1

Biological Games

In this chapter, we present the main GWAPs currently available in biology and biochemistry.

In the highly specialized field of molecular biology, the results of FOLDIT[1] have been so positive (three articles published in the journal *Nature* – [COO 10, MAR 12] and [HAN 10] – and another in the Proceedings of the National Academy of Sciences, or PNAS [KHA 11]) and media coverage so important (a large number of articles in the non-specialized and popular science press) that the concept of GWAPs has quickly spread to biology. Many researchers try, with varying degrees of success, to use an entertaining-contributory approach to solve complex problems.

Zoran Popovic, one of the creators of the game, and director of the *Center for Game Science* at the University of Washington, believes that his laboratory is responsible for the emergence of a new path of scientific discovery. This path takes advantage of the creative capabilities of a wide population, once it is possible to involve it in research mechanisms through an effective initiation.

Adam Gazzaley, professor of neurology, physiology and psychiatry at the University of California and creator of NEURORACER (a game for improving the cognitive abilities of older people), being more restrained, thinks that the field of serious games is still in its infancy and that there should be a selection between that which claims to be based on science and what has actually been validated by scientific methods. According to him, approaches and tools should be multiplied and the results should be verified before making strong recommendations.

---

1 http://fold.it/portal/.

1.1. Foldit

Type of task – Macrotask.

Preliminary remark: FOLDIT is certainly the ancestor of biological GWAPs dedicated to the solution of complex problems. One of its designers, Adrien Treuille, has also participated in the creation of ETERNA[2] (see section 1.2), and the FOLDIT team is also at the origin of the *Center for Game Science*, an organization of the University of Washington dedicated to the universe of gaming for scientific purposes. The *Center for Game Science* hosted a very recent biological GWAP: NANOCRAFTER[2] (see section 1.3), a construction game of molecular nanostructures.

Launch – May 2008.

Audience/popularity – 57,000 players 2 years after launching.

Goal – Create predictive models of three-dimensional (3D) structures of proteins from their amino acid composition.

Significance of crowdsourcing for the problem to be solved – Predicting the 3D structure of a protein by its amino acid composition is a fundamental issue: a large number of diseases are caused by mutations, which by affecting the 3D structure of a protein, alter their normal operation. If the *normal* and the stable structure of a protein can be predicted, it can be understood how a mutation occurs at the level of the spatial conformation, and appropriate adapted therapies can be developed (vaccines, proteins for therapeutic use, etc.).

At the origin of FOLDIT, there is the distributed computation software program Rosetta@home: this is a program that determines the possible conformations that may adopt a protein by calculating the probability of interactions between segments of polypeptide chains according to the amino acids that compose them; interaction chains being all the more probable that the level of energy required for them to take place is minimal. Therefore, the most probable 3D structure is the one that will require the least amount of energy to develop. However, for a given amino acid sequence, there exist so many possible spatial conformations that simulation with algorithms is an extremely long and complex process. Rosetta@home uses home personal computers and runs when they are hardly used or not, thus increasing the computing power available to the project known as *distributed*. FOLDIT has been designed as an interactive and recreational extension of Rosetta@home.

According to David Baker [HAN 10], one of the researchers at the origin of the project, FOLDIT players are not required to have simple skills of visual recognition,

_____

2 http://nanocrafter.org/.

of classification; they are asked to utilize their logic, intuition, ability to see in 3D, initiative and creativity in solving complex optimization problems. Baker says to use three skills of the human brain, three typically and exclusively human talents:

– the ability to know how to take a risk in the short term for a long-term advantage and *vice versa*;

– the ability to see in 3D;

– the ability to realize that a *dead end* has been found and to stop just in time (that is before too much time has been wasted).

Zoran Popovic, one of the main stakeholders of the project (of its software/computing aspect), claims that for the time being, the human brain remains better than the machine as soon as the *creativity* parameter becomes essential and unavoidable. In addition, the game dimension creates the ideal conditions for the emergence of a collective expertise: the designers of FOLDIT have observed that not only do the players improve over time, but also that they organize themselves to add their respective competences. Finally, the game is designed in such a way that the players' findings are reinjected, recycled in order to be integrated in the manipulation mechanisms of the virtual protein, such that new players become increasingly faster experts.

Thus, a typical case (illustrating the first of the three abilities mentioned above) where humans are performing better than machines is that where a structure must be profoundly reshaped to optimize its configuration, that is to reach a stable form with a minimal energy cost. This implies too many sacrifices in terms of computation time for the machine, since this requires, as a first step, disorganizing an existing layout.

The most passionate gamers showed such skill in manipulating the protein chains, that designers have rapidly updated the game so as to provide the ability to create *ex-nihilo* proteins (potential applications: finding molecules likely to catalyze certain metabolic functions, manufacturing vaccine candidates, designing molecules that meet specific biological constraints for biotechnological or medical applications, etc.).

Moreover, David Baker uses the players' findings, that is to say specific folding strategies, to automate them in order to improve the prediction algorithms of protein structures. The community of players is regarded as a scientific partner on its own, and is associated as a coauthor in scientific publications [KHA 11].

Qualities/required human skills – Intuition, logic, spatial vision ("humans have 3D understanding that computers just cannot handle yet, and computers have the number crunching capabilities that humans cannot possibly compete with"), deduction and initiative skills, curiosity and creativity.

Necessary learning/game accessibility – An initiation step, necessary to get familiarized with the concept and the tools, is provided by means of a tutorial. It consists of a succession of 31 *puzzles* which reveal through step-by-step explanations all the mechanisms and modes of actions available, to act on the proposed 3D structure in order to bring it into an accurate conformation. It is possible to confront the real *puzzles* and to compete with other players before solving the 31 steps of the tutorial, but the relative complexity of the mechanisms to control depending on the various possible case studies makes it rather random. The manipulation of the structure modeled in 3D proves to be quite difficult and confusing, and it happens frequently that the solution of a *puzzle* depends largely on a lucky guess rather than on the real mastery of the suggested tools. This corresponds exactly to the *hardgame* configuration described by Good and Su [GOO 13].

Player's education – During the learning phase with the tutorial, the player learns the fundamental biochemical rules that govern the folding of protein chains: he/she must minimize the empty spaces within the molecules by promoting the creation of hydrogen bonds, manipulate the sidechains so that the hydrophobic parts are oriented inward and avoid excessive proximity between the atoms. The modeling of the molecule allows the visualization of these parameters and the mechanisms that can act upon it. Without becoming experts biochemists, regular and passionate players eventually end up acquiring an extensive expertise with regard to the spatial conformation of the protein, and for some of them, the ability to intuitively understand what must be changed to improve the 3D structure. This justifies in the eyes of the developers the benefit of entrusting non-specialists with the design of potentially synthesizable virtual proteins.

Interactivity – It is highly developed: players do not interact through the actual game since each is alone with his/her protein structure to optimize, but the possibilities to communicate with other players and designers are multiple: an instant messaging window is available in the interface where the protein is manipulated, and the number of players connected at the same time on the same configuration can also been seen (several *puzzles* are simultaneously proposed). From the homepage of the game, where the latest news are updated almost daily, a blog is available, where designers detail the scientific progress, and the results are achieved through the activity of the players; a forum and a wiki can also be found.

Challenge/emulation – As a result of the learning phase, where one can practice alone and at his/her own pace on models of proteins whose structure is known, *puzzles* can be tackled, therefore, protein structures to be optimized, which are put into play for a fixed duration. A *puzzle* at the beginner level can be chosen, or a *puzzle* depending on its characteristics (*overall* (generalist), *prediction* (known amino acid composition, unknown 3D structure), *symmetry* (proteins consisting of multiple identical assets arranged along a symmetry axis). The player is then in real-time

competition with all the other players who have chosen this *puzzle* and who strive to improve the structure. There are between 0 and 50 players simultaneously connected to the same *puzzle*, and things take a pretty exciting turn since the objective is to raise his/her score and thus to rise in the rankings, which can be followed in a small window embedded on the page. The points counter reacts to the slightest intervention on the structure, and an animation with a sound effect appears on the page as soon as the score exceeds that of another player (*rank up*), but also if one regresses in the ranking. The desired aim is obviously to stimulate the player so that he/she "hacks" his/her protein until he reaches the top of the rank. The time limitation spices up the challenge.

Design/feeling – The 3D modeling of the molecule is very successful, it can be manipulated and easily directed with the mouse and thus easily seen from multiple angles to identify problem areas (too much vacuum, atoms too close, hydrogen bond to favor, etc.). It is very reactive on the whole, each action generates an effect; fortunately, any action can be canceled, and the possibility of returning to the best configuration obtained is reassuring and allows all the initiatives: the best score and the corresponding conformation can be restored even if starting an attempt to improve that eventually worsens things (which is frequent…). The sound effect of the different actions is nice, the background music is not nagging and anyway, the interface is configurable with in particular the ability to turn off the sounds.

1.2. EteRNA

*Type of task* – Macrotask.

Launch – End of 2010.

Audience/popularity – More than 50,000 registrations, many articles in non-specialized and scientific press, one of which in the *Proceedings of the Academy of Sciences*, where players are associated as co-authors [LEE 14].

Goal – The purpose of ETERNA[3] is to virtually design complex ribonucleic acid (RNA) molecules which will be really synthesized, and tested to verify that they correctly adopt the 3D conformation theoretically predicted, and that they are biologically active. Given the key role that RNA plays in protein synthesis, and the role of proteins in living organisms, it is understood that the mastery of synthesis and RNA conformation is at the base of multiple medical, therapeutic and biotechnological applications.

---

3 http://eterna.cmu.edu/web/.

Benefits of crowdsourcing for the problem to be solved – Human brains prove to be more effective than computers in predicting the ways in which a molecule of a known nucleotide sequence can be folded. It should be noted that this assertion seems controversial: nondeterministic polynomial time (NP)-complexity does not seem proven for the design of RNA, as reported by [TCH 14]. (A problem is known as *NP-hard* when it cannot be solved within a reasonable time by an algorithmic method and that thereby justifies the use of the participatory approach).
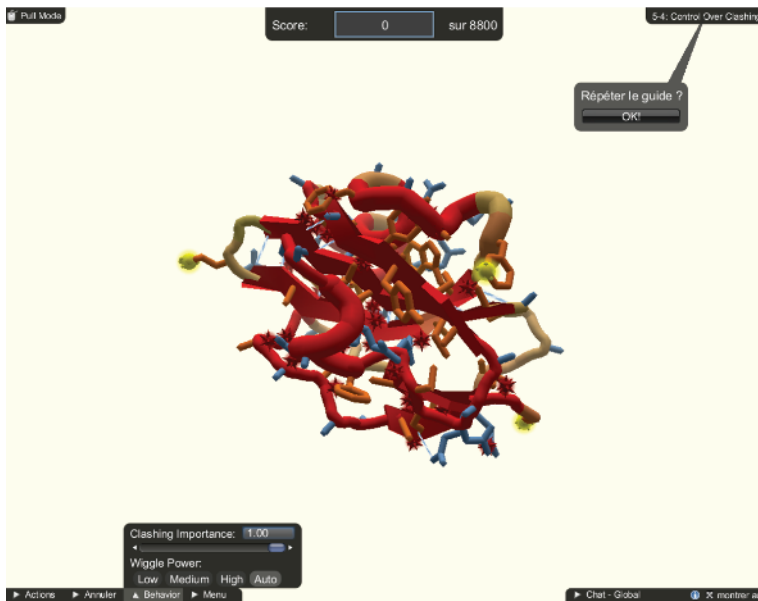
Figure 1.1. *Foldit. The game interface is a three-dimensional view of the protein being studied. The molecular components (hydrogen bonds, hydrophobic chains, etc.) can be manipulated with the mouse, and each action alters the spatial conformation of the protein*

Qualities/required human skills – Logic, deduction ability, initiative, curiosity, creativity, strategy, etc.

Necessary learning – The player is introduced to the rules of pairing of nucleotide bases by means of a tutorial consisting of a series of *puzzles* that he/she can solve through step-by-step explanations.

Player's education – Although the bases pairing rules are very simple, the parameters that determine the stability of the molecule can only be gradually apprehended, as different spatial configurations are found, and by reading what

regular players publish, which eventually end up developing real expertise in this extremely specialized area of molecular biology.

Figure 1.2. *EteRNA. Here, an RNA molecule in the spatial conformation that it must adopt if the proper sequence of nucleotides is performed, the one that will allow the establishment of bonds ensuring the stability of the structure. The circles in the molecule are to be replaced by the A, T, G and C bases chosen at the bottom right*

Interactivity – As in the case of FOLDIT, the interactivity between players is privileged: instant messaging in the game is very active and almost always shows between 40 and 50 players simultaneously connected, which seem to form a community of regulars who know each other and communicate. On the other hand, for each proposed *puzzle*, there is access to a comment space where players who wish to do so can express themselves, give clues or explain how they came to grips. Finally, the forum of ETERNA is also highly frequented and there is also a wiki,

mainly fed by the community of players. This wiki contains a lot of strategies, tips and explanations to solve the *puzzles*.

Challenge/emulation/task gamification – Players are not in direct competition with each other; they solve *puzzles* to earn points, climb in the ranking and cross multiple *grades*: *Tutorial completed*, then *Puzzle master LV1, LV2*, etc. (depending on the number of solved puzzles) and then *Top Player LV1, LV2*, etc. (be part of the best *n* players). At the same time, by solving *puzzles points* are accumulated and the player successively becomes a *Lab Member* and then a *Puzzle Architect LV1, LV2 and LV3*. The ultimate grade is that of *Millionaire*, reserved for players having accumulated 1,000,000 points playing with ETERNA. On the other hand, conviviality and the interactions between players are also parameters of the ranking, and are strongly encouraged by *grades*: *comment* (having at least posted five comments), *follow players* (follow at least five players), *gather followers* (having at least five *followers*). Note: the multitude of *grades* and ranking parameters (i.e. the number of completed puzzles, position in the ranking, earned points, conviviality rewards) mean that even beginner players immediately see the *counters* progress (points, number of *puzzles*, rank, etc.), which is a form of stimulation and encouragement. Their profiles show them what they have *unblocked*, but also all the steps that remain to be done.

Design/feeling – The design is neat, the interface is clear, help in readily availabile and easy to access the colors are harmonious, etc. Animations and sounds give a rhythm to each action, the ergonomics are good and it is possible to zoom at will on the molecule. The deep blue lit by a halo and the bubbles that slowly rise give the illusion of a water environment which is relaxing, serene and zen.

1.3. Nanocrafter

Type of task – Macrotask.

NOTE.– NANOCRAFTER was launched in late April 2014 by the same team as FOLDIT, in the framework of the *Center for Game Science* of the University of Washington, with these words from Zoran Popovic:

> "After more than a year in the making, NanoCrafter is ready for the first public Beta release. Over the many years to come, we expect the game to evolve almost on a daily basis towards a vibrant community of creative DNA designers, hopefully producing many exciting novel designs. As with any Beta we expect many things need to be improved, we look forward to improving the game on a daily basis. I am announcing the beta release of the game at Games for Change in NYC today."[4]

---

4 http://nanocrafter.org/.
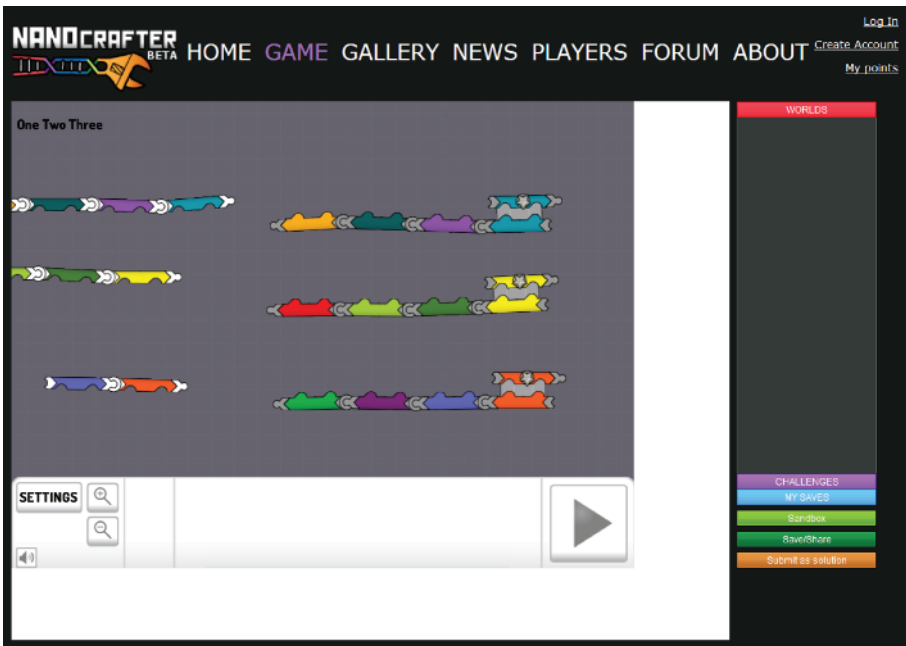
Figure 1.3. *Nanocrafter. In the configuration above, colored items represent fragments of single-stranded DNA that must be assembled respecting the color correspondences to form double-stranded structures*

Goal – NANOCRAFTER approaches the theme of the synthesis of desoxyribonucleic acid (DNA) fragments by using the pairing properties of nucleotides forming DNA, and especially the displacement mechanisms of strands that occur spontaneously when several single strands of compatible sequences are brought together. The objective, through the game, is to think about the construction of nanostuctures whose potential biotechnological applications raise a growing interest in structural biology and especially in nanomedicine.

Benefits of crowdsourcing for the problem to be solved – NANOCRAFTER is directly inspired by what works in FOLDIT and ETERNA; these are, therefore, the same human skills that are looked for through the proposed tasks. The main difference is the emphasis placed on creativity since the purpose is to invent molecular assemblies in order to create structures that do not exist in nature, on the basis of the building blocks of life (DNA) and from what is known of their constraints and properties of assembly. The field of biological synthesis is still in its infancy, but applications in health matters are potentially significant, and according to

Zoran Popovic, it is the privileged domain to express the advance that the human brain still has when compared to the machine.

Quality/desired human skills – Creativity, curiosity, initiative spirit and logic.

Necessary learning/game accessibility – As in other games of this kind, the beginner player is initiated to the mechanisms that govern the assembly of nucleotides, and must pass through the different stages of initiation by performing simple building tasks at the beginning, and which become progressively more complex. The player evolves through *worlds* which correspond to techniques of molecular assembly that should be mastered, each world being divided into several thresholds that must be crossed to unlock the next. Thus, there is a minimum of biochemical parameters to know and whose utilization must be controlled to undertake the biosynthesis of biological nanostructures.

Player's education – As in FOLDIT and ETERNA, even if the player does not know anything about the biochemistry at the beginning, he/she acquires, by simply playing, the basic concepts of nucleotide base-pairing, and the minimum of rules that must be known to manipulate the molecule, rules which become, however, increasingly more complicated as one overcomes levels. As in the previous GWAPs, this might be sufficient for him/her, and he/she does not need to know more in order to play. The game is still too recent, but it is easily imaginable that, as for ETERNA and FOLDIT, the more *hooked* players will quickly acquire expertise nurtured by their practice on the one hand, emulation on the other hand, and the assiduous attendance of discussion spaces of the game (forum and news), where the design team, with a strong presence, regularly communicates information and developments with a more or less pronounced popularization effort. The impression is given that non-scientists, who in appropriating the codes, the vocabulary and discussing issues between them, are gradually acquiring a highly specialized culture, focused on the problems raised by the game. Researchers, for their part, are doing the minimum about popularization in order for the general public to understand what to do (the game has a very detailed help topic available). The reconciliation between researchers and the general public is more pronounced in the sense where the general public acquires specialist knowledge than in that where the specialists try to reach the general public...

Interactivity – The game was recently launched, but like its predecessors, the possibilities of interaction and communication are highly developed: players have access to an instant messaging window embedded inside the game window, to a forum, and a wiki will probably complete the whole.

Challenge/emulation/gamification – The game is too recent to tell, but since a team that wins cannot be changed, the mechanisms that have made the success of

FOLDIT are more or less reused. Outside a solitary progression through *worlds* where levels are gradually unlocked by discovering new ways to act on building blocks, *challenges* are proposed, which are objectives to be fulfilled with constraints to respect, for example *achieve a double-stranded DNA fragment using the parts below*. When it is estimated that the objective has been achieved, the found solution is submitted, which will collect points if it is validated. For the moment, nothing explains clearly how and by whom the proposed solutions are validated, nor the calculation method of the points, probably because the game is still new. Therefore, rather scarce emulation and competition (it is unclear whether several players attempt simultaneously the same challenge, and it is not known whether the players vote for the various proposed designs), the bulk of the interest comes from the *puzzle* aspect, and from the suspense related to the validation or invalidation of the proposed structure. It should be noted that in the levels of the different *worlds*, the answer (valid or invalid) is given at the submission, with as an extra, the reporting of problematic assemblies in the case of failure. Conversely, in the *challenges*, there is no immediate news about the solution that was proposed.

Design/feeling – The interface is nice, clear and colored; the building blocks move with the mouse with fluidity; the manipulation is intuitive; assembly rules are accessible at any time by means of a button in the manipulation window; a structure can be put into the trash and one can start over; in case of failure, there is the possibility of choosing between restarting from scratch or recalling the last configuration achieved and modifying it to try to correct what is wrong.

1.4. Phylo

Type of task – Macrotask.

Generalities – The creator and his team emphasize the fact that PHYLO[5] is an open-free project and define their game as a new tool to support the analysis of the genome available to the international scientific community. A link *contribute to Phylo* invites users to collaborate by improving the code at the base of the game, or by translating the game into different languages (the displayed ambition is that PHYLO be translated in all possible languages; it is currently in 11). Furthermore, since October 2013, researchers around the world have been able upload their sequence alignments on PHYLO and submit them to the ability of the players to improve them. This is done through an interface called OPEN-PHYLO, which requires a separate registration and through which researchers not only upload their own sequences, which need to have been prealigned, but also generate and organize the *puzzles* on the portions of their choice [KWA 13].

---

5 http://phylo.cs.mcgill.ca/.

Jerome Waldispülh, bringing forward the *open-source* status of his project, raises the problem of the status of the data generated by crowdsourcing, deploring the fact that most of the time they are not free. He also points out that the first crowdsourcing projects have, because of the novelty of the concept, received considerable media coverage, which has greatly facilitated their dissemination. Support by strong media, with very wide audiences, is the *sine qua non* condition in order for this type of project to meet the audience it deserves. However, the number of projects known as *citizen science* is constantly increasing. The effect of novelty, therefore, fades away, and the trivialization of the concept will make public adhesion increasingly difficult and random. Even worse, according to Hand [HAN 10], journalist at the journal *Nature*, if the concept of GWAP is disproportionately extended, at some given point the general public will no longer be amazed and flattered to be asked to contribute for science. This is a long way from saying that people are instead likely to feel exploited and manipulated, and that the day will come when scientists will have to pay the volunteers to ensure the support of the public. There is a step that is still far from being taken, but Michael Kearns, computer scientist at the University of Pennsylvania, dreads the development of economic activity around the concept of *citizen science* [HAN 10].

For the creator of PHYLO, web portals such as ZOONIVERSE[6], CITIZEN SCIENCE CENTER[7], or SCISTARTER[8] can to some extent compensate for the problem of the lack of media coverage which new projects will have to face as the concept of GWAP will become commonplace. In order to not dilute the potential power of the crowd in a multitude of projects, he suggests that the research teams come together and use the same game interface when they have the same type of problem to solve, rather than to each create their small GWAP on their own. This is why he puts PHYLO at the disposal of the international scientific community. This is what he explains in the blog of the game by presenting the OPEN-PHYLO interface. The existence of a game such as FRAXINUS[9] (see section 1.5), more or less modeled on PHYLO, is the perfect counterexample to what Waldispülh advocates.

Launch – Launched in October 2010 by Jerome Waldispühl and his team at the McGill University in Montreal, the game has been widely commented in scientific [STR 12] and general media, and as FOLDIT and ETERNA, it has been the subject of a scientific publication to which the players have been associated as co-authors [KAW 12].

Audience – More than 300,000 people since the launch according to the online scientific media *Biomedical Computation Review* .

---

6 https://www.zooniverse.org/.

7 http://www.citizensciencecenter.com/.

8 http://scistarter.com/.

9 https://apps.facebook.com/fraxinusgame/.

Goal **–** Researchers (biochemists, geneticists and evolutionists) need to compare sequences of macromolecules (notably DNA, as well as RNA, proteins, etc.) originating from different species, in order to detect similar areas. One of the applications is to deduct from the rate of similarity between the sequences, valuable information about the relationships between species. Another is also to identify, through alignment zones, important functional sites, or even to highlight the mutations, or to understand the origin of genetic diseases. Multiple sequence alignments are performed by algorithms, and typically represent a problem *NP-hard* (that is it cannot be solved within a reasonable time by a computer given the complexity and the cost in terms of computation time, without even mentioning the financial cost), which justifies the entertaining-contributive approach. The purpose is therefore to improve the sequence alignments obtained through computation algorithms by the players. The game presents itself as a puzzle where the objective is to find the best vertical alignment between successions of colored blocks which represent the four DNA bases. PHYLO thus allows the general public to do what was usually done manually by researchers: reorganize the bits of sequences to try to improve the alignment provided by software.

Benefits of crowdsourcing for the problem to be solved **–** Finding the best alignment compromise for a large number of sequences is thus a *NP-hard* problem. Realizing that performing this task manually did not require any knowledge in genetics but simply a good sense of observation, and abilities of reasoning and logic, Jerome Waldispühl had the idea to transform the problem of alignment of multiple sequences into a game of manipulation of colored geometric forms. In addition, he has found that in more than 40% of cases, players are able to improve the alignment created by computational algorithms. "Unlike an algorithm, human beings are able to circumvent the rules of the game to obtain the alignment" he claims.

Qualities/desired human skills **–** Sense of observation and deduction, reasoning and logic.

Necessary learning/game accessibility **–** PHYLO is designed to be as simple and quickly accessible as the famous Tetris. The simplicity of the task at hand is such that no learning is required, and that the game is immediately accessible: everyone, at any age, is capable of sliding colored squares along superimposed lines, with the objective of creating columns of the same color. Furthermore, since these sequences (lines) are not identical, it is necessary to find the best compromise between the inevitable color differences and *holes* in the line. A tutorial is nevertheless proposed, but mainly to explain how the points are calculated and what strategies should be preferred to improve the score.

Player's education **–** In games such as FOLDIT, ETERNA and NANOCRAFTER , the player is introduced to the rules of base pairing, acquires knowledge of the

compared solidity of atomic bonds, must take account of notions such as concentration, and know and use various biochemical properties. Unlike the above games, PHYLO does not require any genetic or biochemical knowledge and the actual game does not provide any scientific information. This is an option that was chosen and that aims at simplifying the problem to solve into a game as simple and popular as possible, into a colorful puzzle that looks like any little online game that can partially and quickly be played in order to relax. Science becomes almost invisible. . . When the game starts, the subtitle *a puzzle to contribute for the research on genetic diseases* as well as the possibility to choose a *puzzle associated with a disease* are still there to encourage people to play by striking the sympathetic chord of good conscience. Naturally, the curious player can easily find what PHYLO is for, and scientific information is available in a blog and in the *news* on the homepage of the game[4], which are essentially links to press articles. As Jerome Waldispühl highlights, "The player is distracted but this is not lost time, and at the end of the match he is told about which gene related to what pathology he has allowed to move forward".
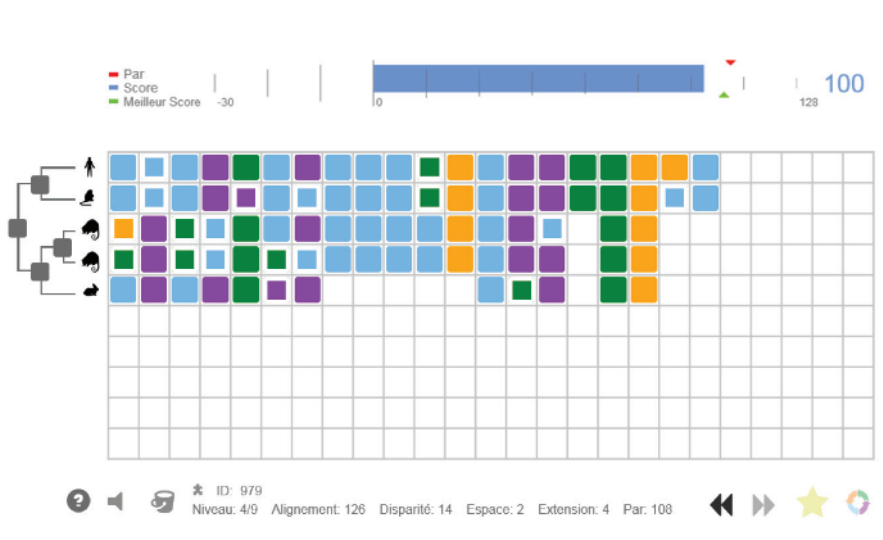
Figure 1.4. *Phylo. The purpose is, by moving laterally the color squares, to find the best alignment compromise possible between the five presented fragments of sequences. Above the sequences, the colored bar illustrates the progression of the score, the small top triangle being the score achieved by the computer, which must be met and exceed to move to the next level*

Interactivity – This is almost not developed. PHYLO is a solitary game, such as *Solitaire*, etc. The player tries to do better than the computer, and the only reference to

other players is the ranking. There is a forum, but it is not really active. On the home page, a window shows the tweets related to the game in real time.

Challenge/emulation **–** The main attraction of the game is its immediate accessibility and the assurance of very easily scoring points at first, sufficiently enough to make the player *hold on* when it becomes more difficult. Thus, a *puzzle* is composed of several *levels*, each level adding sequences to align. Matching the score of the computer (the *Par*) is sufficient to access the next level, and it is rather easy in the early stages. When the player manages to complete the *puzzle*, he/she accesses the statistics and the information about this *puzzle*, which are an element of motivation, since he/she reads his/her score, the mean score, as well as the best score obtained for this *puzzle* and the name of the holder of the *record*...He/she then has the possibility to replay the *puzzle* to try to match or exceed the *record*. Three classifications enables the player to access his/her progress: monthly, daily and overall; the daily ranking is very motivating because the player can quickly progress. Achieving a *record* is also flattering and encourages users to replay. The goal of Jerome Waldispühl was to create a similar game to Tetris, whereby any person could play when he/she has a little spare time, and it seems to be totally successful: the rules are simple enough such that one game suffices to assimilate them, and a game is fast enough so that the time invested is not an obstacle.

Design/feeling – The design of the game is pleasant, the interface is customizable (the color of the plate and the constitutive bases of the DNA can be modified, action sounds and background music can be enabled/disabled) and the language can be chosen. The manipulation of blocks is fluid and the ergonomics is satisfactory. The result of the actions can immediately be seen through a highly visible progress bar, as well as the score to win (the *Par*). However, it is regrettable that the alignment achieved by the computer is not revealed when the player is unable to match the *Par* and when he/she decides to abandon it. This would be instructive...
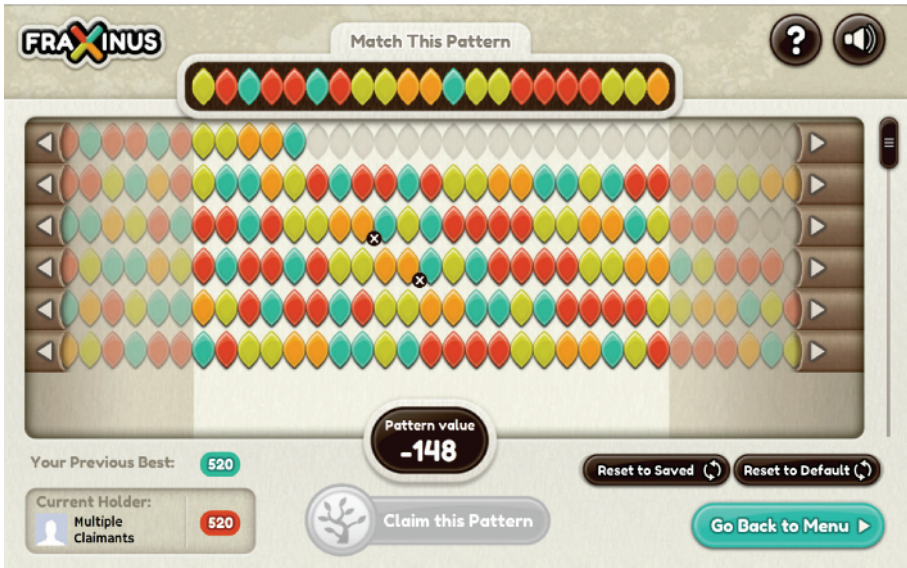
1.5. Fraxinus

Type of task **–** Macrotask.

Goal/launch **–** This game[10] is a game of sequence alignment in all respects comparable to Phylo, launched in December 2012 by the Sainsbury Laboratory, an English research laboratory specialized in plant pathology. Unlike Phylo, it focuses exclusively on research concerning the ash tree disease caused by the *Chalara* fungus and is accessible only to members of the social network Facebook.

----

10 https://apps.facebook.com/fraxinusgame/.

The players improve sequence alignments issued from the pathogen agent and the affected tree to provide information that could help researchers understand how the fungus kills trees. Especially, how and why some ash trees are resistant is of paramount importance to develop a strategy to fight and eradicate the disease that is decimating ash trees of the United Kingdom.
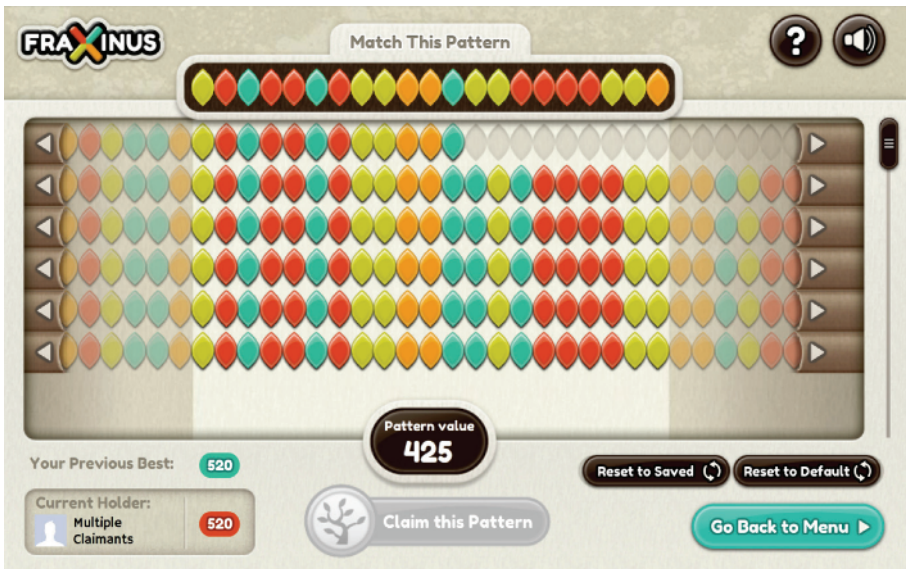

Figure 1.5. *Fraxinus: sequences to be aligned. The purpose is to find the best way to vertically align the colors of the blocks constituting six sequences. They must be aligned between themselves AND with the visible reference sequence at the top. This is achieved by pushing laterally the sequences using the left and right arrow keys*

Benefits of crowdsourcing for the problem to be solved/required human qualifications/game accessibility – Exactly the same as for PHYLO.

Player's education – As for PHYLO, and for the same reasons, it is not necessary to have knowledge of genetics and biochemistry to be effective with FRAXINUS. However, enough detailed information about the disease, the devastation caused to trees and the research strategies to eradicate this scourge is provided at the beginning of the game. This is used to suggest adhesion and motivation by striking the sensitive chords of patriotism and the keen interest for the conservation of nature: "Help us, otherwise 90 to 95% of ash trees in the United Kingdom will die..." At the end of each successfully achieved *puzzle*, the words "You are helping to save the ash tree" appear as a reminder.

Figure 1.6. *Fraxinus: sequences almost aligned. Compared to the previous figure, it can be seen that the blocks of colors of the six sequences are almost perfectly aligned, both among themselves and with the model. But although the score has gone up from −148 to +425, the alignment can still be improved since it can be read, in the bottom left, that the record to beat is 520*

Interactivity – The game, accessible only via Facebook, benefits naturally from the facilities of the social network to attempt to develop interactivity between players and especially encourage them to popularize the game among their *friends*. The player is strongly encouraged to invite *friends* to play, to compare his/her score with those of his/her *friends*, to share results and of course to talk about the game on his/her *wall*.

Challenge/emulation – When the player initiates an alignment *puzzle*, the *record* to beat appears in the game window with the name of its holder. It suffices to just match it to seize it, and then the player is asked to defy his/her *friends* to obtain a better score with the same *puzzle*. The player can either start a new *puzzle* or try to "steal" a *record* held by someone else by improving the alignment. All the completed *puzzles* appear in a pane in the shape of icons, mentioning the score obtained and displaying the words *improve* or *try again* depending on whether the player has beaten the *record* or not. It is exciting to hold a *record* and obviously the game tries to enhance this aspect and arouse the desire to prove either that the player can do better or that he/she is the best.

In addition, designers say that the names of the record holders will be mentioned in the sequence alignment databases and the publications.

Design/feeling **–** The interface is agreeable, clear and well arranged; the manipulation of sequences is intuitive; the progress bar is stimulating; the record to be beaten is highly visible and the help is accessible. The design is well achieved and the four nucleotide bases are represented by small leaves of four harmonious colors.

1.6. Eyewire

Type of task **–** Macrotask.

Goal/launch **–** EYEWIRE[11], developed and launched in December 2012 by Sebastian Seung's team, neurobiologist at the Massachusetts Institute of Technology, is related to the human connectome project, funded by the American National Health Institute. The connectome is a colossal project that aims at mapping the neural relations within and between all the cortical areas of the human brain. EYEWIRE is a game designed to help the reconstruction of the extensions of neurons in 3D from photographs of serial histological sections of the retina. From the 3D mapping of neurons, neuroscience researchers will be able to identify the synapses and relate the connections and brain activity. Seung and his team have just published in *Nature*, with *The EyeWirers* as co-authors, important results on the visual perception of motion through the data provided by the game [KIM 14]. This advance validates, according to them, the use of crowdsourcing through the online game to advance major scientific issues quickly and efficiently.

Audience **–** In May 2014: More than 135,000 recruited players and 150 countries represented (source: Wikipedia[12]).

Benefits of crowdsourcing for the problem to be solved **–** The eye and human intelligence combined together prove to be much more efficient than computer programs in detecting boundaries and cell contours. This is particularly true when the extensions of nerve fibers are entangled in a dense network, as is the case in the retina. The player is faced with a *cube* that represents a piece of retina traversed by a portion of neuronal branch that has been partially and roughly automatically delimited by image analysis. The player must improve the tracing by *coloring*, which he/she identifies as belonging to this neuron on a electronic microscopy photograph that represents the same *cube* in cross-section. Each *cube* is decomposed into 256 slices. The arrow keys of the keyboard allow the player to move through the

---

11 http://eyewire.org/.
12 http://en.wikipedia.org/wiki/EyeWire.

thickness of the *cube* jumping from one slice to another and *to follow* the neuronal branch by correcting the work of the analysis algorithm. This is achieved by *coloring* the portions of neurons possibly omitted, or even by detecting ramifications also ignored by the computer. A whole neuron corresponds approximately to 1,000 *cubes*, each of these 1,000 *cubes* is analyzed by 3–5 different players, and it is the correlation between their tracings that will legitimize the final mapping.
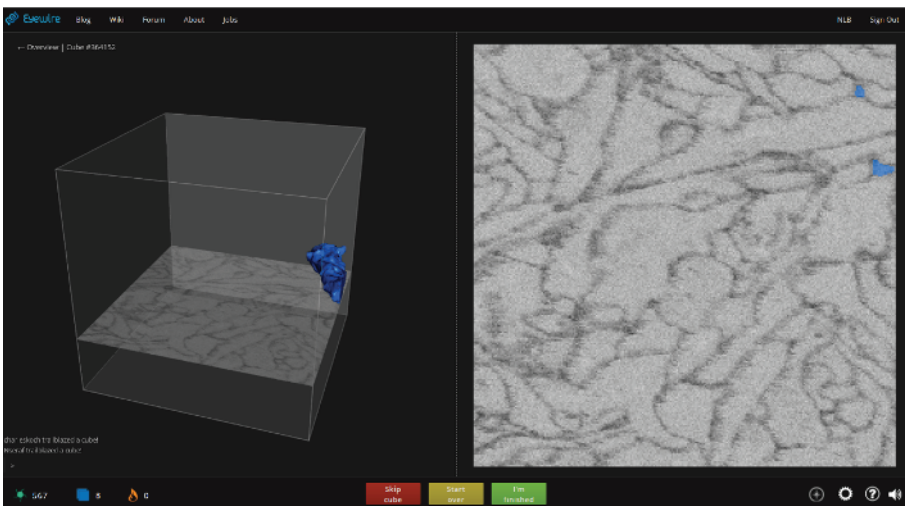

Figure 1.7. *The interface of Eyewire. On the left, the "cube" (fragment of a histological section of the retina) which contains the neural branch to be outlined, of which a fragment can be seen. On the right, the corresponding transversal cross-section where the player "colors" areas that seem to him/her to belong to the neuron. He/she, therefore, "follows" the neural branch by traversing the entire thickness of the cube, through which he/she moves with the arrow keys of the keyboard*

Required human skills – Designers insist on the fact that to become an efficient *Eyewirer*, no knowledge in neurology or even in general biology is required. The game is available to anyone with a good sense of observation and spatial visualization.

Player's education – Even if no knowledge in neurology is required, the players have access to a wealth of scientific information about the project in which they participate by playing. They are also regularly kept informed not only about the evolutions of the game, but also about the resulting scientific progress. On the other hand, elder and experienced players are given the power to supervise the work of the community. Thus, they are recognized as having a true expertise in the visual ability

to detect the contour of a neuron in an electronic microscopy picture, that is a document which most ordinary people only see as a patchwork of gray shades.

Interactivity – Although the task is rather monotonous and each player colors his/her little piece of neuron on his/her own, conviviality and interactivity seem highly developed in the game. An instant messaging window is available in the interface, and the players extensively debate and seem to form a large community of regulars that challenge each other and joke. However, they are also keen to help any newcomer who asks a question. On the other hand, the messaging window also accounts for the activity of the game and gives an idea of the number of players connected by communicating in real time the points obtained by them. This is one way to stimulate emulation and an opportunity for them to congratulate each other.
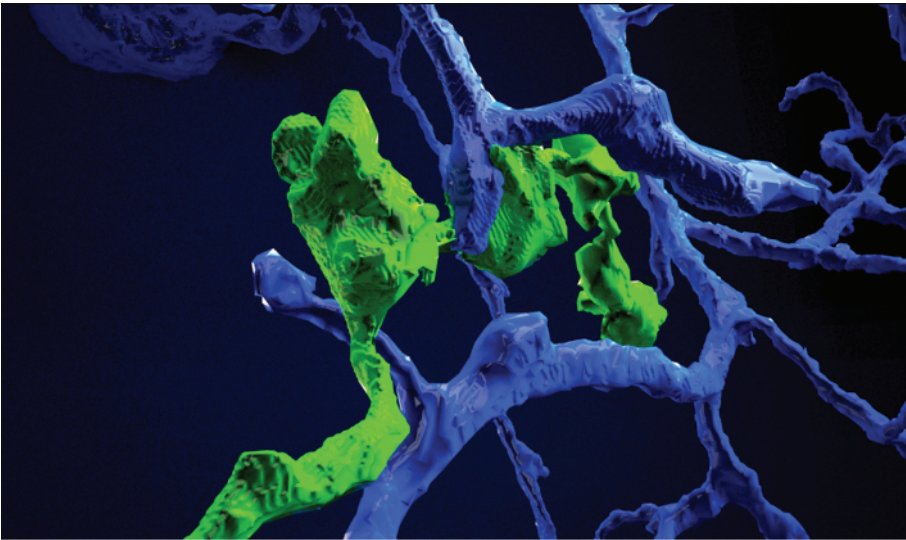
Figure 1.8. *Eyewire. This image from the blog of the game highlights a synapse (the point of junction between two neurons) discovered by means of the activity of the players*

Challenge/emulation – Given the relative aridity of the task (once again, the objective is about scanning grayish pictures looking for continuity and homogeneity), one feels the wish to make it more interesting and encourage players to compete by rewarding them through a rather complex points, titles and classification system. The player receives all the more points when his/her tracing is close to the average of the tracings of the other players. He/she is also rewarded by a *pro rata bonus* of the time spent, intended to reward its application and the care taken in his/her *coloring*. For an

equal amount of work, some cells are rewarded twice as much because they are deemed more difficult to isolate (*starburst cells*). In addition to the points, the meticulousness of the player and the relevance of his/her tracings are evaluated by an accuracy percentage. Once the player has reached an accuracy of 80%, he/she is allowed to become a *pioneer*, that is to be the first to intervene on a *cube*, and thus enjoys a *clearing bonus*; he/she then wins points again whenever another player deals with this *cube*. The players who have demonstrated their skills and pass the tests can be promoted to the ranks of *Scout* or *Scythe*, which gives them the rights to supervise the work of other players and to validate or invalidate some tracings. Thus, the complexity of the classification, the diversity of the evaluated parameters, the seniority as well as the difficulty of the processed cells create a hierarchy within the players and maintain the emulation. In addition, the regularly organized competitions are a way to retain players, who have the opportunity to compete over a specific goal. These *challenges* are of various kinds: for example, *Happy Hours* are held weekly and consist of earning the highest possible number of points during this period of time, with bonuses as reward for the winner. *Marathon* is a challenge: it is necessary to complete an entire cell (i.e. 1,000 *cubes*) in a given time (currently 26 h). *Trivia* is a type of multiple choice questions (MCQ) quiz; the *Diabolic Cube* challenge consists of coloring in the best possible manner regions that are particularly difficult. This difficulty is due to the fact that the neuronal branches of different cells are closely entangled. These one-off events are elements that spice up the game by introducing competition and suspense. Since May 2014, players can form teams, which gives rise to an inter-teams classification. Finally, *Lore of Kor* was launched recently (3 June 2014). It is a neuron-coloring contest based on the background of a science fiction scenario, in which two teams confront each other, with premiums and various bonuses up for grabs. The developers keep breathing life into the game; to this end, they take great care to minimize the monotony of the task. This is achieved with the help of all kinds of devices meant to promote the interactivity and competitiveness, while creating, maintaining and strengthening the sense of belonging to a community.

The other method of securing loyalty and motivation involves an extensive use of the very promising concept of *citizen science*, which results in an extreme valuation of the player as the driving force of the research. Researchers and developers frequently communicate on the blog of the game and do not miss an opportunity to associate the players, known as *The Eyewirers*, with the progress and the results obtained [KIM 14]. The other method of fostering loyalty and encouragement is to *cajole the player* and strengthen, through the granting of titles and diplomas with esoteric soundings, and his/her sense of belonging to the very closed brotherhood of the trailblazers of neural networks.

Design/feeling **–** The game interface is neat, clear and pleasant. The black background highlights the modeling of neurons in 3D which, with all their branching extensions, give rise to quite spectacular figures that can easily be rotated in all

directions. On the home page, a table summarizes the different modes of classification (daily, weekly, monthly, individual and by team). In the actual game interface, the view of the *cube* in 3D is manipulable and adjustable, and it is quite pleasant to gradually see the volume of the neuronal branch that the player is coloring over the two-dimensional (2D) cross-section appear in 3D.

1.7. Citizen sort

CITIZEN SORT[13] is a portal for *citizen science* designed by a group of researchers and students from the School of Information Sciences of the University of Syracuse, in the state of New York. The proposed games have been developed in collaboration with biologists and naturalists. The objective of this initiative is twofold:

– to generate the data relevant to biologists/naturalists (especially in entomology, botany and oceanography) through the games;

– to help researchers in information science and specialists in the field of human–machine interactions to understand how gaming, science and citizenship concepts interact, and to assess the role of gamification as an engine for motivation. The portal CITIZEN SORT allows studying how different types of games, addressing different types of players, can generate different qualities of data.

The portal CITIZEN SORT offers games to classify various species of plants, insects and animals. Two games are currently available: HAPPY MATCH[14] and FORGOTTEN ISLAND[15]; a third game, MARK WITH FRIENDS[16], is in development. The portal CITIZEN SORT claims through the general classification more than 3,000 players, but only 1,200 are active (with a positive score).

1.7.1. *Happy match*

Type of task **–** Microtask.

Goal – This consists of helping the classification of living beings by characterizing photographed specimens according to different criteria. In practice, a series of 5–10 pictures is proposed, and the player will have, for each picture, to give his/her opinion on several morphological criteria by assimilating the specimen to a form of reference, of which a characteristic example is presented below. For

---

13 http://www.citizensort.org/.
14 http://www.citizensort.org/web.php/happymatch.
15 http://www.citizensort.org/web.php/forgottenisland.
16 http://www.citizensort.org/web.php/markwithfriends.

example, if it is about butterflies, the goal will be to assimilate each picture to a general type depending on the shape of the wings at rest, then on the dominant color of the wings and then on the shape of the pattern of the wings, etc.

Thus, the morphological data collected by crowdsourcing contribute to formally identify the sample at the specific or even at the subspecific level. Since the pictures are dated and show information about the location (by geolocalization), the correlation of the taxonomic information with the date and the location can, for example, inform about the impact of certain forms of urbanization on an ecosystem, or highlight climate change, a change in biodiversity, the appearance of an invasive species, etc. Currently, it is possible to play with pictures of moths (HAPPY MOTHS), sharks (HAPPY SHARKS) or rays (HAPPY RAYS).

Benefits of crowdsourcing – Crowdsourcing is used here to achieve a very heavy task in terms of time and data volume to process. As often in the case of microtasks, it is the redundancy and the aggregation of the data provided by the players who, on the condition that they are sufficiently numerous, will provide quality data as good as the annotations of experts.

Required human skills – These are minimal and amount to a sense of observation, an interest in nature, patience, etc.

Player's education – By repeatedly playing, and by using the provided correction elements (see challenge/gamification), the eye can be exercised and one can learn to properly discriminate between some morphological elements. These elements are at the base of the determination keys, and the player can become unbeatable about the family, genus and species Latin names. It can reasonably be assumed that this kind of game delights people who already have expertise in taxonomy (e.g. amateur entomologists).

Interactivity – This is not developed in HAPPY MATCH. The player characterizes his/her images in his/her corner, without contact with what the other players do, without a discussion space such as instant messaging or a forum. On the other hand, users can read on the portal CITIZEN SORT a notification about an upcoming game, MARK WITH FRIENDS which seems, as its name indicates, to place interactivity at the center of the data acquisition strategy.

Challenge/gamification/interface – The interface is visually appealing and one can feel that it was designed with the help of designers. Compared to other games of image annotation (e.g. those of the ZOONIVERSE portal), it can be noted that there is a very pronounced effort to develop the entertaining and esthetic aspects. This starts from the interface which is organized to present the task to achieve in a harmonious and ergonomic way. Skillfully, the essential element of gamification is also the parameter

that makes it possible to assess the quality of the submissions and thus to validate the data provided by the player: in the series of the proposed images, one or two pictures of individuals already known and identified with certainty are *hidden*. If the player correctly classifies these two images on all the proposed morphological parameters, it could reasonably be estimated that the classification that he/she performs on the other images is reliable. At the end of the game, the result reveals if the two known images have been correctly classified on all the parameters; in this case, the player wins *bonus* points and the two species appear as specimens collected in his/her profile; otherwise, for each wrongly assigned morphological characteristic, the correct decision appears, with regard to the picture of the specimen. This allows him/her to know where and why he/she was wrong, and therefore adds an educational element to the ludic aspect.

Figure 1.9. *Citizen Sort: Happy match. The first screen of the game presents 10 pictures of butterflies. At this stage, the player must just validate the pictures, that is to eliminate those that are blurry, truncated or of too poor quality to be used. In the following screens, he/she will categorize butterflies following various morphological criteria (wing shape, dominant color, etc.)*

1.7.2. *Forgotten Island*

Type of task **–** Microtask.

FORGOTTEN ISLAND is the *adventure game* version of HAPPY MATCH. The requested task is the same (classify images of animals according to morphological

criteria), but in a context that mimics adventure games: one plays the role of an adventurer lost on an island where an explosion has ravaged a laboratory and scattered specimens of animals, which must be identified and reclassified. The character that the player embodies moves in a scenery and can glean objects needed for his/her mission, but can also teleport himself/herself from one strategic location of the island to another under the orders of a robot that tells him/her what to do and where to go.

1.8. The Nightjar project

Goal/background – The NIGHTJAR PROJECT[17] is a research program launched in August 2013 by the Sensory Ecology Group of the University of Exeter, in collaboration with the Behavioural Ecology Group at the University of Cambridge. The theme concerns the study of the strategies of camouflage in nature, relative to survival, and the model is that of the *nightjar*, a bird which breeds and lays eggs on the ground. Photographs of nightjars in their natural environment are modified according to the visual parameters of their natural predators (different from ours) to compare the appearance of eggs, chicks and the adults to their natural environment in order to quantify the effectiveness of the camouflage. The study focuses on various species of nightjars, all highly depending on appropriate camouflage strategies to escape their predators. Other birds are also studied (plovers and coursers), but nightjars constitute a model of predilection because eggs, adults and chicks demonstrate different strategies of camouflage. The team of researchers, in collaboration with a game designer, has developed three games to test the effectiveness of the strategies of camouflage of the eggs and of adult nightjars, depending on the type of visual perception of their various predators.

Benefits of crowdsourcing for the problem to be solved – The problem to be solved is the evaluation of the effectiveness of the camouflage strategy, which can be measured by the average time to locate a nest or a bird in a setting. The player will choose to embody a predator category and seek to locate the nest or the bird by watching photographs taken in natural sites. These photographs have been modified to correspond to the di-, tri- or tetrachromatic vision characteristics of each of the three types of natural predators of the nightjar. The data retrieved by crowdsourcing are, therefore, location times, which are closely correlated with the effectiveness of the camouflage.

Interactivity/player's education – The proposed type of game does not lend itself to interact with other players. However, a praiseworthy effort from the designers can be noted to explain the nature of their work: accurate and detailed scientific information

---

17 http://nightjar.exeter.ac.uk/.

on the project is easily accessible via the website of the project, while more technical data concerning the games are provided on the blog of the designer of the game[18].

Figure 1.10. *The Nightjar project. The introduction screen of the Nightjar game, one of the games of the project*

1.8.1. *Nightjar game/Nest game*

Type of task – Neither microtask, nor macrotask.

Goal – WHERE IS THAT NIGHTJAR? (NIGHTJAR GAME)[19] is the first game launched in August 2013, followed in November by WHERE IS THAT NEST? (NEST GAME)[20], which works on the same principle. The player must, in a limited time, locate either a bird or a nest in the picture that is presented to him/her after choosing

---

18 http://www.pawfal.org/dave/blog/.

19 http://nightjar.exeter.ac.uk/story/nightjargame.

20 http://nightjar.exeter.ac.uk/story/nestgame.

the type of predator (monkey = trichromatic vision or mongoose = dichromatic vision) and its type of vision. The timing that it takes to locate (or not) the nest or the bird is directly correlated with the effectiveness of the camouflage strategy.

Challenge/gamification – After accepting that the data of the game are employed in the context of scientific work, after indicating his/her age group and after choosing what predator the player was embodying (which conditions the colorimetrical parameters of the presented pictures), part of the game consists of looking for a bird or eggs in 20 successive pictures. The main ludic element is the task itself: it is fun to find a bird (or eggs) camouflaged in a natural scenery and not necessarily easy to locate it when the landscape is seen in shades of green, that is with the dichromatic vision of a mongoose. The limited time (30 s) spices up the task. If the player clicks on a location where there is nothing, a large red cross appears accompanied by a low-pitched sound. If nothing was found at the end of the allotted time, the solution appears in the form of a rectangle around the camouflaged element, and the failure is hailed with a humorous mention "You will be hungry, tonight!".

Figure 1.11. *Nightjar game. A nightjar (designated by the arrow) is hidden in this setting, and the player has 30 s to locate it and click on it*

1.8.2. *Egglab game*

*Type of task* **–** Neither microtask, nor macrotask.

Audience/popularity **–** The blog of the designer of the games[16] reported, in May 2014, that 9,000 players had played 20,000 games and tested 400,000 shell patterns representing more than 30 generations of artificial eggs. The average overall time of locating an egg has increased by approximately 0.4 s since the beginning of the experience, initiated in April 2014; the launch date was appropriately chosen in connection with Easter.

Principle and goal **–** EGGLAB is a piece of software designed to simulate the genetic variability that characterizes the visible patterns on the eggshells, which play a crucial role in camouflage and are, therefore, directly correlated with predation. The simulated eggs are images that are juxtaposed with pictures of different laying sites, and tested through the game EGGLAB GAME[21]: the player has 30 s to locate the egg in the scenery, and the less noticeable patterns are reinjected in the program to generate a new series of sets. This results in shells increasingly more resembling the ambient scenery, in a similar manner to what happens in nature with the process of natural selection.

Challenge/gamification **–** The game is built on the same principle as the previous two, with the difference that this time synthesis eggs (therefore drawings) must be identified in a natural setting. The natural setting is a picture of the habitat of one of the three species of the studied nightjars. The presentation and the scenery look more like a *cartoon*. The player is asked to enter his/her name by clicking successively on eggs carrying letters. At the end of the game, the average time flashes, and the player is warned that due to him/her, the eggs will become increasingly difficult to detect. He/she is invited to continue to play to see how the difficulty will evolve, which is a way to try to catch his/her loyalty. A clever way to attract a larger number of players is the recent possibility for the player to hide himself/herself the eggs in the setting (*Making an Easter egg hunt*) and to send his/her *Easter eggs hunt* to his/her friends. To this end, he/she is invited to choose a natural setting (picture), and then to slide or place virtual eggs with various shell patterns, selecting himself/herself the place of the scenery where the camouflage seems optimal. When it is finished, a click on *send* generates a url that can be copied and sent by e-mail.

---

21 http://nightjar.exeter.ac.uk/egglab/.
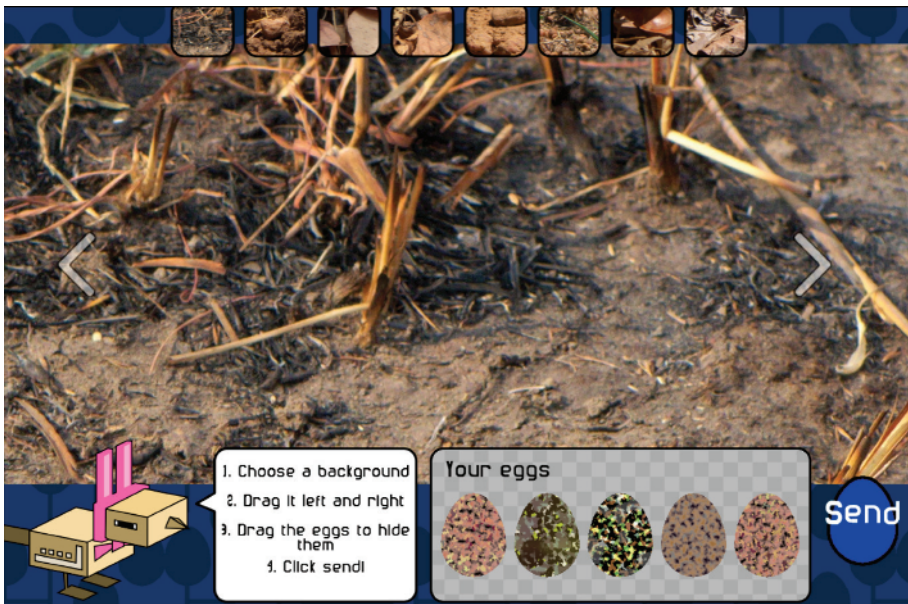
Figure 1.12. *The game Egglab.* Making an Ester egg hunt *is a variant of the* EGGLAB *game: the player chooses a setting, and then hides himself/herself the eggs by clicking and dropping them in areas of his/her choice. He/she can then send the url of the created game to his/her friends*

1.9. References

http://www.pri.org/stories/2014-05-12/your-video-games-may-revolutionize-health-and-scientific-research.

http://boinc.bakerlab.org/.

http://singularityhub.com/2011/09/22/in-3-weeks-video-gamers-defeat-biochemical-puzzle-that-scientists-couldnt-solve-for-years/.

http://www.pri.org/stories/2014-05-12/your-video-games-may-revolutionize-health-and-scientific-research.

http://biomedicalcomputationreview.org/content/biology-game-crowd.

http://www.pourquoidocteur.fr/Jouez-pour-aider-la-recherche-sur-les-maladies-genetiques----4090.html.