode analysis and related applications to proteins and nucleic acids. We developed more in depth the concepts from calculus on functional studies and asked students to perform comparisons of different functional forms to describe molecular interactions and to investigate the consequences of their possible choices. The computer laboratory on protein–ligand interactions was expanded to lead the students to make more quantitative observations and students were asked to write a short report. Instead of the poster group work, a paper on modelling DNA at different scales was chosen to be analysed and presented by the students, with different groups being assigned a different scale (quantum description of bases interactions, atomistic description, coarse-grained description and mesoscale description). A third example around the theme of drugs comes from the workshop offered in Brazil, addressed to master and PhD students in computational biology. The biology, chemistry and physics modules were preserved but adapted to the higher degree of experience of the students, but they were discussed in less time than for the RIGOLE workshop (two full days instead of 2.5). The computer laboratories were expanded and a module on docking was introduced in addition to the analysis of molecular dynamics simulations on protein–ligand systems. The group work on drugs was maintained, but instead of posters, the groups had to prepare an oral presentation.

Taking a wider perspective, the concept, format and methods developed here can be easily exported to other scientific disciplines and subjects beyond the realm of biology/biochemistry. Indeed, the problems with traditional pedagogical methods which motivated us, and which we have outlined in the introduction, are common to the vast majority of the first-year curricula in the hard sciences. The main key to developing similar workshops in other contexts is the choice of an appropriate subject: on the one hand, it should be specific enough to be introduced and explored satisfyingly in a short time frame without the need of too much pre-acquired knowledge; on the other hand, the subject chosen should lend itself to the investigation from different angles and methodologies, to promote the idea that science is not a compartmentalized endeavour and that each single aspect of a university curriculum contributes organically. Interesting examples of this kind can be found in all disciplines.

One example which is particularly well suited in the domain of the physical sciences is cosmology. In this context, an interdisciplinary workshop focused on the theory and observation of the basic features of the evolution of the Universe and its driving forces could be developed along similar lines as the one described in this article. The basic mathematical laws which describe the Universe evolution are very simple to write down and understand even by first- or second-year undergraduates with no prior knowledge in the field. Furthermore, this subject involves many different physics sub-domains (astrophysics, nuclear physics, optics, fluid dynamics, etc.) and features the interplay of phenomena governed by different characteristic scales (as is the case for macromolecules). Also, computer simulations are an important tool in this subject area, and one can easily envision the development of simplified toy versions of the software which is used in real-life research. Finally, interactive online pedagogical tools centred on many different aspects of cosmology (Hubble expansion, cosmic microwave background, etc.) are already available[11] and can be integrated into the workshop.

In conclusion, our experience has shown us that offering an interdisciplinary approach to the study of biomolecular systems is effective at all levels of education, from high school to graduate, especially when this teaching is carried out with a mixture of theoretical and practical activities. Given that many different subjects are addressed in the workshop from various disciplines, this combination of theory and activities becomes essential to lead the students to the understanding of all concepts.[12] Offering a relaxed teaching environment, where fun activities are proposed, is interesting also for more advanced students. Indeed, proposing less academic activities forces them to think out of the schemes they are used to, helping them to acquire a more critical view even toward subjects they have previously studied in disciplinary courses.

We hope this article will allow others to replicate and adapt the workshop in even more contexts.

Data accessibility. This article has no additional data.

Authors' contributions. A.T. and S.P. envisioned and organized the integrity of the workshop. F.N. and M.B. developed the content of the physics and modelling modules and coordinated the contribution of other teachers in their respective fields. All authors contributed to writing the manuscript.

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Endnotes

[1]See https://www.youtube.com/watch?v=y6q9sDO9-tM (2013).

[2]As noted by Burgin and colleagues, VMD offers the advantage of being used in research laboratories, which makes it an authentic activity [12].

[3]See http://mw.concord.org/nextgen/#interactives/physics/pendulums/spring-mass, https://phet.colorado.edu/en/simulation/legacy/mass-spring-lab.

[4]See https://phet.colorado.edu/en/simulation/energy-skate-park-basics.

[5]See http://mw.concord.org/nextgen/#interactives/physics/gas-laws-physics/gasmolecules-motion-physics.

[6]See http://mw.concord.org/nextgen/#interactives/physics/intermolecular-attractions-physics/charged-neutral-atoms-physic.

[7]See http://phet.colorado.edu/sims/html/friction/latest/friction_en.html.

[8]See https://www.codecademy.com/en/tracks/python.

[9]As noted by O'Connor and colleagues, an interactive simulation set-up is very intuitive making it an appealing tool in an education context [22].

[10]More details on the freely available virtual reality implementation and experiments are provided elsewhere [23].

[11]For example, see https://chrisnorth.github.io/planckapps/Simulator/#, https://map.gsfc.nasa.gov/resources/camb_tool/cmb_plot.swf.

[12]One aspect of the activities offered in the workshop that should probably not be neglected is the use of research software that is attractive to students perceiving the authentic nature of the activity they perform [4,12].

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