Systems Biology in STEM open education for teacher training

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Abstract

The fundamental purpose of this project was to design and to implement a creative and reasoned operational innovation in high school teachers training. Motivate teachers in their being masters of culture by creating modern seminars and innovative interactive and participatory STEM teaching laboratories, proposing the culture of teaching biosciences with a systemic approach that identifies in the integrated learning of different disciplines and in Systems Biology an opportunity to cultivate transversal skills that will be increasingly important for the future generations to study complex problems. A systemic perspective with multidisciplinary and transdisciplinary approaches to promote motivating work experiences of teachers today in the classroom during class hours investigating with the research method of research. Concepts, experimental descriptions, analyses, information and contents that are transformed into motivating elements of didactic itineraries that integrate proteomics, genomics, biophysics and biomedicine improving the critical thinking skills and creative skills of students. Approaches to study that lead to overcoming the separation of different disciplinary knowledge in favor of an interdisciplinary approach introduced into the world of science by the american biologist Leroy Hood who has well presented reflections also on the possible didactic implications in terms of methodological innovation of this method of investigation in scientific research. Research methods that require an interdisciplinary theoretical and practical approach to study, involving bioscience, chemistry, computer science, proteomics, genomics and postgenomics, analysis of interactions between complex macromolecules, cellular morphofunctional analysis, promoting the integration and interaction between different skills. The educational value in making high school students aware of this new method of analysis of living beings is significant, seeking and identifying biochemical and physiological connections at a cellular and molecular level. It is exciting and engaging in the scientific communities of the classroom to introduce in teacher training open science education for bioscience. Research that studies organisms as systems that change over time, biological systems that are the result of different dynamics, parts and structures organized at different degrees of complexity. Modern action research activities that promote educational passion in teachers into integrated training innovation for a new perspective in science education.

Keywords: *STEM Systems Teaching and Learning; Innovative Teacher training; Interdisciplinary science education; multidisciplinary didactics ; Biology Systems for science open education*

Introduction

The training system in international context should ensure that young students meet new charismatic figures, teachers capable of cultivating in them a passion for effective methodological innovations in respect of traditional culture, not simple practices [1]. Therefore, teachers would be convinced that the time spent with their students in the classroom, in laboratorial didactic experiences or in the laboratory is of real significance to promote soft skills and cognitive skills. For different groups of interviewed high school teachers think het is fundamental to participate at the plan of science education training offer not just as performers of pre-established organizational and standardized tasks, but as people with high passion and skills for communication and STEM didactic researches, who can be valued for their personal training and professional specificity. This question was proposed by the course teachers: *how to train teachers who with educational passion want to build an effective educational and training dialogue with their students in STEM open science education*? Teachers consider fundamental the need of a solid cultural preparation in the area of competence, which depends on the seriousness of the results achieved in the training path prior to accessing the teacher's job and which for consistency should not be underestimated. Methods of teachers training could be implemented with an international model which favor the importance of articulated lessons with multidisciplinary and interdisciplinary approaches to promote the motivation in lesson plans.Teachers that work as people primarily enthusiasts of their own disciplines, but oriented towards overcoming content hyper-specializations; characterized by the desire for continuous personal cultural updating, not standardized, to be built with criteria over time. Science teachers who should know how to explain during curricular lessons using differentiated sources of information in an integrated way, know how to ask questions, identify useful answers also supported in a reasoned way for some aspects by artificial intelligence. It is believed that teaching at different levels is a job in which every professional of his own disciplines, before being a teacher, should be a credible and coherent reference for young people able to guide them to critical reasoning, beyond simple STEM notions of single disciplines.

Methods

In order to actively involve teachers in a training course on systems biology aimed at making the teacher an actor in an integrated renewal process of sciences, the project began with theoretical and operational elements of bioinformatics into participatory STEM teaching laboratories. It was considered that not all teachers have the same educational background and that many enter science teaching in secondary schools even with little in-depth knowledge of molecular-cellular biology and genetics. Some participatory seminars for teachers were therefore organized regarding fundamental concepts of cellular and molecular biology useful for better understanding the theoretical and operational insights of Bioinformatics and key contents of Systems Biology.

Bioinformatics is characterized by multidisciplinary operational approaches and is used to analyze biological data in order to formulate hypotheses on the processes characterizing phenomena specific to living beings.

Bioinformatics helps to build a common language between biologists and computer scientists with a high procedural or multidisciplinary didactic, in fact it allows to connect disciplines such as *mathematics*, *computer science*, *molecular biology*, *biochemistry*, *biomedicine* and *genetics*. Cultural approaches that are increasingly widespread in scientific research and that unfortunately schools often ignore.

In classes the unidisciplinary approaches are mainly proposed, therefore separate learning of key concepts common to different disciplines, generally making it difficult for students to have a unitary vision of knowledge, knowledge of the scientific contexts of investigation. In Europe and around the world, the culture of STEM (Science, Technology, Engineering and Mathematics) teaching has been spreading for some years, which identifies the "integrated" learning of different disciplines as fundamental opportunities to cultivate in students skills that are interesting for personal culture, but also useful in the world of future professions where transversal skills, and not just unidisciplinary ones, will be increasingly important for studying complex problems. [2]

The main purpose of this training itinerary - project was therefore not to give «bioinformatics recipes» already present in different contexts, defined as «protocols» with rigid operational schemes, but to propose some reflections and suggestions to invite teachers to a «creative and reasoned operational innovation», not pure adoption or adherence to initiatives created and promoted for the school context.

A working method that has been implemented in curricular activities of fifth groups of science teachers in scientific high school and university with elements of theoretical Systems Biology (interactive seminaries also in e learning) and with innovative STEM operational Biology systems activities (research works).

Bioinformatics allows researchers two working methods: a «static» method to memorize and extract significant data; a «dynamic» method to evaluate the functional and temporal relationships of phenomena, the interactions between different parts of a system.It is therefore possible to convey the idea of biology as a science of discovery in which the system to be studied is identified and its characteristics are studied, beyond reductionist approaches [3].

Bioinformatics for STEM Education

Since 1960, and especially after the scientific acquisitions of the study of the genomes of organisms with different degrees of complexity, the scientific community has tried to systematically archive and analyze the biological data that have accumulated at high speed.

The bioinformatics activities integrated into the training course for teachers on biological molecules represent an excellent tool to introduce in the classes young people to the STEM profession of

biologist, computer scientist, medical researcher and in general to the world of scientific research; they do not require special equipment but only a computer room with computers connected to the network. An "educational mix" between basic biochemical and molecular biology knowledge with an opening to biomedicine.
In biological databases it is also possible to search for affinities between DNA sequences or affinities between protein sequences, therefore it is necessary to design paths also in relation to the specificity of the different class group and,
if necessary, proceed with differentiated activities, guiding them to work as in the teachers training in small groups, almost creating virtuous work communities oriented towards mutual help even for students with less computer skills.

Bioinformatics Banks

To fully understand the structure of a database and to be able to participate in operational activities, teachers and students must first have a good knowledge of biochemistry and molecular biology. As the number of available databases increases, it is important to be able to quickly integrate with critical approach different information from multiple sources thanks to specific computer software.
Numerous data are present in DNA banks: non-coding and coding sequences, partial/complete genomic sequences, cloning vectors, mitochondrial viral genomes, chondrial, polymorphisms, therefore DNA sequences with variants of a few bases that code for different proteins.
For rapid searches for sequence similarities in DNA and protein databases, for example, the *FASTA* program and the BLAST program (Basic Local Alignment Search Tool, 1990) are used, which use algorithms based on indexing all the positions in which each possible word appears within a sequence.

Working in the Classroom as "Protein Bioinformaticians"

The didactic innovation for the teachers involved in this project was to find a way to translate this technical and specialized knowledge into teaching activities for high school students and also for students of the first year of bioscience university courses. Bioinformatics allows the study of proteins that have an evolutionary relationship: by comparing amino acid sequences from different species, and their arrangement in space, it is also possible to precisely establish the evolutionary level of the organisms that contain these biological molecules.
The comparison between homologous sequences serves to identify the most important regions from a structural and functional point of view. Comparing the sequences of proteins allows to identify which amino acids are responsible for the common characteristics and for the differences. Amino Acid sequences undergo mutations, insertions, deletions and these variations are reflected in the encoded proteins. If a protein sequence is conserved during evolution and is present in many different organisms, it is very likely that in all organisms it performs the same function that depends on a particular sequence of amino acids.
The functional characteristics of biological macromolecules depend on the three-dimensional conformation that they assume in space. How are the fundamental units of macromolecules arranged in space? In particular, it is useful to reflect with teachers on the fact that protein molecules with a similar primary sequence tend to have similar secondary and tertiary structures; if two proteins are 50% identical, it is very likely that their three-dimensional structure is completely superimposable. Therefore the educational training course path began from the contents also about the four organization levels of proteins (primary, secondary, tertiary and quaternary structure) and from the question of whether it is possible to observe and analyze these structures. In fact, over the last thirty years researchers have managed to identify the three-dimensional structure of thousands of proteins, starting with the discovery of hemoglobin and myoglobin. The only database that collects this information is the *PDB* (Protein Data Bank). After having carried out some bioinformatics research activities in small groups, the teachers divided into groups of three used an artificial intelligence platform AI by making a specific request to develop two written tests with open questions for high school students: one test regarding elements of bioinformatics and a second relating to elements of systems biology.

The teachers were invited to analyze the tests proposed by AI and reflect on proposed changes or considerations regarding concepts to be discussed and explored with the students regarding these complex topics with particular reference to the scientific language used.

Bioinformatics Written Test for High School students- AI
Instructions: Answer all open-ended questions clearly and in detail. Each answer should demonstrate your understanding of bioinformatics concepts.
Questions:
1. Define bioinformatics.
Explain its main purpose and how it integrates biology, computer science, and statistics.
2. Describe the process of sequence alignment.
What is the importance of sequence alignment in the field of bioinformatics? Give a practical example of its use.
3. What are biological databases?
List three examples of databases used in bioinformatics and describe the type of information each contains.
4. Explain the concept of comparative genomics.
What are the benefits of studying the genomes of different species and how does this contribute to our understanding of evolution?
5. Discuss the importance of omics data analysis.
What is 'omics' in bioinformatics? Refer to genomics, transcriptomics, and proteomics in your reasoning.
6.What are machine learning algorithms and how are they used in bioinformatics?
Give an example of an application of machine learning in this field.
7. Analyze the role of bioinformatics in personalized medicine.
How does bioinformatics help develop personalized therapies for patients?

Systems Biology Written Test for high school students - AI
Directions: Answer each question clearly and concisely. Each answer should demonstrate your understanding of systems biology concepts.
Questions:
1. Define systems biology.
Explain how this approach differs from traditional biology.
2. Describe the concept of a biological network.
What are some examples of biological networks and what role do they play in organisms?
3. What are computational models in systems biology?
Explain how they are used to represent complex biological processes.
4. Discuss the importance of interactions between genes, proteins, and metabolites.
How do these interactions influence the behavior of cells?
5. What is meant by negative and positive feedback in a biological system?
Give an example of each and explain their role in biological regulation.
6. Discuss the concept of homeostasis.
How do biological systems maintain internal equilibrium despite environmental changes?
7. Explain how 'omics' technologies (genomics, proteomics, metabolomics) contribute to systems biology.
Refer to how these technologies provide data for systems modeling.
8. Discuss the role of systems biology in understanding disease.
How can this approach help in the search for cures for complex diseases?
9. What are metabolic pathways?
Describe an example of a metabolic pathway and its significance to the cell.
10. Discuss the importance of systems biology in biological engineering.
How does this field apply to the design of genetically modified organisms or biomanufacturing?

Results

In the computer science classroom the teachers working in pairs, connected to the PDB homepage gradually explored the tabs called up in the menu on the left: *Welcome*, *Deposit*, *Search*, Visualize, *Download*, Learn. In particular, by clicking on Search, teachers discover which are the main categories that can be used for a targeted search and how many structures referable to human macromolecules are deposited to date. After a brief introduction, the tutor of the project asked the teachers to search for a series of information for the proteins indicated below: how many amino acids is the protein composed of, when the structure was deposited and by whom, with which method it was obtained. It is also possible and interesting to view the amino acid sequence and download the pdb file (text) from the download menu. Each pair had to choose three structures to search and download

among the following: *hemoglobin* (PDB ID 2N2), collagen (PDB ID 1CAG), Na-K pump (PDB ID 3KDB), insulin (PDB ID 4INS), adrenaline receptor (PSB ID 2RH1), immunoglobulin (PDB ID 1IGT).
The visualization and analysis of the structures was carried out with the protein software RasMol downloadable at the link *http://rasmol.org/* or with Deep View - *Swiss-Pdb* Viewer downloadable at the link *http://spdbv.vital-it.ch/.*
Thanks to these softwares, the teachers observed the conformation of the chosen proteins describing their secondary, tertiary and quaternary structure. At the end of the work, the teachers presented the results obtained to the whole group and, subsequently, prepared a written paper about the perspectives of application in respective classes of the work discussing the projected didactic itinerary and the interconnection between different STEM disciplines.

The Evolution of Hemoglobin and its Genes in Class

To consolidate awareness of the link between sequence, structure and function, was carried out an in-depth study on hemoglobin starting from reading some sections of Marta Paterlini's book "*Little Visions*: *The Great Story of a Molecule"*, a very rigorous publication that presents the historical-experimental development that led to the discovery of hemoglobin with an interdisciplinary cultural approach. In particular, the book presents the story of Max Perutz and all the scientists (physicists, mathematicians, biologists, chemists) who collaborated in the discovery of the structure of hemoglobin and helps to understand a multidisciplinary approach to science with elements of learning itinerary "from molecules to organisms" with particular study of the protein myoglobin and protein hemoglobin: from the analysis of structural anomalies to the modifications of important functions in complex organisms and related references to some related pathologies. Reasoned analysis of parts of the text in this book can also involve teachers of different disciplines, a constructive collaboration for STEM education in schools, aspects discussed with the teachers of the training group with high participatory enthusiasm.
In front of the computer, the small group of selected teachers proceeds with the research on the NCBI (*National Center of Biotechnology Information)* website of the human genes for hemoglobin (HBB and HBA1, HBA2), myoglobin (MB) and other proteins of the same family.

Comparison between the Y Chromosome of the Mouse and the Chromosomes of the Human

Another activity explained and realized with teachers was about comparison between Chromosome Y of the mouse and chromosome Y of the human answering also the question "why all the mice used in the scientific experiments are female". The female mice used as guinea pigs in the laboratory allow us to verify the effects of gene silencing, understand the functions of hormones and are models for the study of metabolic diseases.
In the last part of this experience, the tutor guided the teachers to study the synteny between the chromosome 2A and 2B of the chimpanzee and the chromosome 2 of the human. Chimpanzees have one more chromosome than humans, but during evolution, the fusion between chimpanzee chromosomes 2A and 2B generated human chromosome 2. In particular, chimpanzee chromosome 2A constitutes the upper part of human chromosome 2, while chromosome 2B presents the same genes as the lower part of the human chromosome.
At the end of the course a computer archive of all the activities was shared with the attending teachers: the different comparative tables developed, the reports of the working groups, the operational reflections on the integrated scientific reading, the key points of the discussions about the transferability of the activities carried out in the classes, also involving teachers of other disciplines.

Discussion

Bioinformatics provides researchers with predictive working methods on the biological functioning of living things and prescriptive methods that can impose a certain behavior on the biological system, opening up a new integrated approach to investigation called "Systems Biology", a dynamic model in the study of the behavior of biological systems that evaluates the biochemical, physiological, and genetic interactions between the different parts of the system. An
an approach of this type allows us to overcome a fragmented study of the different parts in favor of an interdisciplinary approach with interconnections between different disciplines. Witness to this cultural

approach is the American biologist Leroy Hood who, in an interview reported by the magazine Science in School - EMBL Heidelberg also presents reflections on the possible educational implications of this method in terms of methodological innovation.
The educational value in making high school students aware of this new method of analysis of living beings is significant for teachers, seeking and identifying biochemical and physiological connections at a cellular and molecular level. It is exciting and engaging in the scientific communities of the classroom to introduce in teacher training some
elements of open science education for bioscience. Research that studies organisms as systems that change over time, biological systems that are the result of different dynamics, parts and structures organized at different degrees of complexity. Modern action research activities that promote educational passion in teachers into integrated training innovation for a new perspective in science education.
International studies believe that the good STEM teacher is the result of reasoned reworkings of cultural, professional
and didactic experiences skillfully conceived and coordinated over time, combined with passion and educational sensitivity, all important elements also to promote in the training of teachers the creativity at different levels, analyzing the better work conditions to realize modern STEM teaching activities with methods of research [4].
At the end of the seminars and the research activities carried out by the teachers with short reports also about the possible applications of these researches in didactic itineraries during curricular lessons, an open-ended questionnaire was carried out in which the participants reported their satisfaction expressed in a scale for different indicators on the quality and training effectiveness of this course. The 88 percent of the course evaluation sheets analyzed indicated the course as having a high training level and excellent training value, evaluations also integrated with different reflections on the possible use of these activities in their classes, hoping for future opportunities for similar training also for other colleagues.

Conclusion

In all these proposed activities the teachers participated interactive seminaries and in different practical research activities proposing some operational ideas for curricular teaching to create multidisciplinary STEM didactic itineraries and to introduce students of their classes to the consultation of computer databases relating to proteins or DNA sequences, genomes belonging to different organisms, tools for obtaining essential information that leads to the comparison between species with different degrees of evolutionary complexity with elements of different disciplines. The operational aspects of bioinformatics lead to obtaining useful information for the understanding of biological phenomena and for the development of new biomedical and biotechnological strategies.
Today, in scientific laboratories, researchers can communicate new data in real time by comparing their results with the work already carried out by the scientific community [5]. These dynamic aspects of bioinformatics flow back, even in high school and university classes, through learning paths that also result in orientation towards new professionists in the world of work. For all of this, collaborative teachers are needed who do not follow predefined schemes, rigid procedures, who adopt models or copy protocols, very forced modernisms perhaps conceived in contexts very foreign to the world of school [6]. At different levels teachers are creators of strategies and ways of working, oriented to overcome operational individualisms to involve and create paths of deep cultural and educational significance, reinterpreting the way of proposing knowledge in a transmissive way. Innovative, attractive teaching not through forced modernity, to keep up with the times in extracurricular projects, but above all to win the interest of students during curricular lessons, to remove operational liabilities, to give everyone the opportunity to understand the beauty of knowledge, of reasoning with awareness on facts and events, of producing new knowledge for oneself and for others.

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