UČNI NAČRT PREDMETA / COURSE SYLLABUS	
Predmet:	Načrtovanje učinkovin na osnovi molekulskega in QSAR modeliranja
Course title:	Drug Design Based on Molecular and QSAR Modelling

Študijski program in stopnja Study programme and level	Študijska smer Study field	Letnik Academic year	Semester Semester
Nanoznanosti in nanotehnologije, 3. stopnja	/	1	1
Nanosciences and Nanotechnologies, 3rd cycle	/	1	1

Vrsta predmeta / Course type Izbirni / Elective

Univerzitetna koda predmeta / University course code: NANO3-814

Predavanja Lectures	Seminar Seminar	Sem. vaje Tutorial	Lab. vaje Laboratory work	Druge oblike	Samost. delo Individ. work	ECTS
15	**15**			**15**	**105**	**5**

**Navedena porazdelitev ur velja, če je vpisanih vsaj 15 študentov. Drugače se obseg izvedbe kontaktnih ur sorazmerno zmanjša in prenese v samostojno delo. / This distribution of hours is valid if at least 15 students are enrolled. Otherwise the contact hours are linearly reduced and transfered to individual work.*

Nosilec predmeta / Lecturer: Prof. dr. Marjana Novič

Jeziki / Languages:		
	Predavanja / Lectures:	slovenščina, angleščina / Slovenian, English
	Vaje / Tutorial:	

Pogoji za vključitev v delo oz. za opravljanje študijskih obveznosti:	**Prerequisites:**
Zaključena druga stopnja bolonjskega študija ali diploma univerzitetnega študijskega programa. Potrebna so tudi osnovna znanja matematike in kemije.	Completed Bologna second level study program or an equivalent pre-Bologna university study program. Basic knowledge of mathematics and chemistry.

Vsebina:	**Content (Syllabus outline):**
- Predstavitev podatkovnih bank, ki so dostopne preko interneta in eventualno urejanje lastne banke podatkov za različne biološke lastnosti (doze in razredi toksičnosti, teratogenost, karcinogenost, vezavne konstante z določenimi encimi, itd.). - Kodiranje kemijskih struktur (notacija SMILES, MDL, SDF, MOL). - Izračun deskriptorjev (topološki, empirični, kvantno-kemijski, itd.) in uporaba ustreznih računalniških programov (DRAGON, CODESSA, itd.). - Uporaba različnih programskih paketov za gradnjo in validacijo QSPR modelov (linearna	- Presentation of data banks, which are accessible via the Internet, and possibly compilation of students' own data banks for the different biological properties (dose and grades of toxicity, teratogenicity, carcinogenicity, binding constants of certain enzymes, etc.). - Encoding of chemical structures (SMILES notation, MDL, SDF, MOL). - Calculation of descriptors (topological, empirical, quantum-chemical, etc.) and use of relevant computer programs (DRAGON, CODESSA, etc.). - Use various software packages for the construction and validation of QSPR models

regresija, metoda glavnih osi, nevronske mreže, itd.). - Izdelava modelov (linearni, nelinearni) V okviru tega poglavja bodo študenti spoznali osnove večkratne linearne regresije (MLR) kot primer linearne regresije, med nelinearnimi tehnikami pa bomo predstavili različne umetne nevronske mreže. - Transformacije merskega prostora Predstavili bomo nekatere pogoste transformacije merskega prostora (npr. PCA,...), ki jih uporabljamo za boljšo predstavitev več dimenzionalnega merskega prostora. - Grupiranje Predstavili bomo enostavne postopke grupiranja podatkov v večdimenzionalnem merskem prostoru kot tudi uporabo umetnih nevronskih mrež v te namene. - Vrednotenje modelov Spoznali bomo osnovne postopke za delitev podatkov v več setov, potrebnih za učenje in testiranje modela. Prav tako bomo obravnavali metode, ki jih uporabljamo pri testiranju različnih modelov. - Matematične reprezentacije kemijskih struktur Obdelali bomo nekaj enostavnih predstavitev kemijskih struktur z namenom uporabe v QSAR in QSPR modeliranju. - Praktična uporaba pridobljenih znanj – na primeru načrtovanja inhibitorjev izbranega encima.	(linear regression, principal component analysis, neural nets, etc.). - Modeling (linear and nonlinear) In this chapter, students will learn the basics of multiple linear regression (MLR) as an example of the linear regression. As example of the non-linear techniques various artificial neural networks will be presented. - Transformation of the measurement space Some common measurement space transformation will be presented (e.g. PCA, etc.), which are used to enable the graphical presentation of the multi-dimensional metric space. - Clustering We will present a simple procedure for clustering of data in a multidimensional space of measurements, as well as the use of artificial neural networks for the same purpose. - Model validation We will learn the basic procedures for dividing data in different sets needed for model validation (learning and testing set). We will also discuss the methods used in various model validations. - Mathematical representation of chemical structures. Some simple representations of chemical structures that can be used in modeling the relationship between chemical structure and properties of molecules (QSAR, QSPR) will be discussed. - Practical application of the knowledge obtained – a case study of design of inhibitors of a selected enzyme.

Temeljna literatura in viri / Readings:

Izbrana poglavja iz naslednjih knjig: / Selected chapters from the following books:

1. D.L Massart et al., Handbook of Chemometrics and Qualimetrics, Elsevier, Amsterdam, 1997. Part B, pp. 383-417

2. J. Zupan, J. Gasteiger, Neural Networks in Chemistry and Drug Design: An Introduction, VCH, Weinheim, 1999. pp. 125-358

Additional literature (Selected chapters)

3. L. Hansch, A. Leo, Exploring QSAR Fundamentals and Applications in Chemistry and Biology, American Chemical Society, Washington, DC 1995.

4. MINOVSKI, Nikola, NOVIČ, Marjana. Integrated in silico methods for the design and optimization of novel drug candidates : a case study on fluoroquinolones - Mycobacterium tuberculosis DNA gyrase inhibitors. V: ROY, Kunal (ur.). Quantitative structure-activity relationships in drug design, predictive toxicology, and risk assessment, (Advances in chemical and materials engineering book series (Print), ISSN 2327-5448). Harsley: Medical Information Science Reference (an imprint of IGI Global), cop. 2015, str. 269-317.

Additional literature available for the individual seminars in case of the tutoring approach.

Cilji in kompetence:

- Spoznavanje računalniških metod za modeliranje lastnosti molekul. Poudarek je na lastnostih, ki so zanimive pri raziskavah novih zdravilnih učinkovin in za ocenjevanje nevarnosti spojin v okolju (kemijska regulativa).
- Spoznavanje ustreznih podatkovnih bank, ki vsebujejo podatke o strukturah in lastnosti spojin, in metod za delo s podatkovnimi bankami.
- Spoznavanje metod za kodiranje molekulskih struktur in za izračun molekulskih deskriptorjev.
- Spoznavanje statističnih metod modeliranja in validacije modelov.
- Spoznavanje osnov molekulskega modeliranja – rešetanje, sidranje.

Objectives and competences:

- Getting acquainted with the computer methods to model the properties of molecules. The properties that are of interest in drug design and in chemical regulations - risk assessment of compounds in the environment will be addressed.
- Collecting knowledge about the databases that contain information about the structures and properties of compounds, and about the methods for data handling.
- Learning about the methods for encoding of molecular structures and for calculating molecular descriptors.
- Acquiring the knowledge about the statistical modeling and validation of models.
- Acquiring basic knowledge about molecular modelling – virtual scrambling, docking.

Predvideni študijski rezultati:

Razumevanje problematike, ki nastaja pri obdelavi velikega števila podatkov, spoznavanje mehanizmov delovanja spojin v bioloških sistemih.

Študenti bodo z uspešno opravljenimi obveznostmi tega predmeta pridobili:
Zmožnost interpretirati in analizirati pred kolegi njihovo lastno razumevanje vsebine znanstvenih člankov. Pokazali bodo praktično uporabo pridobljenega znanja in ovrednotili literaturne in praktične podatke.

Intended learning outcomes:

Understanding the problem, which occurs when processing a large number of data, learning about the mechanisms of action of compounds in biological systems

Students successfully completing this course will acquire:
Ability to interpret and analyze in front of the colleagues their own understanding of the the content of articles in scientific journals. He/she will have to use practically the acquired theoretical knowledge and evaluate the issues presented in the literature / practice.

Metode poučevanja in učenja:

Predavanja, konzultacije, individualno delo

Learning and teaching methods:

Lectures, consultancy, individual work

Načini ocenjevanja:	Delež (v %) / Weight (in %)	**Assessment:**
Seminarska naloga	50 %	Seminar work
Ustni zagovor seminarske naloge	50 %	Oral defense of seminar work

Reference nosilca / Lecturer's references:

1. ROY CHOUDHURY, Amrita, PERDIH, Andrej, ŽUPERL, Špela, SIKORSKA, Emilia, ŠOLMAJER, Tomaž, JURGA, Stefan, ZHUKOV, Igor, NOVIČ, Marjana. Structural elucidation of transmembrane transporter protein bilitranslocase : conformational analysis of the second transmembrane region TM2 by molecular dynamics and NMR spectroscopy. Biochimica et biophysica acta, Biomembranes, ISSN 0005-2736. [Print ed.], 2013, vol. 1828, iss. 11, str. 2609-2619.

2. MARTINČIČ, Rok, KUZMANOVSKI, Igor, WAGNER, Alain, NOVIČ, Marjana. Development of models for prediction of the antioxidant activity of derivatives of natural compounds. Analytica chimica acta, ISSN 0003-2670. [Print ed.], Apr. 2015, vol. 868, str. 23-35,
3. BORIŠEK, Jure, VIZOVIŠEK, Matej, SOSNOWSKI, Piotr, TURK, Boris, TURK, Dušan, MOHAR, Barbara, NOVIČ, Marjana. Development of N-(functionalized benzoyl)-homocycloleucyl-glycinonitriles as potent cathepsin K inhibitors. Journal of medicinal chemistry, ISSN 0022-2623, Sep. 2015, vol. 58, iss. 17, str. 6928-6937.
4. FJODOROVA, Natalja Stanislavovna, NOVIČ, Marjana, GAJEWICZ, Agnieszka, RASULEV, Bakhtiyor. The way to cover prediction for cytotoxicity for all existing nano-sized metal oxides by using neural network method. Nanotoxicology, ISSN 1743-5390, 2017, vol. 11, iss. 4, str. 475-483.
5. DRGAN, Viktor, ŽUPERL, Špela, VRAČKO, Marjan, CAPPELLI, Claudia Ileana, NOVIČ, Marjana. CPANNatNIC software for counter-propagation neural network to assist in read-across. Journal of cheminformatics, 2017, DOI 10.1186/s13321-017-0218-y.