

NAME OF THE COURSE		Molecular Evolution				
Code	PMB706	Year of study	2			
Course teacher	Branka Bruvo Mađarić, PhD, Research Associate	Credits (ECTS)	3			
Associate teachers	Prof. Đurđica Ugarković, PhD, Scientific Advisor; Martina Podnar Lešić, PhD, Research Associate; Željka Pezer, PhD, Research Associate	Type of instruction (number of hours)	L	S	E	F
			15	15	15	
Status of the course	Elective	Percentage of application of e-learning				
COURSE DESCRIPTION						
Course objectives	<p>Molecular evolution involves processes of change in the composition of cellular molecules such as DNA, RNA, and proteins through generations, leading to the evolution of organisms. The field of molecular evolution uses the principles of evolutionary biology and population genetics to explain, from an evolutionary perspective, the patterns of molecular changes in the genome.</p> <p>The aim of this course is to introduce students to recent insights into the molecular evolution of the genome, with a focus on eukaryotic organisms. Students will gain basic knowledge of the theory of evolution (common descent, natural selection, genetic drift, models of growth and selection), about the content and organization of eukaryotic genomes and about the molecular mechanisms that lead to evolutionary changes in organisms. The lectures will also provide introduction to theory and algorithms in the field of computational molecular evolution. Practical computer work will introduce students to the application of molecular phylogeny and phylogeography methods as well as exploring and interpreting high-throughput sequencing data. Through the preparation and presentation of seminars, students gain additional insight into various relevant topics and techniques in the field of molecular evolution. Overall, the course will cover main concepts in evolutionary and population genomics in order to provide understanding of how and why genomes change in time, enabling the students to make evolutionary interpretations and functional predictions.</p>					
Course enrolment requirements and entry competences required for the course	<p>Students should be comfortable with key concepts in evolutionary biology and genetics. Students are expected to do a self-assessment of their knowledge in these disciplines and complement potential caveats through the background reading on specific topics.</p>					
Learning outcomes expected at the level of the course (4 to 10 learning outcomes)	<p>Upon completion of the course the student will be able to:</p> <ul style="list-style-type: none"> <li>• Explain and discuss the basic evolutionary theory;</li> <li>• Describe the organization of eukaryotic genome and the evolutionary mechanisms involved in evolution and shaping of the eukaryotic genome;</li> <li>• Browse and extract DNA and protein sequence data from public databases (NCBI, BOLD, EBI), and create multiple sequence alignments using appropriate alignment software (Clustal W, MAFFT, MUSCLE, T-Coffee, etc.);</li> </ul>					

	<ul style="list-style-type: none"> <li>• Understand and explain the principles of major phylogenetic methods (distance matrix-based, parsimony-based, maximum likelihood, and Bayesian methods) and choose relevant method for the given phylogenetic/phylogeographic problem;</li> <li>• Select and apply commonly used software packages (MEGA, PhyML, RAxML, MrBayes, BEAST, TCS, Network, etc.) to infer and interpret phylogenetic trees and networks, estimate divergence times, and test phylogenetic hypotheses;</li> <li>• Define types of genetic variation and perform variant discovery from high-throughput sequencing data;</li> <li>• Interpret and analyze population structure, quantify genetic diversity and identify differentiated loci;</li> <li>• Explore public catalogues of variation and genotype data (1000 Genomes project, dbVAR).</li> </ul>
<p>Course content broken down in detail by weekly class schedule (syllabus)</p>	<p><b>Lectures (15 hours)</b></p> <ol style="list-style-type: none"> <li>1. Basic evolutionary theory and processes which shape the eukaryotic genome (2 h);</li> <li>2. Genetic diversity as a core concept in evolutionary biology - types of genetic variation, their abundance and genomic distribution, mutation rate, effects on phenotype and genomic methods of detection (2 h);</li> <li>3. Types of genomic sequences and their organisation in the eukaryotic genome (1 h);</li> <li>4. Evolution of coding DNA (protein-coding and regulatory regions) (1 h);</li> <li>5. Evolution of non-coding DNA (repetitive sequences, introns, transposons, pseudogenes etc.) (1 h);</li> <li>6. Biological species concepts, macroevolution, microevolution (1 h);</li> <li>7. Cross-species genomics - the principles of comparative genomics and examples from vertebrate genome evolution (2 h);</li> <li>8. Population genomics - aims and approaches (adaptation; speciation; neutral vs. non-neutral evolutionary processes etc.) (2 h);</li> <li>9. Molecular phylogeny and phylogeography - theory and principles (2 h);</li> <li>10. Methods of data analyses in molecular phylogeny and phylogeography (2 h);</li> <li>11. Models of sequence evolution and hypothesis testing (2 h);</li> <li>12. Molecular clock and divergence time estimation (2 h);</li> </ol> <p><b>Computer exercises (15 hours)</b></p> <ol style="list-style-type: none"> <li>1. Sequence databases - NCBI GenBank, EBI, BOLD - searching, retrieving and storing nucleotide data; BLAST algorithm (1 h);</li> <li>2. Formatting and alignment of nucleotide sequences - application and comparison of various algorithms (Clustal W, MAFFT, MUSCLE, T-Coffee etc.) (2 h);</li> <li>3. Nucleotide substitution models of evolution (MEGA, jModeltest) (1 hour);</li> <li>4. Phylogenetic tree construction methods - distance, parsimony, likelihood, Bayesian (MEGA, PhyML, RAxML, MrBayes, BEAST etc.) (4 h);</li> <li>5. Phylogenetic networks construction methods (TCS, Network) (2 h);</li> <li>6. Exploring public catalogue of variation and genotype data (1000 Genomes projects, dbVAR) (1 h);</li> </ol>

	<p>7. Using multi-locus genotype data to investigate population structure, identification of differentiated loci from SNVs and CNVs based on Fst and Vst calculation (2 h);</p> <p>8. Discovery and interpretation of variants from high-throughput sequencing data (Genome Analysis Toolkit, CNVnator) (2 h);</p> <p><b>Seminars (15 hours)</b></p> <p>Seminar topics will be offered to students to prepare a presentation based on recent scientific literature (the list of suggested papers covering each topic will be provided):</p> <ol style="list-style-type: none"> <li>1. Evolution of the genome and chromosomes;</li> <li>2. Evolution of eukaryotic organisms (eukaryogenesis);</li> <li>3. "Junk DNA" and mobile elements in eukaryotic genome: transpozones, highly repetitive DNA, SINE, LINE, microsatellites, pseudogenes, NUMTs, etc.;</li> <li>4. Horizontal gene transfer;</li> <li>5. Gene birth and death;</li> <li>6. Evolution of tumor genome;</li> <li>7. Viral genome evolution;</li> <li>8. Phylogenomics;</li> <li>9. NGS, WGS;</li> <li>10. "Orphan genes";</li> <li>11. Phylostratigraphy;</li> <li>12. Molecular clock;</li> <li>13. Metagenomics;</li> <li>14. DNA barcoding and metabarcoding;</li> <li>15. Genetic adaptation;</li> <li>16. Selective sweeps;</li> <li>17. Adaptive copy number variants;</li> <li>18. Speciation;</li> <li>19. Ecological divergence.</li> </ol>					
Format of instruction	<input checked="" type="checkbox"/> lectures <input checked="" type="checkbox"/> seminars and workshops <input checked="" type="checkbox"/> exercises <input type="checkbox"/> <i>on line</i> in entirety <input type="checkbox"/> partial e-learning <input type="checkbox"/> field work		<input type="checkbox"/> independent assignments <input type="checkbox"/> multimedia <input type="checkbox"/> laboratory <input type="checkbox"/> work with mentor <input type="checkbox"/> (other)			
Student responsibilities	Attending class lectures and practical exercises; preparation and presentation of seminar essay; oral exam.					
Screening student work ( <i>name the proportion of ECTS credits for each activity so that the total number of ECTS credits is</i>	Class attendance	1	Research		Practical training	1
	Experimental work		Report		(Other)	
	Essay		Seminar essay	1	(Other)	
	Tests		Oral exam	1	(Other)	

<i>equal to the ECTS value of the course)</i>	Written exam		Project		(Other)	
Grading and evaluating student work in class and at the final exam	<p>During the semester, the attendance to class lectures and exercises will be recorded for each student. Active participation and independent task solving will be additionally noted.</p> <p>The preparation and presentation of the seminar essay on the selected topic and the discussion at the oral exam will be evaluated.</p> <p>The final grade for the subject is the mean of the grade of seminar work and oral examination (50%) as well as of total commitment and active participation in classes, exercises and discussion throughout the entire course (50%).</p>					
Required literature (available in the library and via other media)	<b>Title</b>			<b>Number of copies in the library</b>	<b>Availability via other media</b>	
	M. Nei, S. Kumar (2000) Molecular evolution and phylogenetics. Oxford University Press, USA; 1st edition					
	W-H. Li (2006) Molecular Evolution, Sinauer Associates.					
	B.G. Hall (2011) Phylogenetic trees made easy: A how-to manual. Sinauer Associates, Inc.; 4th edition					
	J.C. Avise (2000) Phylogeography: The History and Formation of Species. Harvard University Press; 1st edition					
	Alföldi J, Lindblad-Toh K. 2013. Comparative genomics as a tool to understand evolution and disease. Genome Res 23: 1063–1068. doi:10.1101/gr.157503.113					
Optional literature (at the time of submission of study programme proposal)	<ul style="list-style-type: none"> <li>• J. Felsenstein (2003) Inferring phylogenies. Sinauer Associates; 2nd edition;</li> <li>• J.C. Avise (2004) Molecular markers, natural history, and evolution. Sinauer Associates; 2nd edition;</li> <li>• J.C. Avise (2006) Evolutionary pathways in nature: A phylogenetic approach. Cambridge University Press; 1st edition;</li> <li>• Z. Yang (2006) Computational Molecular Evolution. Oxford University Press; 1st edition</li> <li>• D.H. Huson, R. Rupp, C. Scornavacca (2010) Phylogenetic Networks. Cambridge University Press; 1st edition;</li> <li>• Quintana-Murci L. Understanding rare and common diseases in the context of human evolution. Genome Biol. 2016;17: 225. pmid:27821149</li> </ul>					
Quality assurance methods that ensure the acquisition of exit competences	Upon completion of the course, an anonymous student survey will be conducted, the results of which will be used for the purpose of evaluating the subject and the teachers, and monitoring of the learning outcomes.					

Other (as the proposer wishes to add)	
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