Machluf, Y., Dahan, O., Shpalter-Avidan, C., Mitchel, A., & Yarden, A. (2011).
Bioinformatics in the service of biotechnology (A web-based learning environment
http://stwww.weizmann.ac.il/g-bio/bioinfo, The Amos de-Shalit Israeli Center for
Science Teaching, grades 11-12).

Short summary of the main features

We recently developed a web-based learning environment that is aimed at introducing bioinformatics into a high-school biotechnology curriculum. Bioinformatics is an elective topic in the curriculum of biotechnology majors (45 hours, 12th grade). In the bioinformatics learning environment both pedagogy and technology were recruited for educational purposes aiming at keeping the biotechnology curricula current and engaging students with scientifically authentic inquiry activities that brings the fruits of bioinformatics to bear on human health.

The learning environment contains various units that are aimed to support students' learning and teachers' instruction, in light of the unique characteristics of bioinformatics education.

At the core of the learning environment lays first-hand active learning processes in which high-school students are invited to take part in five authentic inquiry activities in biotechnology using eight different bioinformatics tools and databases (Figure 1). The activities were developed based on research articles selected according to several features: relevance of the scientific context to students' interests; a clear biotechnological application; use of a variety of bioinformatics tools and databases that are suitable for high-school students’ cognitive level; representation of diverse organisms and different molecules (DNA, RNA, proteins); leading-edge, high-impact subjects that are broadly covered in the popular scientific literature and in the public media; and clear connections to principles and techniques in the biotechnology syllabus.

The topics of the activities focus around authentic investigations that are aimed at improving human life quality and expectancy:

1. Identifying alleles of hemoglobin conferring resistance to malaria;
2. Screening for novel genes involved in antibiotics biosynthesis;
3. Exploring the genotype-phenotype relations in Cystic Fibrosis;
4. Searching for a competitive inhibitor to the Anthrax toxin;
5. Characterizing the Green Fluorescent Protein (GFP).

In each multistep activity, the students are introduced to the rationale and main goals of the research at hand, and learn how to utilize the bioinformatics tools and databases, resembling the original research plan. In three 'in-depth activities' (1-3 above) the students first get familiarized with the bioinformatics tools and databases, therefore emphasis is placed on prompting understanding through hand in hand guidance along each step of the inquiry process, mainly focusing on procedures and concepts. The remaining two 'integrated activities' (4-5 above) are based on this previous experience, hence highlighting the research strategy, considerations of selecting bioinformatics tools and their contribution to basic and applied scientific research. Students enact most tools once in 'in-depth activity' and once in 'integrated activity' (Table 1). Clearly, 'in-depth activities' should be enacted before the 'integrated activities', yet in each category of activities, teachers are free to decide on the instruction sequence.

The selected bioinformatics tools (Entrez, Blast-N, Blast-P, ClustalW, ORF Finder, Primer3Plus, Prosite and Jmol) and databases are basic yet fundamental and commonly used by scientists and allow the acquisition of central bioinformatics principles and approaches. The tools are introduced to the learners in a virtual "Bioinformatics Tool-Box" that includes detailed interactive tutorials and written texts.

Each activity begins with a detailed background to the scientific investigation, including images and external links and animations, presenting the rationale, goal, design and 2-4 key steps/tasks of the investigation. In order to execute a task, a problem-solving endeavor, utilization of one bioinformatics tool is required. Throughout the inquiry process, which is embedded with a large number of questions and assignments, the students experience different scientific practices, they are required to coordinate between different types of knowledge from different scientific disciplines, to apply procedural skills of using bioinformatics tools, to reason scientifically and make decisions following the strategic plan. Some questions guide them to analyze the tool-derived textual and graphical data, whereas others ask to conclude about the biological meaning of the bioinformatics findings, or to explain which bioinformatics tool they would select considering the data and strategic plan. Students' answers to the questions embedded in the learning environment are stored on-line in a database. Scaffolding is provided by reflections on students' answers and reference to a scientific dictionary. A summary of each investigation, including the use and contribution of each bioinformatics tool to each task, appears at the end of each activity.

Presented below are the features of two representative activities:

Identifying alleles of hemoglobin conferring resistance to malaria ('in-depth activity'): Researchers wished to evaluate the possible role of genetic alterations in the gene for an oxygen-transport molecule called hemoglobin in the resistance or susceptibility to severe malaria, which in Africa kills 3000 children each day. Students utilize the Entrez search system to find the sequence of normal gene for hemoglobin in the databases, and to analyze it. Then, they use the sequence alignment tool ClustalW to compare hemoglobin sequences from malaria resistant and susceptible people, resulting in the identification of a mutation. Finally, by applying evolutionary approach students determine the more ancient hemoglobin sequence.

Searching for a competitive inhibitor to the Anthrax toxin ('integrated activity'): Virulence of the Anthrax toxin depends on the ability of two factors (termed EF and LF) to bind a third protein (termed PA). To map the critical site for PA binding, scientists compared between EF and LF. Likewise, students employ Entrez to search for EF and LF proteins sequence, identify the homologous sequence between EF and LF by ClustalW, and analyze their structures by the free 3D molecule viewer, Jmol. In addition, students used the alignment search tool (BLAST) to compare the query PA gene sequence to the databases, enabling the identification of homologous anthrax toxins in a reduced violence closely related strain.

An introductory unit lays the groundwork for learning comprising the subject matter knowledge in biology, biotechnology and bioinformatics. It covers basic concepts and core ideas in biology such as the path from gene to function. The bioinformatics field is presented from historical and research perspectives, highlighting its integration in and contribution to modern basic and applied biological research.

An assessment unit includes short exercises as well as matriculation exam-like questions to provide students deeper understanding of the bioinformatics approach and to improve their skills of bioinformatics practices.

A teachers' guide is inherent to the learning environments. Suggestions for instruction, enactment and evaluation are provided in each activity, as well as answers to the questions, a close forum for teachers, presentations and learning materials. A teacher interface for analysis of students' performance (answers to questions) is also integrated in the learning environment.

Altogether, the bioinformatics learning environment is designed to provide students with opportunities to engage in authentic inquiry activities similar to those carried out by scientists.

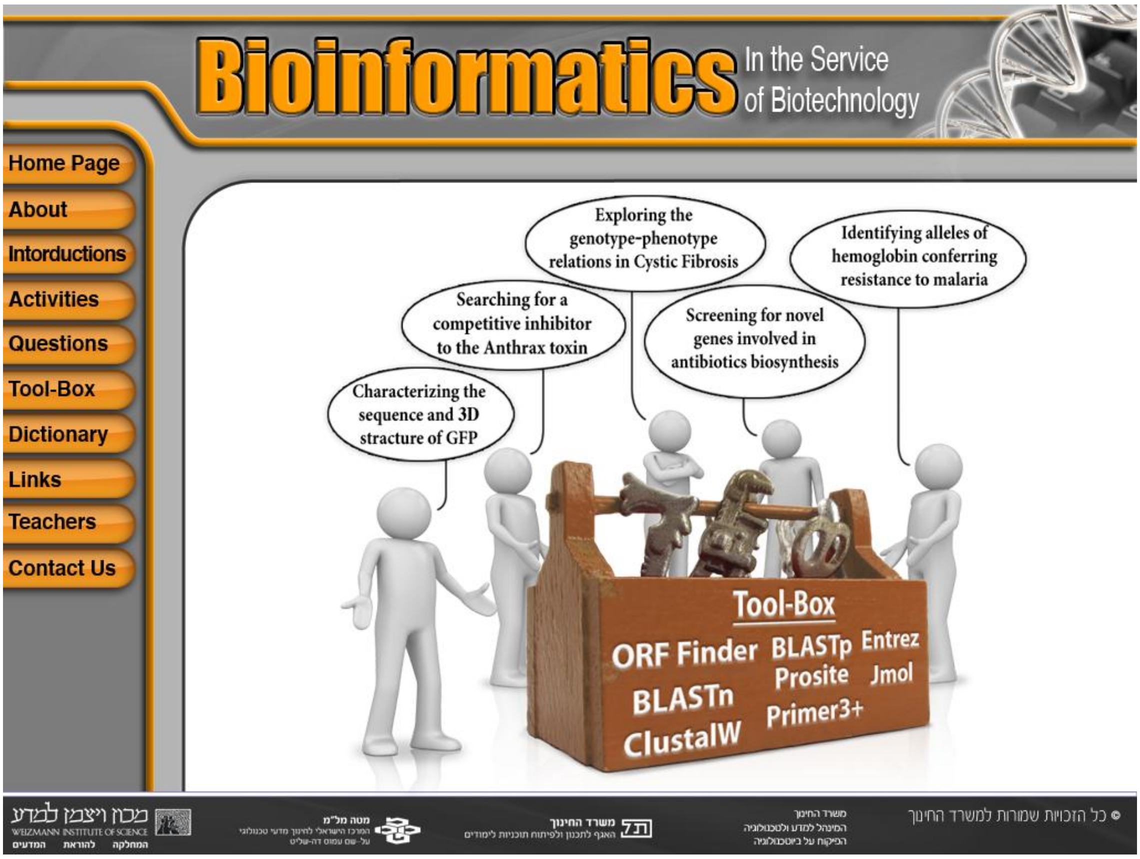

Figure 1: The home page of the learning environment. The various units are presented, as well as the scientifically authentic inquiry activities and the bioinformatics tools.

Table 1: Details of the bioinformatics tools in each activity

Bioinformatics tool	'In-depth activities'			'Integrated activities'	
	Identifying alleles of hemoglobin conferring resistance to malaria	Screening for novel genes involved in antibiotics biosynthesis	Exploring the genotype-phenotype relations in Cystic Fibrosis	Characterizing the sequence and 3D structure of Green Fluorescent Protein	Searching for a competitive inhibitor to the Anthrax toxin
Entrez	☑			☑	
Blast-N		☑		☑	
Blast-P		☑			
ClustalW	☑			☑	☑
Primer3+			☑		☑
ORF Finder		☑			☑
Prosite			☑		
Jmol		☑		☑	☑