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Learning the Cell Cycle with a game: virtual experiments in cell biology

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***Abstract*—Cell Cycle Learn (CCL) is a learning game designed for undergraduate students in Biology to learn common knowledge about the cell-division cycle along with practical skills related with setting up an experiment and the scientific method in general. In CCL, learners are guided through the process of formulating hypotheses, conducting virtual experiments and analysing the results in order to validate or invalidate the hypotheses. The game has been designed in the University of Toulouse and introduced last year as part of the curriculum of a cellular biology class. This paper presents early results of an evaluation of the game enabled by questionnaires filled by the participants and game data collected during the training sessions. The results demonstrate with examples that both types of data can be used to assess the game's utility.**

***Keywords*—Cellular biology, learning game, game data.**

I. Context and related work

Cell Cycle Learn (CCL) is a learning game designed by a multidisciplinary group of researchers and teachers for undergraduate students to learn about the cell cycle and its regulation. Learning about the cell-division cycle is a crucial prerequisite to study proliferation for any curriculum in Biology and therefore the matter is taught early to students. The objective is to understand elementary concepts of the cell life, among which lie the different phases of the cell cycle, their duration and the checkpoints enabling the cell to progress through the cycle up to mitosis.

The cell cycle is often drawn as a circular timeline consisting of four phases named G1, S, G2 and M. By the end of G1 phase, at checkpoint named "commitment", the cell integrates environmental signals before proceeding towards G1/S transition. A lack of these signals will lead the cell to enter a quiescent state (G0), a subsidiary phase of the cell cycle which consists for the cell to wait for better environmental conditions. In addition to proceeding in its cycle or wait in G0, the cell can also decide to die (apoptosis) or to differentiate. When a cell progresses in the cell cycle, it must accurately duplicate all its internal material (DNA, centrosome, etc.) and double its mass before preparing for division. Before entering into S phase where DNA synthesis occurs, the cell must check for the integrity of its genetic material, which is called the G1/S DNA integrity checkpoint. Then, after replication, the cell switches to G2 phase in order to complete doubling its mass and organelles. During these last two phases (S and G2), duplicating centrosomes will allow the assembly of the mitotic spindle required for M phase (mitosis) to occur. However, before proceeding to this last stage, the cell checks once again the integrity of its genetic material. This is usually named G2/M checkpoint. When mitosis occurs, the cell (meaning all its internal material as well as its membrane) divides and produces two new cells that will restart their cycle in G1 phase. The cell cycle is dependant on internal or external conditions, the checking of which is the very purpose of the checkpoint mechanism. Therefore, in a cell culture, the cycle can be controlled [1] by endogenous or exogenous factors.

Most of these concepts were discovered during the second half of the nineteenth century and are considered general knowledge. For this reason, they are now delivered to students via lectures and tutorial and expected to be learnt by heart and retained permanently. Yet, experimentally controlling the cycle is the way scientists have first highlighted and then understood its mechanisms and properties. Experiential learning, as theorised by Kolb [2] is empirically supported by expert teachers as the most effective way to teach the cell cycle to students. For this reason, the teaching should ideally be supplemented by practical works in the lab with actual cell cultures. Unfortunately, this is seldomly the case for several reasons.

Firstly, growing cells in *in-vitro* culture is a costly activity. Cell lines are expensive, and so is the sterile equipment and its maintenance. In addition to this, the cell cycle is a fundamental matter which must be taught early in the student's graduate program and therefore a large number of students is concerned, which multiplies the costs. Secondly, for meaningful observations to be made, the duration of the experiment must be over 48 hours, during which measures must be performed manually at an interval of 6 to 12 hours. Of course, this is hardly compatible with the time table. Thirdly, experiments studying the cell cycle demand precision. Many parameters must be controlled and many manipulations are necessary before obtaining any result: Make one mistake and the result is flawed or spoiled, and the experiment must be started from scratch. As a consequence of these constraints, practical experiments studying the cell cycle have been removed from the program and this matter is only learnt in the classroom. From an educational point of view, this causes two problems. Practical works represent a form of active learning, which has been evidenced as an improvement over more classic forms of knowledge delivery by Richard Hake in physics education [3]. Learning by practising is therefore likely to help understanding the underlying processes and grounding them in concrete experience, so as to facilitate their later recollection. Without practice, knowledge related to the cell cycle is repeatedly reported by teachers to be a tough obstacle for undergraduate students. Moreover, carrying out experiments allows students to get familiar with the scientific method. Designing, planning and setting an experimental protocol is an important part of the required skills in biology.

To deal with the difficulty for students to understand the cell cycle and its mechanisms, a lot of material has been designed and can be found on the Internet. Explanatory animated clips illustrating the processes underlying the cell cycle are plentiful on video-sharing online platforms, and such content seems to be of interest, according to the high number of views. Serious games are another form of content freely and easily available. Most of them are quiz games helping students rehearse newly acquired knowledge, like “The Cell Cycle” [4]. “Cell Craft” [5] offers a more compelling gameplay. Through the incremental exploration of several levels, the player is led to build a properly functioning cell, and doing so, understand cellular metabolism and the role of DNA, mitochondria, ribosomes, etc. “Inky the squid and the scientific method” [6] is not a game dealing with cell biology *per se*, but it promotes the scientific method. It is a metaphorical game where facts about the scientific method must be collected by a squid in an underwater world. Virtual labs represent a form of training closer to the experience of practical works. They aim to recreate virtually the process of conducting an experiment through an interactive yet guided path of activities, engaging “the students [to] mimic the work methodology of a scientist and [to] rediscover laws of nature” [7]. The Howard Hughes Medical Institute has designed a series of virtual labs consisting of a graphical reconstruction of a lab including several pieces of equipment (Petri dish, microscope, etc.) covering various topics (bacterial identification, stickleback fish evolution, etc.) with interactive observation or manipulation activities. More labs in biology are available online (see [8] for a list). Maciuszek et al. make the case for designing digital experiments in virtual labs in Second Life in [7], taking advantage of the features offered out-of-the-box by the online virtual environment and the provided scripting language for immersing the learner into a relatively realistic experience (depending on the complexity of the script). This is the approach of medical education where scientific simulators are resorted to in order to produce accurate outputs with respect to the parameters set by the learner and the actions carried out during the experiment (see [9] for examples of medical simulators).

In CCL, we have opted for a mixed design compromising between scripted scenarios offering user guidance and the use of a dedicated cell cycle simulator allowing for free exploration and trial and error learning. CCL follows two objectives: Firstly, overcoming the constraints of real-life experiments by means of a virtual lab offering to every learner as many trials and errors as it takes for the knowledge (concept, calculation, protocol, manipulation, technique, etc.) to be understood once and for all, without any regard for time, cost or risk. Secondly, training them to the scientific method which is: formulating one or several hypotheses about a property to study, design an experiment scheme, conduct the experiment, obtain the results and analyse them in order to confirm or invalidate the initial hypotheses.

II. Simulation background

Simulating the cell behaviour for the biologists to help them understand the underlying mechanisms of cell cultures has been a prolific research domain [10], [11], [12], [13] in which various cell types have been modelled and simulated in very different contexts, specifically designed for very precise research questions. In a previous work, some members of the CCL project have proposed an individual-based model in which the cell behaviour is modelled using a check-point oriented paradigm [14], [15]. Such models have been demonstrated to represent accurately complex biological system dynamics [16]. The aim of this model is to easily take into account various cell lineages and environmental conditions naturally, only by modifying transition probabilities between the different stages. Pascalie et. al [14], [15] showed that the simulator is able to reproduce *in-vitro* data generated from cell cultures with various cell lineages and in environmental conditions.

III. Game design

CCL has been engineered on top of this simulator to take advantage of its capabilities to simulate the actual evolution of a population of virtual cells, thus allowing the students to experiment freely in a safe environment. The remaining challenges have consisted to i) provide a friendly user-interface to facilitate the control of the game by the learners in comparison to the simulator, and ii) to add a narrative for them to be guided through the process of conducting virtual experiments and analysing the results in order to acquire the targeted knowledge and skills.

A. Presentation

The learning game is presented as a web application available via a Web browser. The game currently runs on its own page but it has been designed to be integrated within a Learning Content Management System (LCMS) with minor adaptations. Figure 1 presents a view of the main panel. The top bar displays the title of the sequence and the current activity. It also regroups icons for side-tools of the game: a timer (that can be paused) to help learners keep track of time, a notepad for recording important things like calculation results, and a calculator. The left-side panel lists the activities of the sequences being played along with icons depending on their type (cf. next section). It has been designed mainly for the learner to control their progress through the scenario but can also be used to jump back to the memo sheet (cf. next section) of any previous activity if required. Finally, the central panel hosts the current activity. Buttons at the bottom are used by

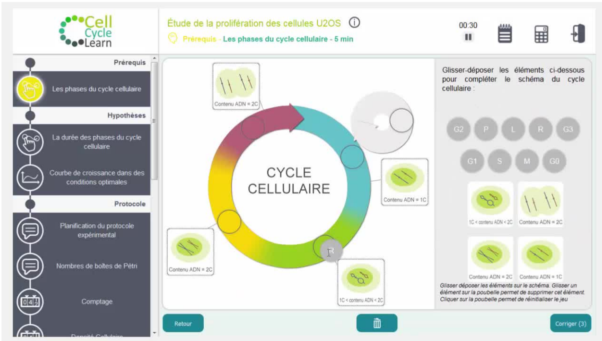


Fig. 1. The game is presented as a slideshow of interactive activities and transitions which must be unlocked one after the other. The progress within the scenario is outlined by a bullet-point-like progress list on the left.

the learner to clear or submit their answer, or to advance to the next activity once unlocked.

B. Content

A sequence is the virtual re-enactment of an experiment. It consists of 6 sub-sequences, each being composed of one or several activities:

Requirements	Activities to assess the knowledge required for the sequence. Whether the learner succeeds or not, such an activity is corrected and the results are afterwards available throughout the entire sequence and can therefore be assumed to be known in any further activity.
Hypothesis	Activities where the learner is required to formulate hypotheses concerning the one or several properties which are targeted by the sequence. Hypotheses are not corrected since the objective of the scenario is for the learner to experiment and find by themselves the correct answer (step 5: Results).
Protocol	A sub-sequence of activities whose objective is to set up the experiment. The protocol mostly addresses mathematical competencies like counting cells, measuring or calculating dilutions. Hands-on skills to manipulate the equipment is out of the scope of the game and must be practised during actual practical works.
Experiment	Once the protocol is established, the experiment is launched. It does not correspond to any interactive activity. Setup data are uploaded to the cell simulator and results collected within seconds.
Results	The collected results are presented to the learner for analysis. The analysis is usually guided through a step-by-step progression of activities where the learner is pointed to the relevant data and asked to correct their own hypotheses.
Synthesis	In this final activity, the learner summarises the knowledge covered by the scenario by means of filling the blanks of a cloze test.

A sequence is therefore composed of several interactive activities distributed among the 6 stages. Each stage is announced by a transition slide. The activities are of several types:

activity type	instructions
Drag & drop	Place tags on a drawing or a chart at their correct locations.
Curve	Draw a curve with the mouse to sketch a pattern.
Planning	Sketch a plan of the experiment using a form and a timeline-like graphical representation.
Pipette	Prepare a mix of cell/medium/serum using graduated pipettes.
Count	Estimate a cell count on a hæmocytometer.
Calculation	Perform a calculation.
Cloze text	Fill in the blanks in a text.

Unless designed otherwise (e.g. hypothesis activity, read paragraph below), each activity is corrected as soon as the learner submits their answer. Good answers are classically accentuated in green colour, bad answers in red. The learner is always granted 3 attempts, after which a memo sheet is displayed. The memo sheet of an activity is critical for the pedagogy. It displays the complete correction of the activity along with additional explanations. Each of them has been designed by hand so that the most adequate illustrations and layout were used regardless of the type of the activity. The memo sheet of every completed activity remains conveniently available until the end of the sequence. That way, learners can refer back to any of them at any time of the game.

Some activities are endowed with special attributes. For instance, "hypothesis" activities are not corrected automatically by the game but the answer is recorded and retrieved at the end of the sequence for the learner to correct by themselves on the basis of the experiment results. This self-correction is achieved in a "time limited" activity where the players are timed and score accordingly.

IV. Experiments

The experiments studied in this paper have taken place between September and November 2016 in two locations of Toulouse University: Paul Sabatier in Toulouse and Jean-François Champollion in Albi. The results (questionnaires and game-data presented in section V) were similar for both groups and were therefore grouped for the study.

The game was introduced in the classroom as part of a course of cellular biology. Each session is composed of two sequences, each featuring a different educational scenario and thus exploring a different set of knowledge and skills. Sequences are independent from one another but both are scripted following the same framework, as described in section III-B. Sequence 1 deals with the duration of the cell-cycle phases. It is composed of 9 playable activities, detailed in table I. The learner is led to understand that the duration of each phase is proportional to the number of cells currently in the phase (assuming the population is desynchronised) which can be observed on a macroscopic scale by the FACS (Fluorescence-activated cell sorting) method. Secondarily, the scenario also allows to observe, by counting the cells at a regular time interval, that a cell population grows following a non-linear (exponential) pattern.

TABLE I. ACTIVITIES COMPOSING THE FIRST SEQUENCE

#	activity	type	special
1	Requirements	Transition	
2	The stages of the cell cycle	Drag & drop	
3	Hypothesis	Transition	
4	The duration of the cell cycle phases	Drag and Drop	hypothesis
5	Growth pattern under optimal conditions	Curve	hypothesis
6	Protocol	Transition	
7	Experimental planning	Memo sheet	
8	Petri dish count	Memo sheet	
9	Cell count	Count	
10	Evaluating the cell density	Calculation	
11	Number of cell per dish and dish size	Memo sheet	
12	Cell seeding	Pipette	
13	Experimentation	Transition	
14	Results	Transition	
15	Cell counts along the experiment	Drag and Drop	
16	Concluding on growth pattern under optimal conditions	Curve	time-ltd
17	Proportion of each phase of the cycle	Drag and Drop	
18	Proportionate duration of each phase of the cycle	Drag and Drop	time-ltd
19	Synthesis	Transition	
20	Summarising on the cell cycle under optimal conditions	Cloze text	

Sequence 2 comprises 11 playable activities, detailed in table II below. This sequence deals with how the cell cycle can be controlled by exogenous factors. By an action on the culture medium, namely a starvation of growth factor, the learner witnesses the population of cells synchronising on a specific phase (G1). By assuming that the cells are unable to progress to the next phase (S), the learner is expected to identify the specific role of the checkpoint of G1 phase (restriction point), which is to ensure the cell will have at disposal in its immediate environment enough material before engaging into cell cycle propagation.

TABLE II. ACTIVITIES COMPOSING THE SECOND SEQUENCE

#	activity	type	special
21	Requirements	Transition	
22	The cell cycle checkpoints	Drag and Drop	
23	DNA content by phase	Drag and Drop	
24	Hypothesis	Transition	
25	Checkpoint influenced by deprivation of growth factor	Drag and Drop	hypothesis
26	Evolution of cell number	Curve	hypothesis
27	Protocol	Transition	
28	Experimental planning	Planning	
29	Petri dish count	Drag and Drop	
30	Evaluating the cell density	Memo sheet	
31	Number of cell per dish and dish size	Memo sheet	
32	Cell seeding	Memo sheet	
33	changing the cell culture medium	Pipette	
34	Experimentation	Transition	
35	Results	Transition	
36	FACS profiles over time during experiment	Drag and Drop	
37	Concluding on checkpoint influenced by deprivation of growth factor	Drag and Drop	time-ltd
38	FACS profiles and evolution curve	Curve	time-ltd
39	Synthesis	Transition	
40	Summarising on the cell cycle control	Cloze text	

Note that in the two scenarios above, the cell simulator is not involved: since every activity in the protocol is corrected before proceeding to the experiment, the results are logically known in advance without any computation required. However, the simulator is used to generate most of the data presented to the learners, which allows both a realistic data presentation and data quality control for a cost close to zero. Besides, a third scenario has been developed where the simulator is fully utilised. In this scenario, learners are required to confirm/invalidate a list of hypotheses by planning and launching experiments with the greatest freedom and autonomy. However, the lack of guidance was deemed problematical by biology teachers during the first testing of the game and therefore the third scenario was excluded from later use in class.

Fig. 2. Cell Cycle Learn being used in the classroom with undergraduate students in a Cell Biology class.

V. EDUCATIONAL SETTING AND DATA COLLECTION

Although the game was introduced in two institutions, the set-up was identical for both. The experiment was conducted as part of an actual class of cellular biology followed by 2^{nd} and 3^{rd} year undergraduate students in Biology ($n = 337$, 286 in Toulouse + 51 in Albi). One 2-hours game session was added to the course program which is usually only composed of lectures and tutorials since practical works cannot be organised for that part of the program due to technical and cost reasons (cf. section I).

Groups of approximately 20 students, supervised by one teacher, attended the virtual technical work in computer rooms, each student in front of a computer as illustrated in Figure 2. Each student was expected to play and progress through the 2 sequences at their own pace, and ask for help whenever they were confused by the instructions or puzzled by a result or an explanation.

The scientific methodology applied to the evaluation of this game aimed to assess three criteria, as per the framework described by André Tricot in [17].

- Utility describes how well the game has reached its objectives, namely how effective was the training achieved by/using the game.
- Usability measures how easily and fast the students got familiar with the game and its mechanics. It is also related to satisfaction and pleasure of use.
- Acceptability measures to what extent the game is endorsed by the audience. Although many factors play on acceptability, depending on the context, it is generally related to how compatible or aligned the objectives of the game are with those of the learner.

Data were collected in two ways: A survey was conducted at the end of the session; it contained questions related to both usability and acceptability, looking to evaluate how readily and efficiently the students could use the game but also the extent to which they would play the game on their own will or recommend it to a self. Computer logs were also silently collected during each session; they record every interaction of the player (visual element clicked, answer submitted, etc.) along with their time-stamp. Analysing those traces is likely to help shedding some light upon the utility of the game but it is also useful for cross-checking the answers of the questionnaires.

VI. Results

A. Questionnaire

The survey was taken by 279 students out of 337 who used CCL in the classroom in 2016 (response rate : 83%). The answer distribution is presented in figure 5. The chart shows an overall positive welcome of the game by the student audience. The software ease-of-use (comfort, navigation) is recognised by a large majority of users (96%). The content is well adapted to the level of the students, which was an expected result considering it was designed by biology teachers from previously existing teaching material to blend naturally into the educational scenario. A large majority of students agree to say that the game allowed them to make progress. Two results stand out: Firstly, a significant number of students complain about the instructions not being always clear and precise. Secondly, the statement that the game could replace practical works is disputed by nearly half the population, although the majority agrees on the game to be a good supplement to practical works.

Figure 6 presents word clouds generated from the answers given to the last two questions of the survey, which are open-ended questions. The more a word is used within the answers, the bigger it appears on the cloud, so that meaningful observations can be made at a glance (although a complete semantic analysis should be envisaged if those results were to be used for drawing scientific conclusions). In the first question, the participants were asked to report only the positive points of the game and/or the teaching type. What we first learn from the answers is that they found the experience playful. Words like knowledge, acquired and reviews indicate the students have acknowledged the scientific reach of the game. Among other positive assets, the students identified that the game promotes autonomy and allows practice without consequences. Regarding areas where improvements are needed, the questions and the instructions were the most challenged aspects, particularly a lack of clarity in the wording of some explanations and corrections. Two specific problems were also pointed out: the learners found some calculations very complex and they wished they were provided with more help; the pipette activity (activity #12) was criticised for its difficulty as any dosage error required the activity to be restarted from scratch since no undo action was provided.

B. Computer log analysis

The second part of the evaluation is the analysis of in-game user-traces reported by the game during the sessions. This process known as learning analytics or educational data mining, applied to learning games, is a promising path of research whose purpose is as much to study and evaluate learners as to improve the learning process itself. Indeed, collected data can be used at two levels, as described in [18]: in-game logging analysis is performed at learner's scale and used online (e.g. in real time) for the learner's benefit (personalisation, profiling, etc.) whereas posterior logging analysis aims to use population-scale data for evaluating or improving the game offline. Game-data processing can therefore be used to discriminate between different learner profiles, to build a learner model, to measure how similarly to an expert a learner behaves [19] or to evaluate how much of the "lesson" or skills are being acquired by the learner [20], [21]. Game-data processing can also entail changes in the learning environment: for example by pointing bottlenecks in the gameplay and suggesting improvements accordingly or, in a more adaptive fashion, adapt the narrative to the learner in response of their interactions [22], [23] in real time, which is referred to as adaptive storytelling.

The early analysis of this paper focuses on the usability of the game, which is a primary concern for the project since it is now scheduled to be used regularly by two institutions. Although utility and acceptability are also important evaluation criteria, we consider them secondary in this project since i) the game is included in the program as part of a compulsory course and therefore students' acceptance would be biased if not irrelevant and, ii) this part of the program was overlooked before the game was introduced and therefore its benefits are undeniable although its utility could not be readily demonstrated. In the following paragraphs, we report the most interesting results we have obtained from investigating potential ways for game-data to be interpreted as usability metrics. User-traces are very low-level, as they record every action from the players; they were therefore aggregated into meaningful data in order to reveal relationships or patterns.

Figure 3 illustrates the distribution of attempts in playable activities of sequences 1 (leftmost sub-figure) and 2 (rightmost). Each stacked bar reflects the distribution for each activity of the 1^{st}, 2^{nd} and 3^{rd} attempts.

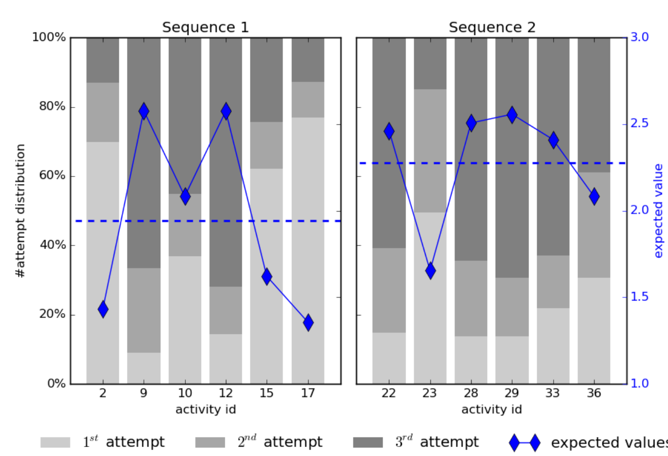


Fig. 3. The distribution of attempts on each playable activities indicates that sequence 2 is more difficult than sequence 1.

For each activity an expected value is calculated using the standard formula of a binomial distribution (1) with x_i being the number of attempts and p_i the probability of completing the activity in x_i attempts.

$$\mu = \sum_{i=1}^{n} x_i . p_i \tag{1}$$

This expected value reflects the average number of attempts necessary for completing the activity. Thus, it stands as a good indicator of an activity's difficulty. For each sequence, a mean expected value is computed by averaging the expected values of each activity in the sequence. Similarly to the activities, this measure represents a good indicator of a sequence difficulty. Applying this method, sequence 1 is showing a difficulty rate of 1.9 and sequence 2 of 2.3. In consequence, we can infer that sequence 2 is harder than sequence 1, which is consistent with our expectations since the scenarios were designed with increasing complexity and length.

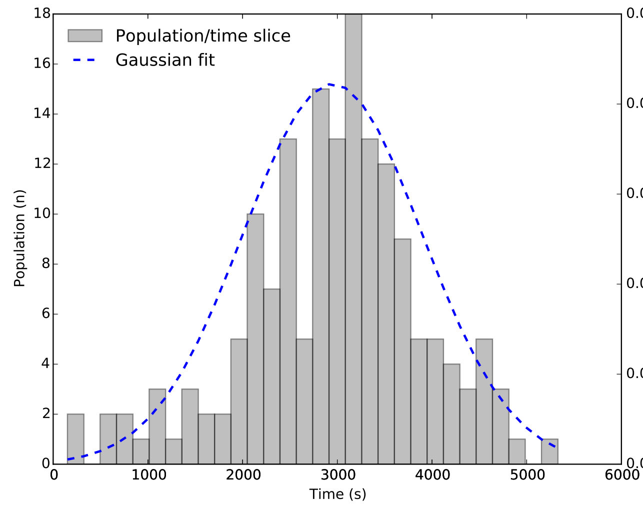
The same estimators can serve another purpose. Individually, the level of difficulty of each activity can be compared to the average level in the sequence in order to identify activities whose complexity may be discrepant with the others within the same sequence. For instance, the chart on the left in Figure 3 makes clear that activities #9 and #12 from sequence 1 stand out from the others, whose average level of difficulty is otherwise rather consistent. This is an indication that these activities should be reworked to match the average level of difficulty in this sequence. In the case of activity #12, this observation is corroborated by the survey (cf. section VI-A) where bad game design was pointed out by the learners. The difficulty of activity #9 however is unexpected and the instructions should be rethought by the experts. In contrast, the same method allows to detect that activity #23 is overly simple with respect to the other activities within sequence 2. Although overly simple activities are less detrimental than overly difficult ones since they do not hamper the progression of the learner, they could reveal that the educational challenge was not carefully adjusted. Moreover, too many trivial activities could yield boredom and negate the positive impact of the game on the learner's engagement.

Figure 4 displays the time spent playing sequence 1 (a) and sequence 2 (b). In both charts, the average time was estimated assuming a normal distribution, logically suggested by the shape of the probability density. The mean value for sequence 1 is 50 minutes (3007 seconds) whereas sequence 2 is expected to be completed in 30 minutes (1805 seconds). Both standard deviations represent 32% of their respective mean values, which indicates that the disparity is steady from sequence 1 to sequence 2.

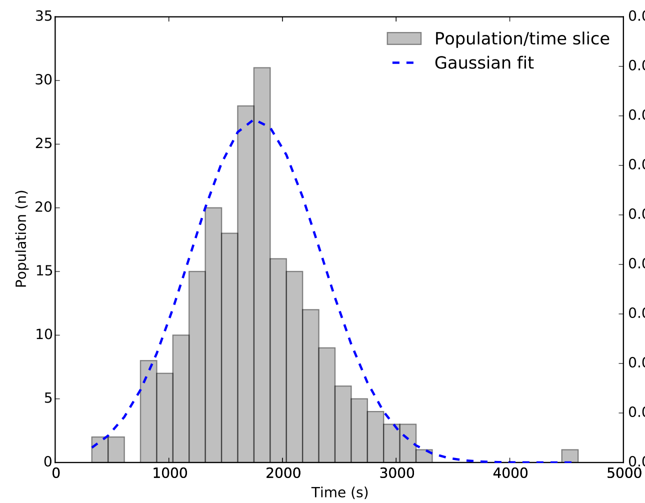
Considering that sequence 2 is more difficult (cf. Figure 3) and contains more playable activities ($11 > 9$) than sequence 1, this result indicates that the learning curve was overcome quickly. This is a good objective indicator that the game usability is satisfactory. Observations conducted in the classroom support this result as students showed increasing skilfulness and confidence during the session.

VII. Conclusion

In this article, we have presented the design principles of a learning game for teaching students with the concepts of the cell cycle and the experimental method. We have shown how both survey data and user-traces collected within the game could be used to evaluate the game's usability, that is to estimate how well the audience familiarises itself with the game. Measuring the game's utility and acceptability proved more complex than anticipated and will necessitate further investigation and possibly additional data. The game's utility could be assessed using a standard pre- and post-evaluation. Since the game is integrated into a course, another way could consider gaining access to each student's final grades and comparing them to their respective data collected within the game. With regard to the game's acceptability, we think the teacher's opinions and willingness to integrate the game within their course should be considered first. We trust their opinion towards using learning games to be positive on the grounds of more interactive and personalised teaching (differentiated instruction is a recognised good practice but actually hard to organise) and the capacity to alleviate their work. Regarding students, experience reveals that in the context of the class-



(a) Sequence 1, $\mu = 3007$, $\sigma = 963$



(b) Sequence 2, $\mu = 1805$, $\sigma = 581$

Fig. 4. Durations of sequences 1 and 2. Sequence 2 lasted less although the complexity of the scenario was higher.

room, their criteria for acceptability is far from what is generally envisioned by game designers. Games' inherent criteria such as fun and entertainment are less valued by students than its efficacy to facilitate their learning and ultimately help them passing the exam.

This first round of analysis has shown promising results as per the soundness of the project and our future ability to improve the game using data collected from the users. A lot of work remains to be done with the data, as suggests the rich literature on the topics of game analytics and educational data mining. For instance, the time spent per activity show large standard deviations, suggesting that either their duration is totally unpredictable due to a great variability in the profiles or that several subgroups with specific profiles and behaviours could be clustered. Insights could also be gained by comparing the answers provided by the students to the questionnaire to their respective game user-data. so far, confidentiality reasons have prevented us to do so but we expect to solve this legal matter shortly.

Collaboration is another aspect of learning that we could observe in the classroom but failed so far to evidence or measure objectively. The experiment described in this article was organised during regular teaching classes. On the one hand, it allowed us to reach a large population of participants and therefore consolidate the data. On the other hand, we could not prevent the emergence of collaborative behaviours between students. Indeed, although each student was supposed to play on their own computer, we observed peer-to-peer behaviours such as students waiting for a neighbour classmate to catch up or students working with a classmate on the same computer and reporting their result once the activity collaboratively completed, etc. This collaboration, whose immediate and adverse consequence on this study is to distort the data, is nevertheless a positive strategy for progressing and learning and therefore it should not be fought but encouraged and captured as a measurable component of the game's evaluation.

Finally, on a more technical note, we found that low-level user-traces are cumbersome and that collecting and logging them on the server in real time is a network-intensive process likely to threaten the game's playability or the collection process itself on low-spec computers. As an immediate future work, we intend to integrate the data required for evaluating the game and the learners as high-level metrics aggregated locally in real time and uploaded into a database.

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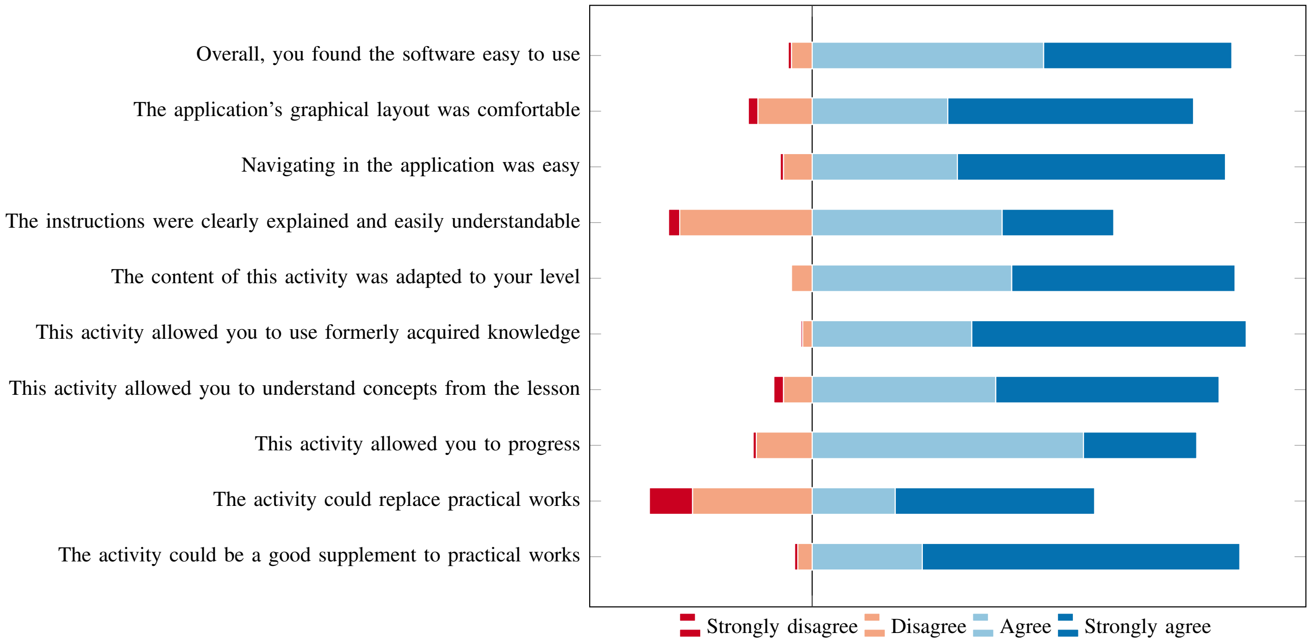

Fig. 5. A questionnaire was presented to the student after the training session for them to evaluate the usability and the acceptability of Cell Cycle Learn. The answers (n=279) reveal a warm welcome towards the game. A few negative observations point out some flaws in the content and the limit of the approach which cannot replace an actual experiment.

(a) "Which are the main assets of this game/teaching type" (Pros)

(b) "which points of the game should be improved" (Cons)

Fig. 6. Word clouds generated from the answers given to the open-ended questions concerning the assets/flaws of the game experienced by the users.