PROTOKOL I ZAPISNIK OBRANE DOKTORSKOG RADA

Povjerenstvo ulazi u prostor za obranu, doktorand stoji ispred Povjerenstva. Članovi Povjerenstva i ostali nazočni sjednu, a potom Predsjednik čita:

Dear applicant, members of the Committee for the defense of doctoral thesis, dear colleagues and guests. I am pleased to announce that today, on the 9th of December 2013, our applicant

Ana Sofia Pedrosa Pinto

PRIRODOSLOVNO-MATEMATIČKI FAKULTET, SPLIT
Primljeno: 02. 12. 2013
Klasifikacijska ozn.: 643-02/13-13/0001 02-02
Urudžbeni broj: 2181-204-03-02-13-0009

Will defend her doctoral thesis entitled:

Naslov doktorskog rada:	*Jezik pisanja rada:*	Engleski
	Hrvatski:	Računalna analiza genotipova i N-glikoma ljudske plazme
	Engleski:	Computational analysis of human plasma N-glycome and genotypes

And which was supervised by one mentor:

	Titula, ime i prezime :	**Ustanova, država:**
Prvi mentor:	Prof.dr.sc. Kristian Vlahoviček	Prirodoslovno-matematički fakultet, Sveučilište u Zagrebu, Hrvatska

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Predsjednik čita **životopis** doktoranda/doktorandice:

The applicant, Sofia Pinto, was born in Coimbra, Portugal 1984.

She graduated from the University of Coimbra, Portugal, in Biomedical Engineering in 2007.

She has been a researcher in the Bioinformatics Group at the Molecular Biology Department, Faculty of Science, University of Zagreb, since 2007. While in the group, she was a teaching assistant on the Algorithms and Programming Course.

She is the author of two publications, one related to the present thesis and one related to a side project.

She enrolled the Interdisciplinary PhD Program in Biophysics at the University of Split, Croatia, in 2008.

Predsjednik čita **obrazloženje** ocjene doktorskog rada.

PhD dissertation of the applicant Ana Sofia Pedrosa Pinto contains 5 chapters: 1. Introduction; 2. Materials and methods; 3. Results; 4. Discussion; 5. References. Lists of figures and tables are presented at the beginning of the document, CV of the applicant, abstracts, and additional figures and tables are presented at the end of the document. Dissertation is written in English language and contains 165 pages, 31 figures, 8 tables, 148 references, and additional 12 figures and 10 tables organized in 2 Appendices.

The applicant has published 2 papers in scientific journals:
Pinto, S., Vlahoviček, K. and Buratti, E. (2011) PRO-MINE: A Bioinformatics Repository and Analytical Tool for TARDBP Mutations. Human Mutation, 32: E1948–E1958.
Pučić, M., **Pinto, S.**, Novokmet, M., Knežević, A., Gornik, O., Polašek, O., Vlahoviček, K., Wei, W., Rudd, P. M., Wright, A. F., Campbell, H., Rudan, I., and Lauc, G. (2010) Common aberrations from normal human N-glycan plasma profile. Glycobiology 20:970-975.

Diverse computational methods were employed to the integrated analysis of glycan, physiological/biochemical and genotype data in three isolated population cohorts in order to explore the genomic and environmental regulation of glycosylation. A general data processing pipeline to treat and prepare glyco-related data prior to analysis was established. Specific glyco-phenotypes possibly related to pathologies were identified in the general population and the potential use of glycan modifications as biomarkers was evaluated for the particular case of diabetes. Analysis of the internal structure of populations revealed the presence of similar cluster profiles. Additionally, several patterns of associations between glycans and phenotypes were shared across populations despite their geographical and environmental separation. Multivariate methods based on polygenic modeling were used to investigate gene polymorphisms affecting glycosylation. Identification of possible novel links suggest that these efficient methods could be an alternative to traditional univariate genome-wide association studies.

Our opinion is that doctoral dissertation of the applicant Ana Sofia Pedrosa Pinto contains original scientific contribution and all the necessary requirements to be accepted. The applicant has systematically explained and supported known scientific facts with a comprehensive literature survey. Research results are described simply and clearly, and follow goals of the thesis and used methods. Discussion presents the importance and potential of the methods developed within the framework of this work for further research of glycomic profiles and their correlation with population genotypic and phenotypic characteristics, as well as a potential use of glycans as biomarkers for diabetes. Therefore, our proposal is the acceptance of the doctoral dissertation of the applicant so she can proceed with defense of the thesis.

Nakon što je pročitao Izvještaj, Predsjednik daje riječ doktorandu/doktorandici) riječima:

*I invite the applicant **Sofia Pinto** to present her doctoral thesis. The presentation can last up to 45 minutes.*

I invite the members of the Committee to ask questions related to the dissertation.

(Note: The mentor will not ask).

2 At the end President of the Committee asks questions.

Pitanja Povjerenstva za obranu doktorskog rada	
2. član	Vidi prilog
3. član	Nema
Predsjednik Povjerenstva	Nema

If anyone in the audience has a question, please ask now and please introduce yourself.

Pitanja nazočnih	
(ime i prezime)	
(ime i prezime)	
(ime i prezime)	

President ends the procedure by saying:
If there are no more questions, I declare the defense of the dissertation completed and suggest that the Commission withdraw for the counseling.

* * *

After returning President reads:

The doctoral thesis was defended in front of the Committee for the defense of doctoral thesis composed of 3 members:

	Titula, ime i prezime:	**Ustanova, država:**	**Potpis**
Izabrano povjerenstvo za obranu doktorskog rada	1. Prof.dr.sc. Igor Weber	Institut Ruđer Bošković, Hrvatska	
	2. Prof.dr.sc. Gordan Lauc	Farmaceutsko-biokemijski fakultet, Sveučilište u Zagrebu, Hrvatska	
	3. Doc.dr.sc. Andreja Ambriović-Ristov	Institut Ruđer Bošković, Hrvatska	

Which was elected by

The Faculty Council of the Faculty of Science, University of Split
on: 10.07.2013 (63. Faculty meeting)

The Doctoral dissertation was accepted by

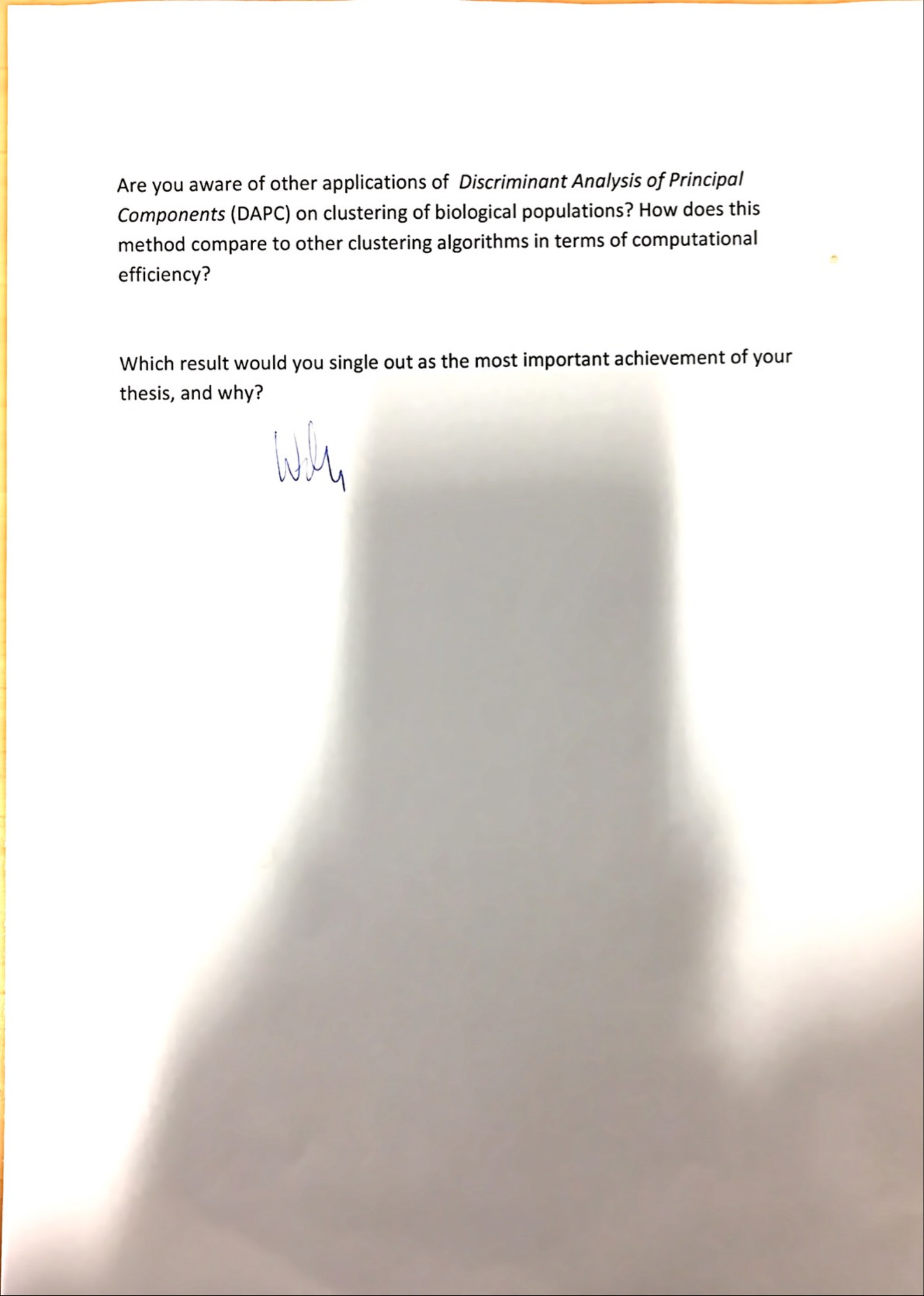
The Faculty Council of the Faculty of Science, University of Split
on: 27.11.2013 (68. Faculty meeting)

at the proposal of the elected Committee for the evaluation of doctoral thesis, which consisted of the same members as the Committee for the defense of doctoral thesis.

Upon public defense of the doctoral thesis, the Committee for the defense of doctoral thesis issued a unanimously – majority of votes (please underline).

Are you aware of other applications of *Discriminant Analysis of Principal Components* (DAPC) on clustering of biological populations? How does this method compare to other clustering algorithms in terms of computational efficiency?

Which result would you single out as the most important achievement of your thesis, and why?



Andreja Ambriović Ristov, PhD
Division of Molecular Biology
Laboratory for Genotoxic Agents

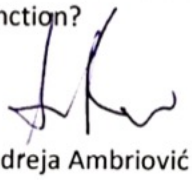
Zagreb, December 9th 2013

Questions asked at the PhD defence

1. What do you know about glycosylation pattern of monoclonal antibodies? Does glycosylation pattern change with changes in composition of the growth media, type of cells, species, type of antigen, etc?

2. In your thesis you described that the IgG glycan profiles were measured with the gel method for Vis and Korčula cohorts and with the solution method for Orkney. Therefore, an evaluation of the agreement between the two methods was necessary to allow a proper comparison and interpretation of results from analyses involving the IgG profiles of the three populations.
Can you please briefly describe the difference between these methods? Can you please compare them regarding sensitivity, specificity, etc?
Do you believe that an exact formula could be found to enable the transformation of values between the two methods and allow a more accurate comparison of results?

3. In you thesis you emphasize the association between calcium and glycan structures:
„Another interesting pattern which was only observed for the Orkney population is the positive association between calcium and glycan structures containing bisecting GlcNAc and the negative association with glycan structures without bisecting GlcNAc. While the presence of bisecting GlcNAc on IgG increases its effector function [antibody expression book], calcium signalling has an important role in immune function by participating in diverse mechanisms of the immune system (Diamantstein & Odenwald, 1974). Moreover, N-glycans on T-cell glycoproteins are found to be involved in triggering T-cell functions (Walzel *et al.*, 2006).
Why do you think that the association that you found in your data concerns primarily immune function?



Andreja Ambriović Ristov, PhD

In your study you have used GWAS and GEMMA to identify genetic loci. Can you explain the difference between the two approaches?

This analysis was performed on individuals from isolated populations. Can you tell us advantages and disadvantages of this type of experimental design.

C. Lace