

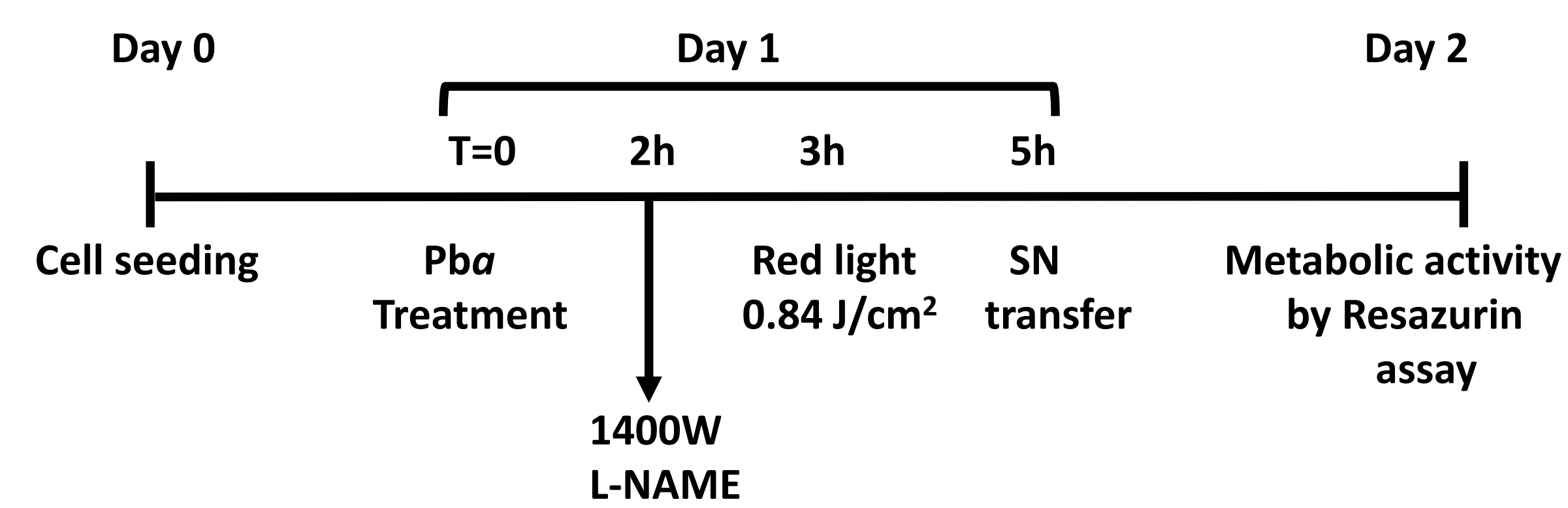
## Can NO released by photooxidative stressed tumor cells affect the bystander cells?

**BACKGROUND:** Photodynamic therapy (PDT) is a minimally invasive technique used in cancer treatment. It is based on the combination of a photosensitizer (PS), light and oxygen. This triad produces oxidative damage with the release of ROS and  $^1\text{O}_2$ . Not all cells in a given tumor are uniformly targeted by PDT. This situation depends on PS cellular uptake and on the light tissue penetration in the tumor, which may condition PDT efficacy. A high PDT insult leads to cell growth arrest, whereas a low PDT insult stimulates tumor cell growth, invasiveness and resistance.

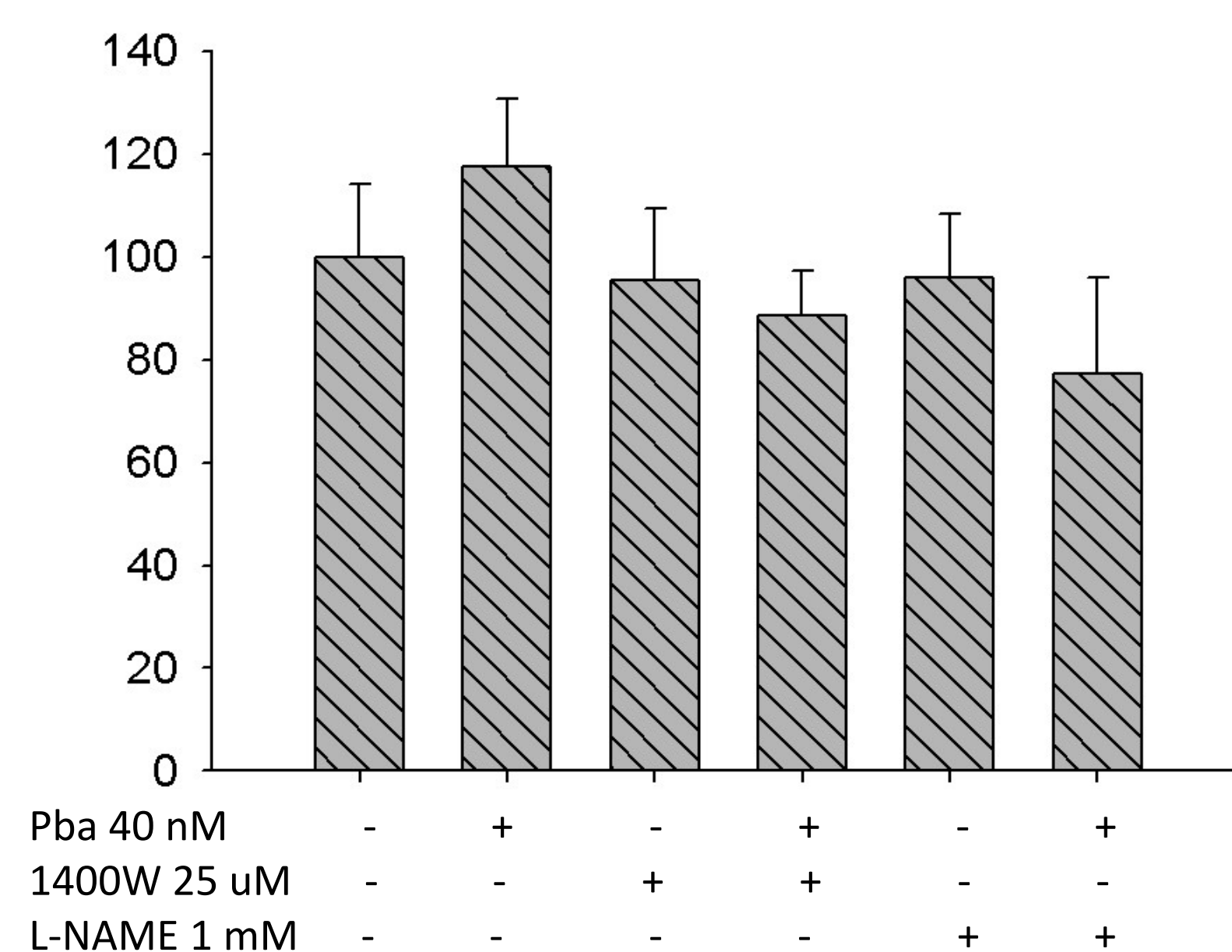
**AIM:** Considering that low doses of NO, induced by Pba/PDT in PC3 cells, play a cytoprotective role, we wanted to investigate whether this effect could be extended to «bystander» tumor cells.

### RESULTS:

#### 1. Low NO levels induced by Pba/PDT are able to stimulate «bystander» PC3 cancer cells

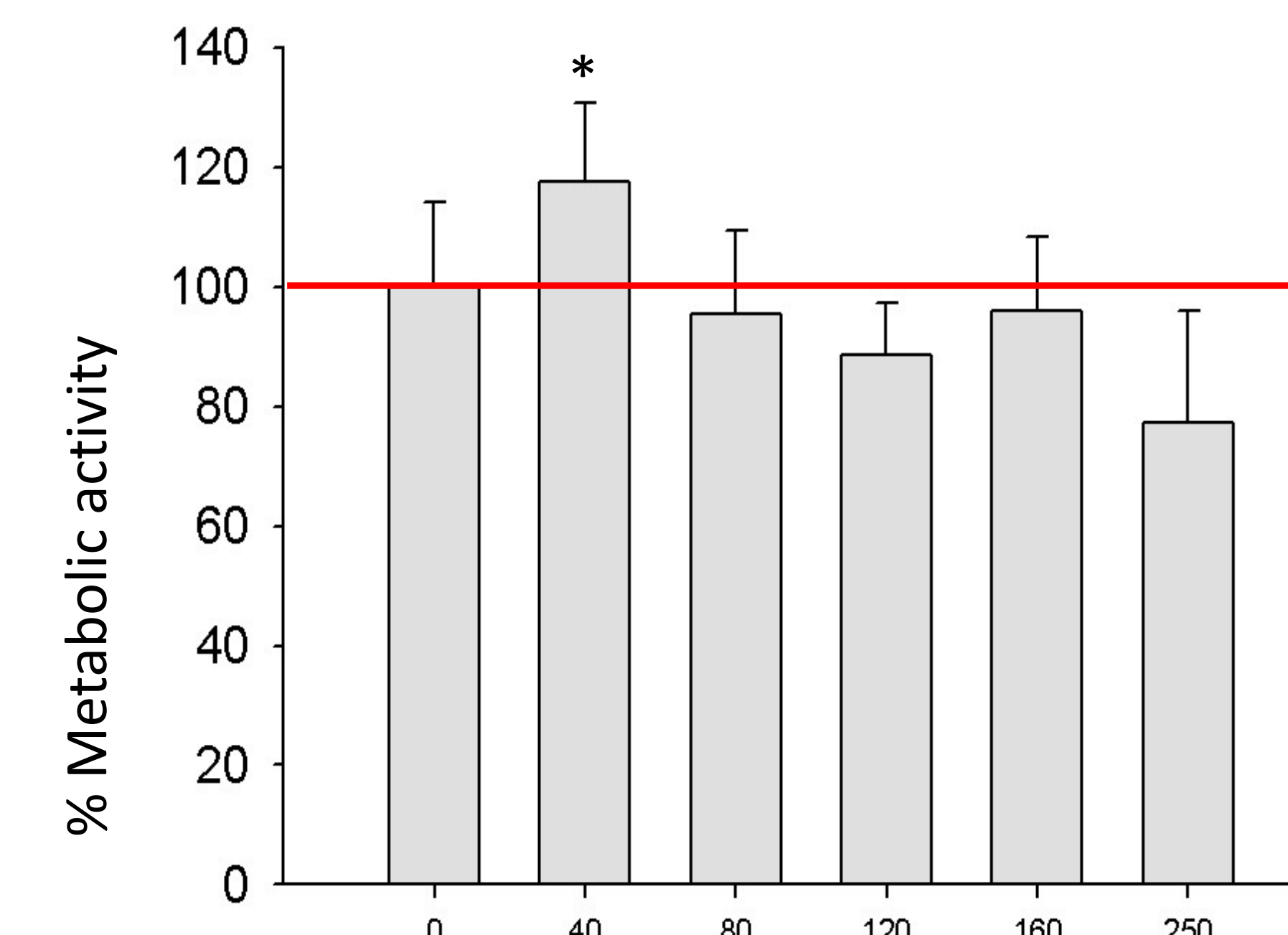


The supernatant (SN) of Pba/PDT treated PC3 cells was transferred to untreated PC3 cells 2 h after irradiation.



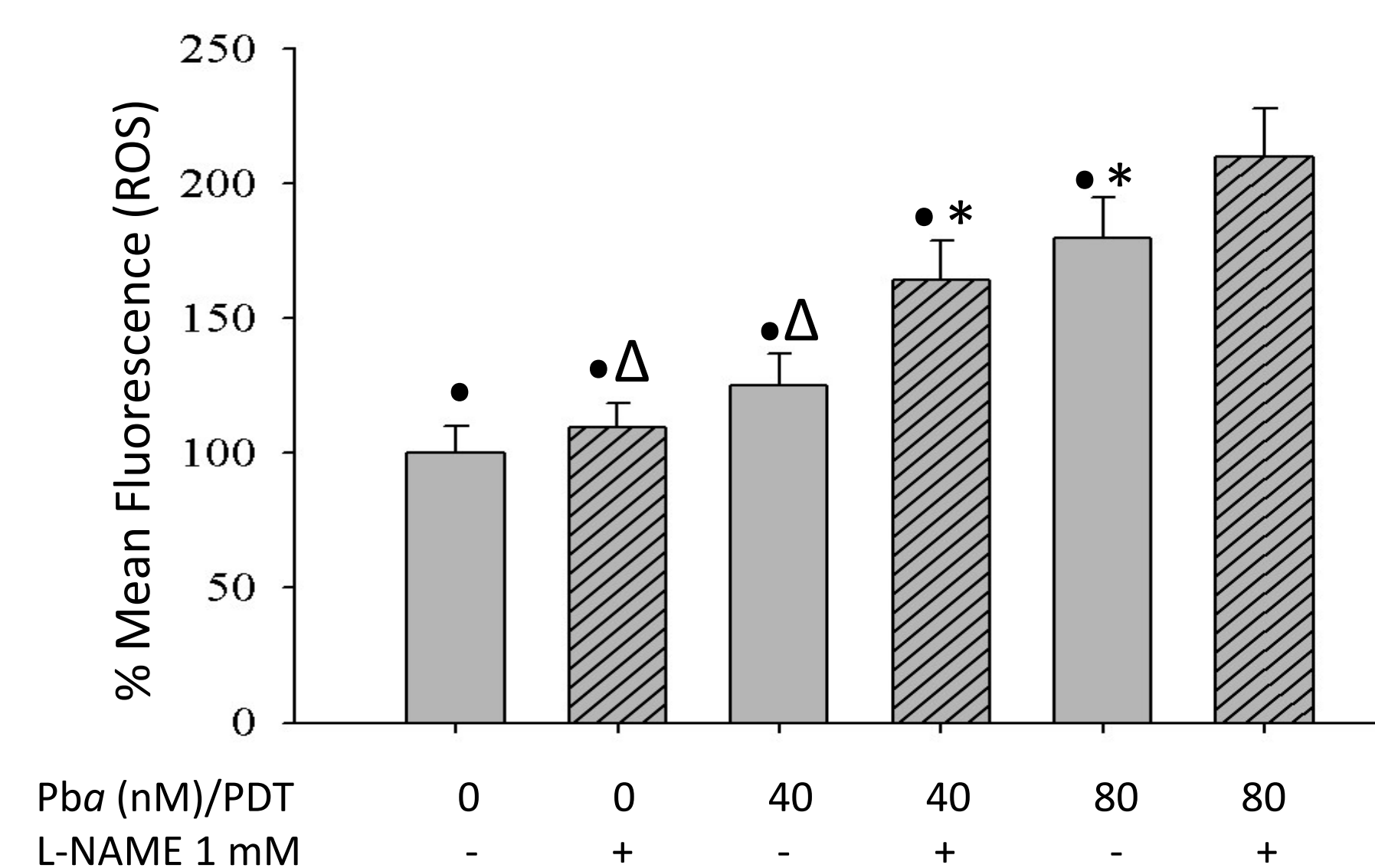
**Fig. 1.** Effect of NO derived from Pba/PDT in stimulating untreated "bystander" cells using L-NAME and 1400W iNOS inhibitors. PC3 cells were treated in different ways as indicated in the x-axis. Values represent the mean  $\pm$  SD obtained in two independent experiments.

#### 2. The SN from PC3 cells treated with 40 nM Pba/PDT is able to induce untreated «bystander» PC3 cells



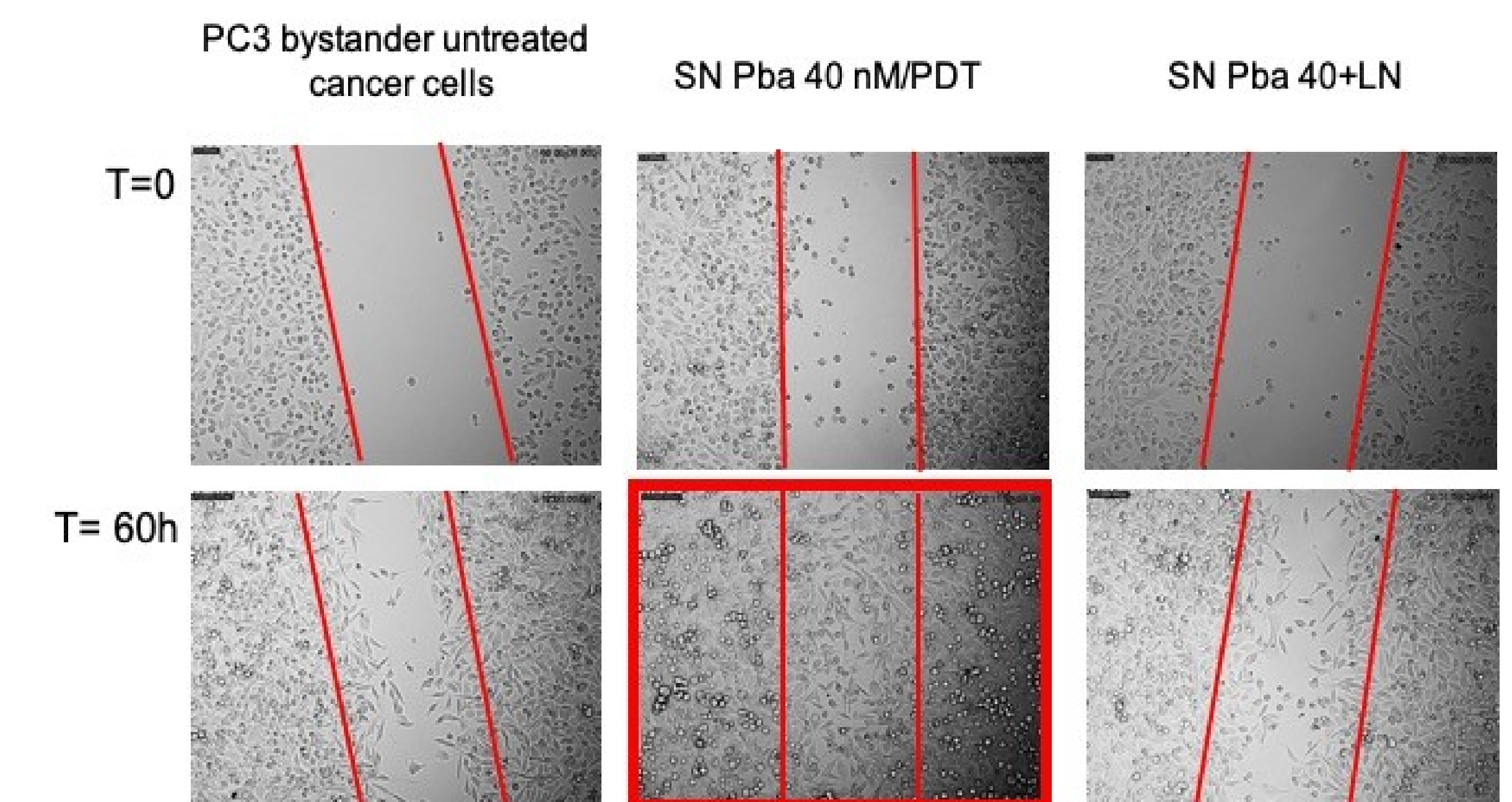
**Fig. 2.** Metabolic activity of Pba/PDT-treated PC3 cells vs that of untreated «bystander» PC3 cells receiving the SN of PDT-treated cells. PC3 cells were treated in different ways as reported in the x-axis. Values represent the mean  $\pm$  SD obtained in three independent experiments (Student's t-test;  $P < 0.05$ ).

#### 4. iNOS inhibition increases the efficacy of a low dose of Pba/PDT, due to an increase in ROS production.



**Fig. 4.** ROS production in PC3 cells using Pba/PDT and L-NAME iNOS inhibitor. PC3 cells were treated in different ways as indicated in the x-axis. Values represent the mean  $\pm$  SD obtained in two independent experiments (Student's t-test;  $P < 0.05$ ).

#### 3. The SN derived from PC3 cells treated with 40 nM Pba/PDT stimulates the migration of untreated «bystander» PC3 cells



**Fig. 3.** PC3 cells vs untreated PC3 «bystander» cells receiving the SN of Pba/PDT-treated cells. PC3 cells were treated with 40 nM Pba/PDT. After the treatment a scratch wound was performed and the SN was transferred to untreated «bystander» PC3 cells. Images were taken every 6h.

### CONCLUSIONS:

Our previous studies showed that a low dose of Pba/PDT induces proliferation and survival of PC3 prostate cancer cells, while a high dose of Pba/PDT inhibits cell growth.

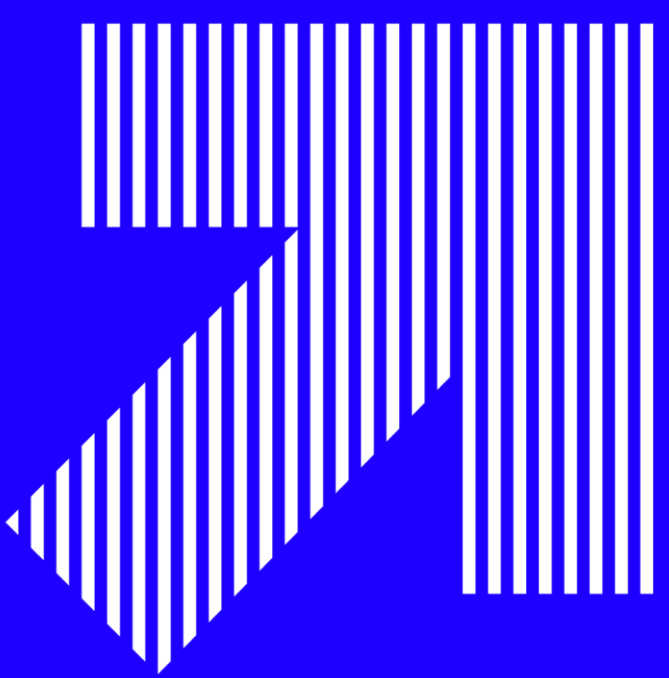
A low dose of Pba/PDT is able to stimulate the metabolic activity and migration of untreated «bystander» PC3 cancer cells, due to low NO levels that have cytoprotective and antioxidant properties.

### FUTURE PERSPECTIVES:

To evaluate the molecular signaling pathways involved in «bystander» cancer cells stimulation.

To evaluate whether NO, induced by low Pba/PDT, stimulates the tumor microenvironment (healthy prostate cells, macrophages,...).





# Increased MtCK and ANT in aging Pin1 KO mice as a basis of augmented ADP sensitivity of mitochondrial respiration

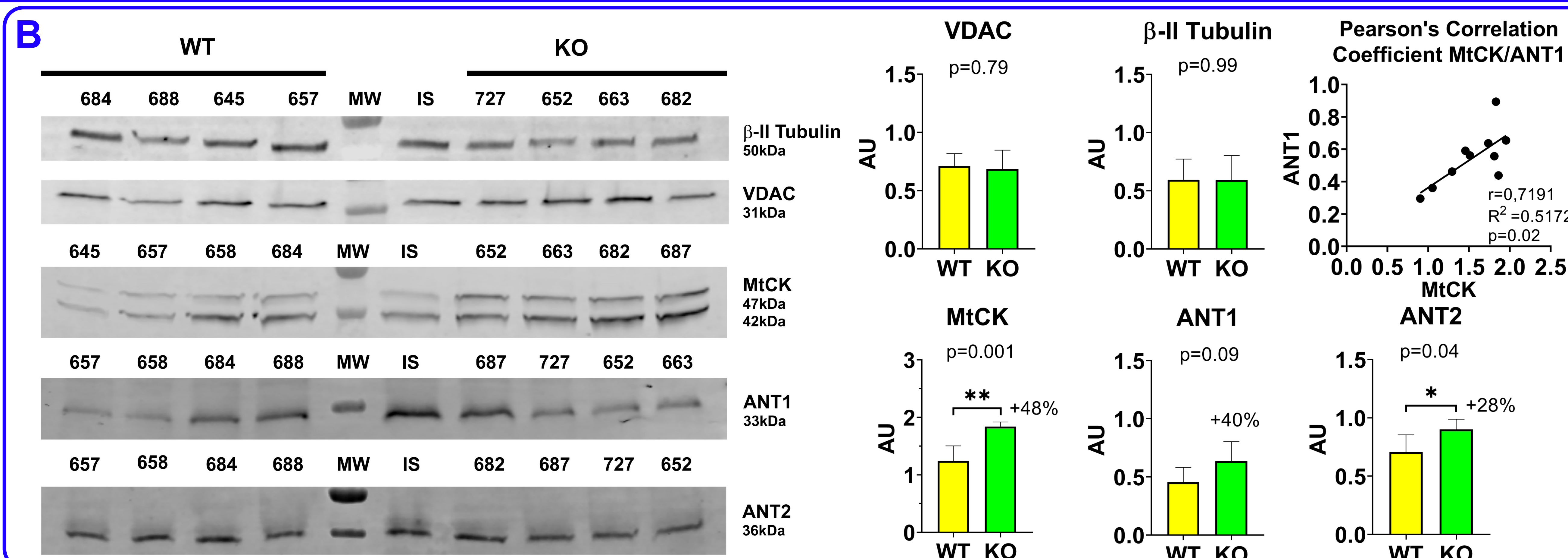
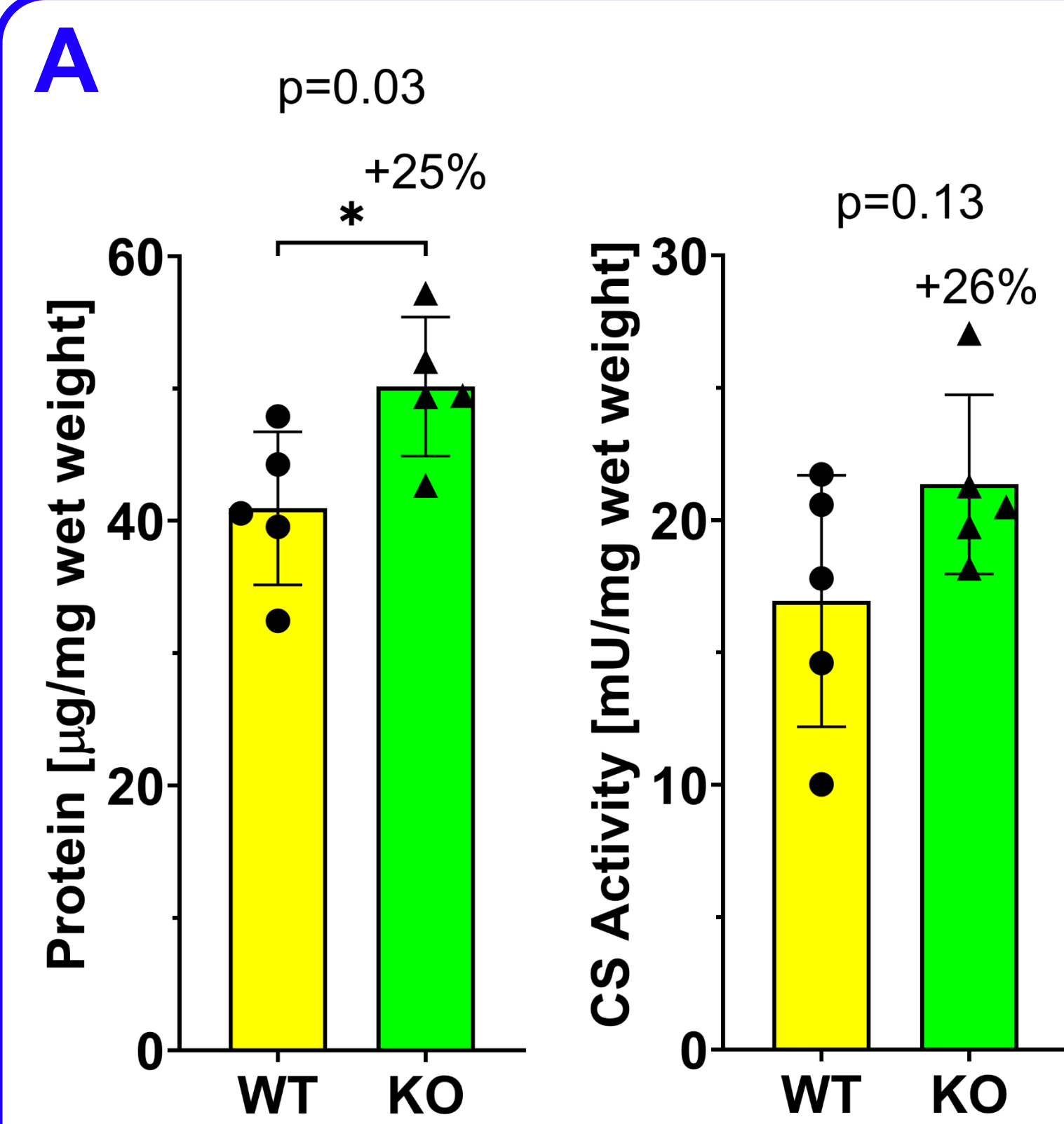
Gissi C.<sup>a</sup>, Zuccarelli L.<sup>a</sup>, Comelli M.<sup>a</sup>, Brocca L.<sup>b</sup>, Rossi M.<sup>b</sup>, Battini R.<sup>c</sup>, Uchida T.<sup>d</sup>, Pellegrino M.A.<sup>b</sup>, Bottinelli R.<sup>b</sup>, Grassi B.<sup>a</sup>, Molinari S.<sup>c</sup>, Mavelli I.<sup>a</sup>.

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**INTRODUCTION:** Mitochondrial impairment associated to a severe motor neuron loss occurs frequently during aging, causing muscle wasting and sarcopenia. Pin1, Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1, is a prolyl isomerase that binds to and isomerizes specific phosphorylated Ser/Thr-Pro motifs of target phosphoproteins, thereby affecting the stability and activity of numerous signalling proteins and transcription factors. Thus, Pin1 plays a crucial role in numerous cellular processes. Importantly, a role of Pin1 was recently suggested as a regulatory mechanism of the adult myogenesis<sup>[1]</sup>.

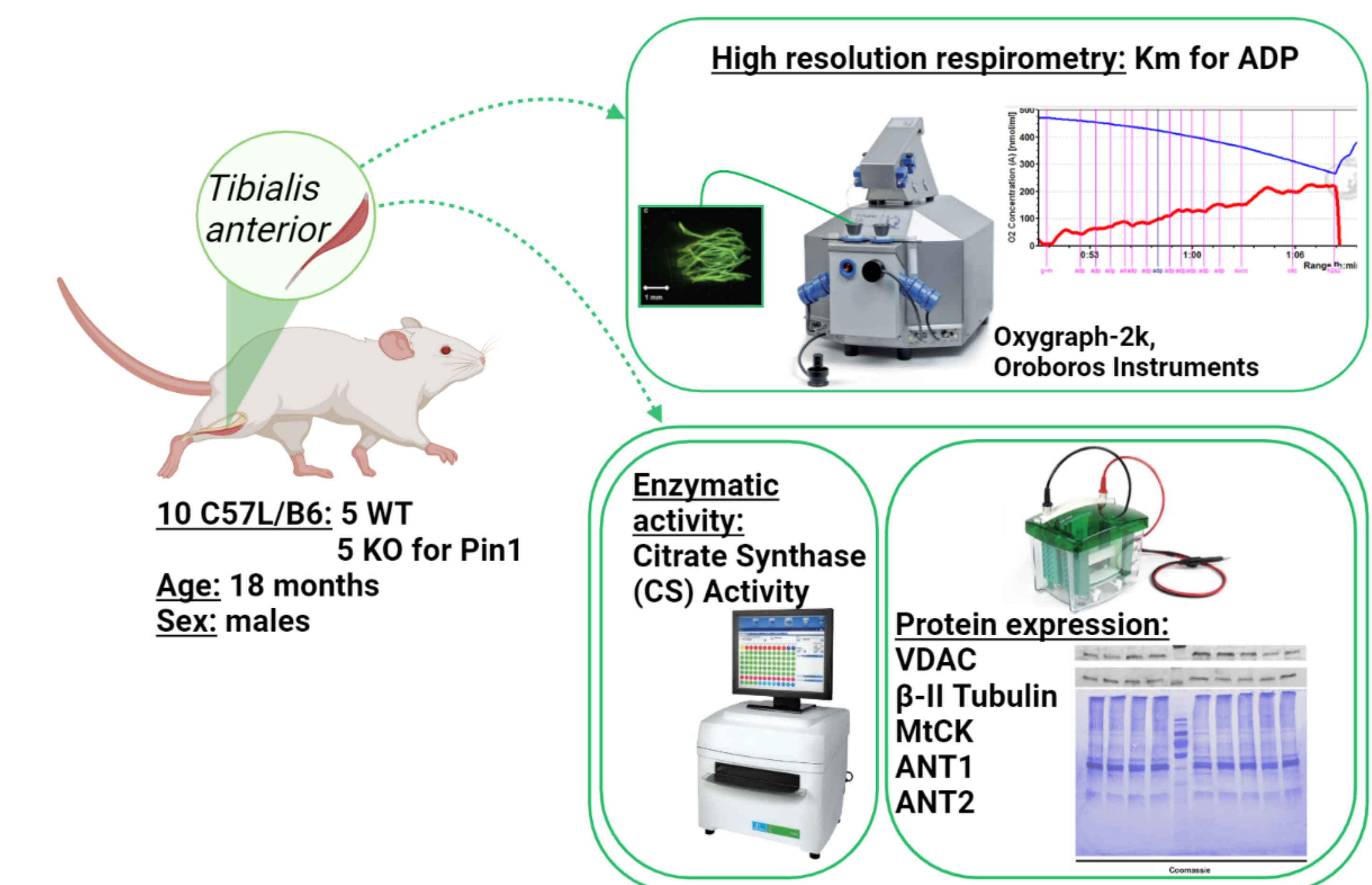
**AIM:** To assess the effects of Pin1 loss on mitochondria structural/functional aspects, in order to evaluate if they might counteract loss of skeletal muscle function in aging mice. To this aim, we quantified some proteins residing in different mitochondrial sub-compartments, as well as responsible for regulation of the ADP sensitivity of respiration, in the skeletal muscle of *in vivo* Pin1 KO mature adult mice.

## RESULTS:



The increase observed in KO for CS activity, a mitochondrial matrix marker, mirrored the increment of the protein quantity in total muscle homogenates (**A**). The expression levels of VDAC and its interactor β-II Tubulin did not differ between KO and WT. Instead, higher expression levels in KO vs. WT were observed for MtCK, ANT1 and ANT2. The 40% increase of ANT1 expression did not result statistically significant, but a Pearson's correlation analysis revealed a moderate positive correlation between MtCK and ANT1 or ANT2 variations (**B**). The apparent Km for ADP decreased (increased ADP sensitivity of mitochondrial respiration) by 73% in KO compared to WT, although the difference did not reach the statistical significance. (\*  $p<0.05$ ; \*\*  $p<0.005$ )

## EXPERIMENTAL DESIGN AND METHODS:

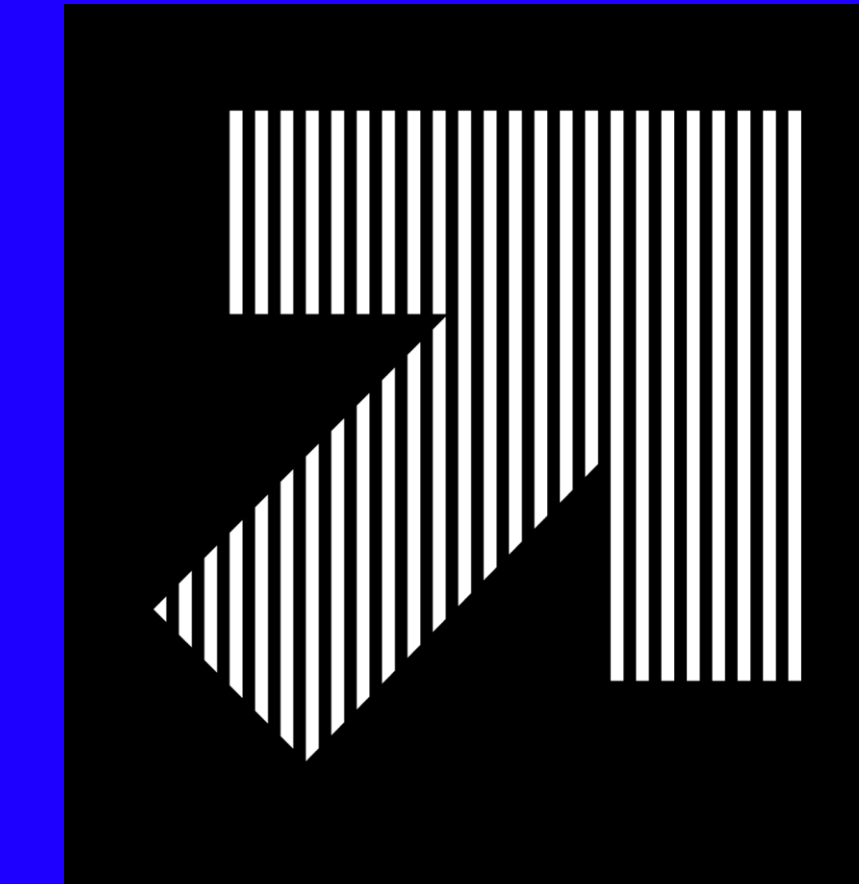
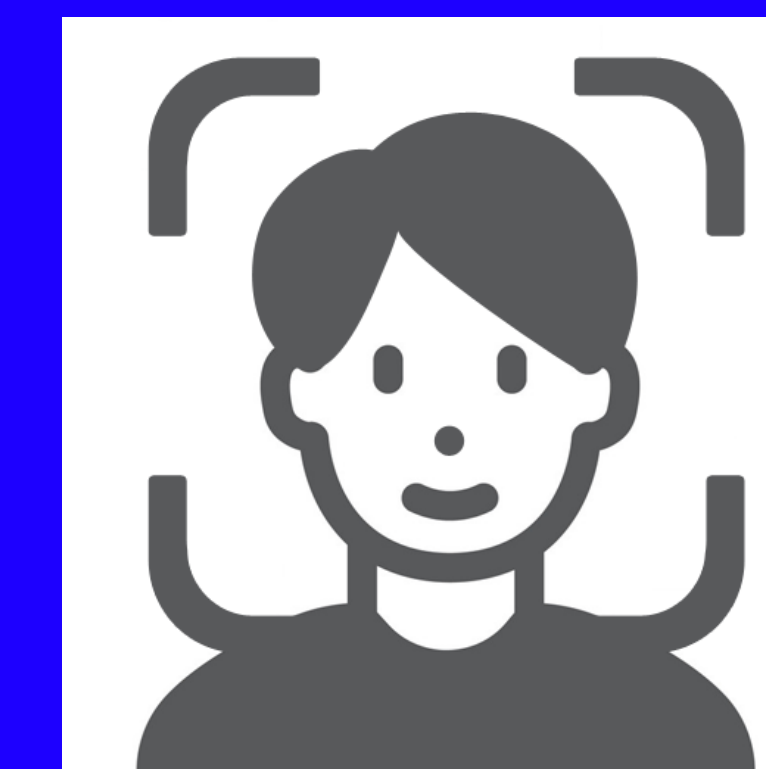


**CONCLUSION:** These preliminary data suggest that the selective increase observed in Pin1 KO for MtCK, ANT1 and ANT2 may explain the increased sensitivity of mitochondrial respiration to submaximal ADP, by favouring ADP recycling from the inter-membrane space to the matrix. The data also show that, while there was no change in proteins residing in the mitochondrial matrix and outer membrane, there was a selective increase in proteins associated to the inner membrane, suggesting a remodelling of such membrane improving mitochondria function.

**REFERENCE:** [1] A. Magli, C. Angelelli, M. Ganassi, F. Baruffaldi, V. Matafora, R. Battini, A. Bachi, G. Messina, A. Rustighi, G. Del Sal, S. Ferrari, S. Molinari, J Biol Chem (2010), 285(45), 34518-27.

**ACKNOWLEDGEMENT:** This work was supported by the Ministero dell'Istruzione dell'Università e della Ricerca, PRIN Project 2017CBF8NJ.





# EVALUATION OF DIFFERENT HDACS INHIBITORS IN THE CONTEXT OF LEIOMYOSARCOMA

Department of Medicine, Udine

Compound	Molecular structure	IC50	MW	Energy Kcal/Mol	TS**
BML-210		29.9	339.43	-77.45*	1.000
NKL-54		15.5	393.41	-81.43	0.719
MC2991		51.3	333.44	-76.89	0.388
MC2983		N.A.	333.44	-80.25	0.521
MC2984		19.8	333.44	-79.69	0.723
MC2985		10.6	378.49	-79.37	0.510

Figure 1: Chemical structures of HDACi derived from PAOA.

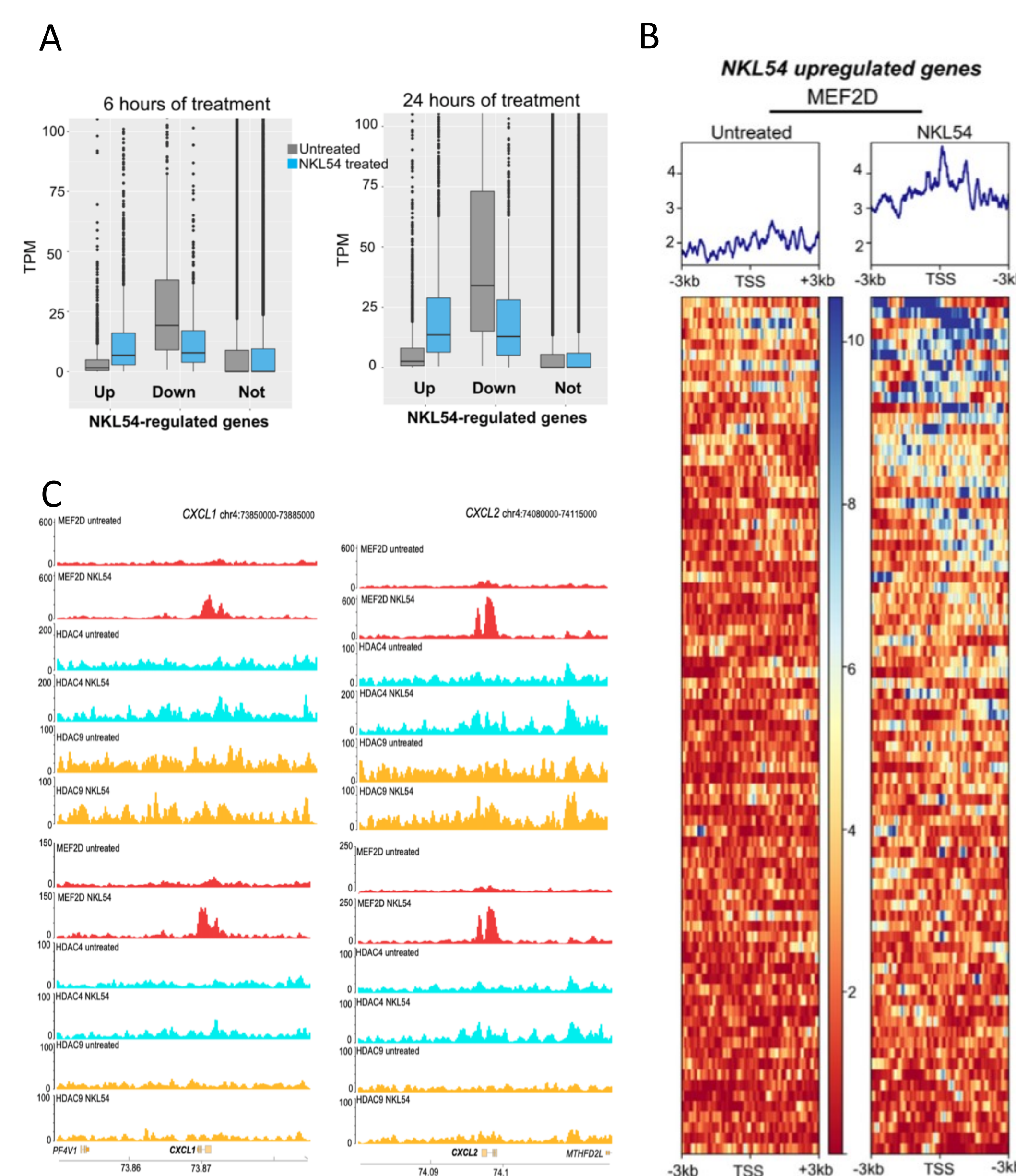


Figure 2A: TPM values are shown after treatment or not with NKL54. B: Heat-maps of the MEF2D signal distribution in a region of  $\pm 3$  kb around the TSS of 90 genes upregulated by NKL54 treatment. Data derived from Chip-seq experiment. C: Detailed view of the MEF2D, HDAC4 and HDAC9 tracks at two representative loci (*CXCL1* and *CXCL2*) upregulated by NKL54.

## BACKGROUND:

Histone deacetylases (HDACs) are a group of 18 enzymes involved in the epigenetic and transcriptional regulation. HDACs are dysregulated in different diseases and many HDACs inhibitors (HDACi) have been generated. HDACs of class IIa (HDAC4,5,7,9) interact through an extended N-term domain with different transcription factors, such as myocyte enhancer factor 2 (MEF2) family members. We have investigated different HDACi in the context of leiomyosarcoma (LMS), a rare and aggressive cancer characterized by a poor immune infiltration and by dysregulations in the HDACs IIa-MEF2 axis.

## AIM and APPLICATION:

The aim of our study is the evaluation of HDACs IIa-MEF2 axis in LMS cells where the complex resulted dysregulated. To do that, we have investigated different HDACi in order to restore the normal epigenetic landscape under the control of HDACs IIa-MEF2; we used some HDACi derivatives from pimeoloyanilide-o aminoanilides (PAOA), mainly NKL-54 (Figure 1A). Moreover, we compared SAHA, a pan-HDACi, and TMP-195, a specific class IIa inhibitor (Figure 3A). Our findings suggest the existence of a HDACs IIa-MEF2 repressive complex at the level of some genomic loci including some chemokines. The inhibition of this complex could potentiate the antitumor immune response in LMS, a cancer with a poor immune infiltration enhancing in this way the effect of immune-therapy.

## RESULTS:

NKL-54 causes a resetting of gene transcription and in particular it leads to an increase of genes normally low expressed and a downregulation of the highly expressed ones (Figure 2A). Interestingly, NKL-54 induces an increased number of MEF2D peaks at the level of TSS of genes regulated by the inhibitor (Figure 2B). Analyzing in detail some of these genes, it emerged an effect on *CXCL1* and *CXCL2* loci, where the increased binding of MEF2D after the treatment with NKL-54 is evident (Figure 2C). These data pointed out an activation of MEF2D after the treatment with NKL-54 which has an effect also on genes codifying for chemoattractants.

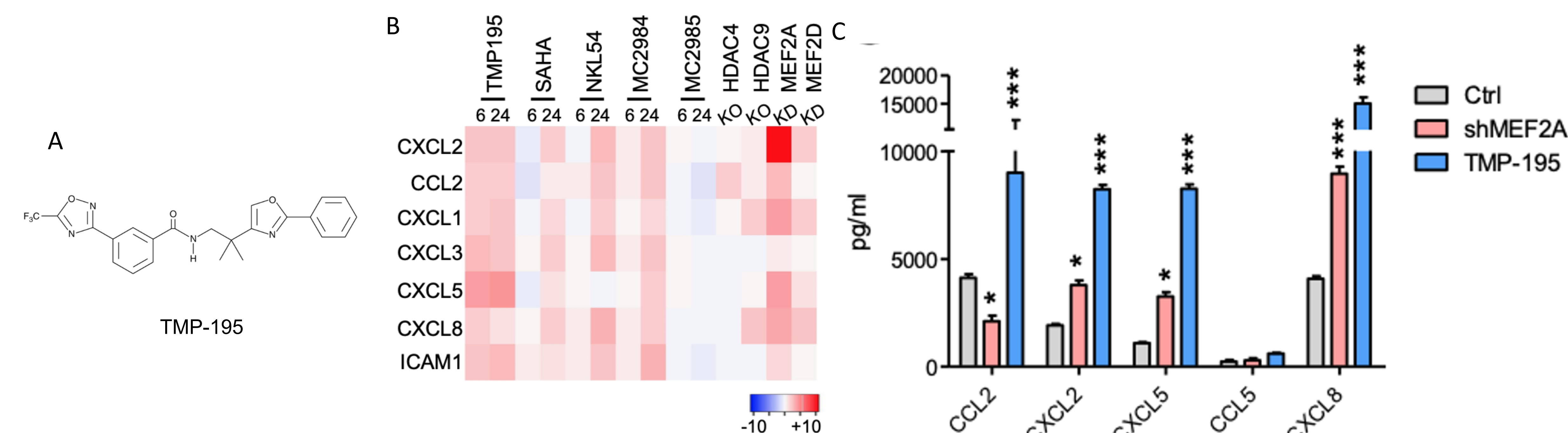
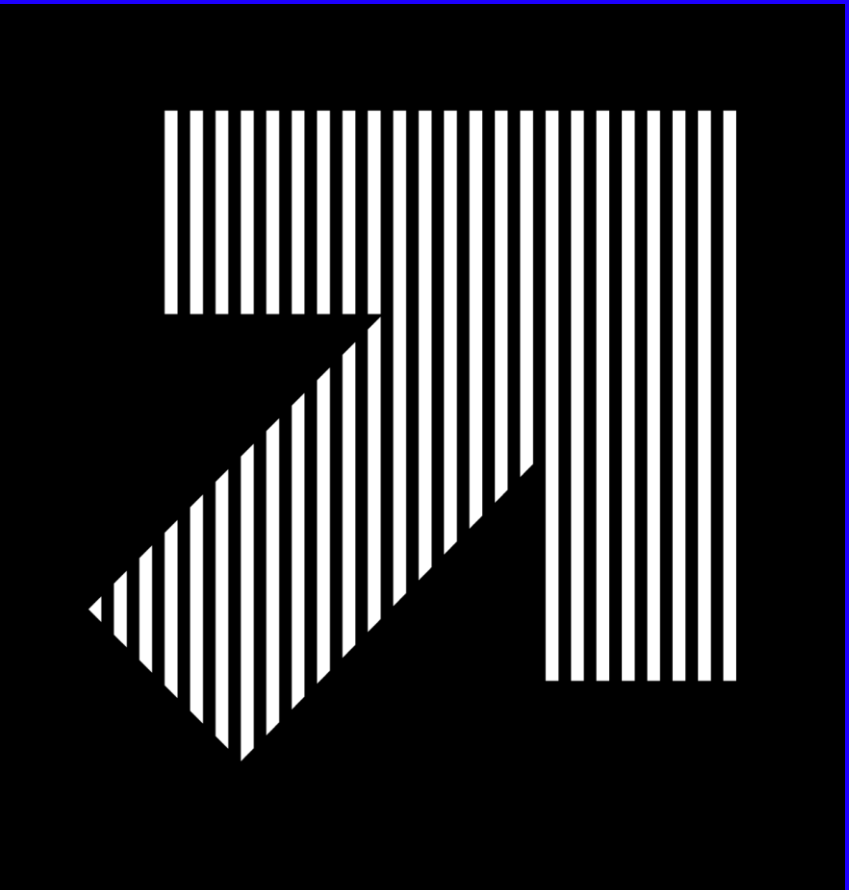


Figure 3A: Chemical structure of TMP-195. B: Heat-map showing the chemokines expression after the treatment with HDACi in LMS cells from RNA-seq compared with microarray of *HDAC4,9* ko and *MEF2A*, D kd. C: Levels of chemokines release in the supernatant of LMS cells treated with TMP-195 or sh for MEF2A.

We focused the attention on TMP-195 in order to better analyze the contribution of class IIa HDACs. Interestingly, we found that TMP-195 leads to an upregulation of some specific chemokines: *CXCL1*, 2, 3 and 5, in an early time point compared with other HDACi. We also compared the RNA-seq data with microarray of *HDAC4* or *HDAC9* knockout (ko) and *MEF2A* or *MEF2D* knockdown (kd) in LMS cells. A strong increase on *CXCL2*, 1 and 5 expressions after the downregulation of *MEF2A* was found (Figure 3B). Next, we evaluated the release of chemokines after the downregulation of MEF2A (short-hairpin MEF2A). As reported in figure 3C, the decreased level of MEF2A induces a high release of different chemokines in LMS cells supernatant and the effect is even stronger after the treatment with TMP-195.





# HDAC4/HDAC3 COMPLEXES ANTAGONIZE p300/AP-1 ACTIVITIES ON WELL-DEFINED SUPER-ENHANCERS

**keywords: HDAC4, senescence, SEs, SASP, HDAC3, p300, AP-1**

## AIMS:

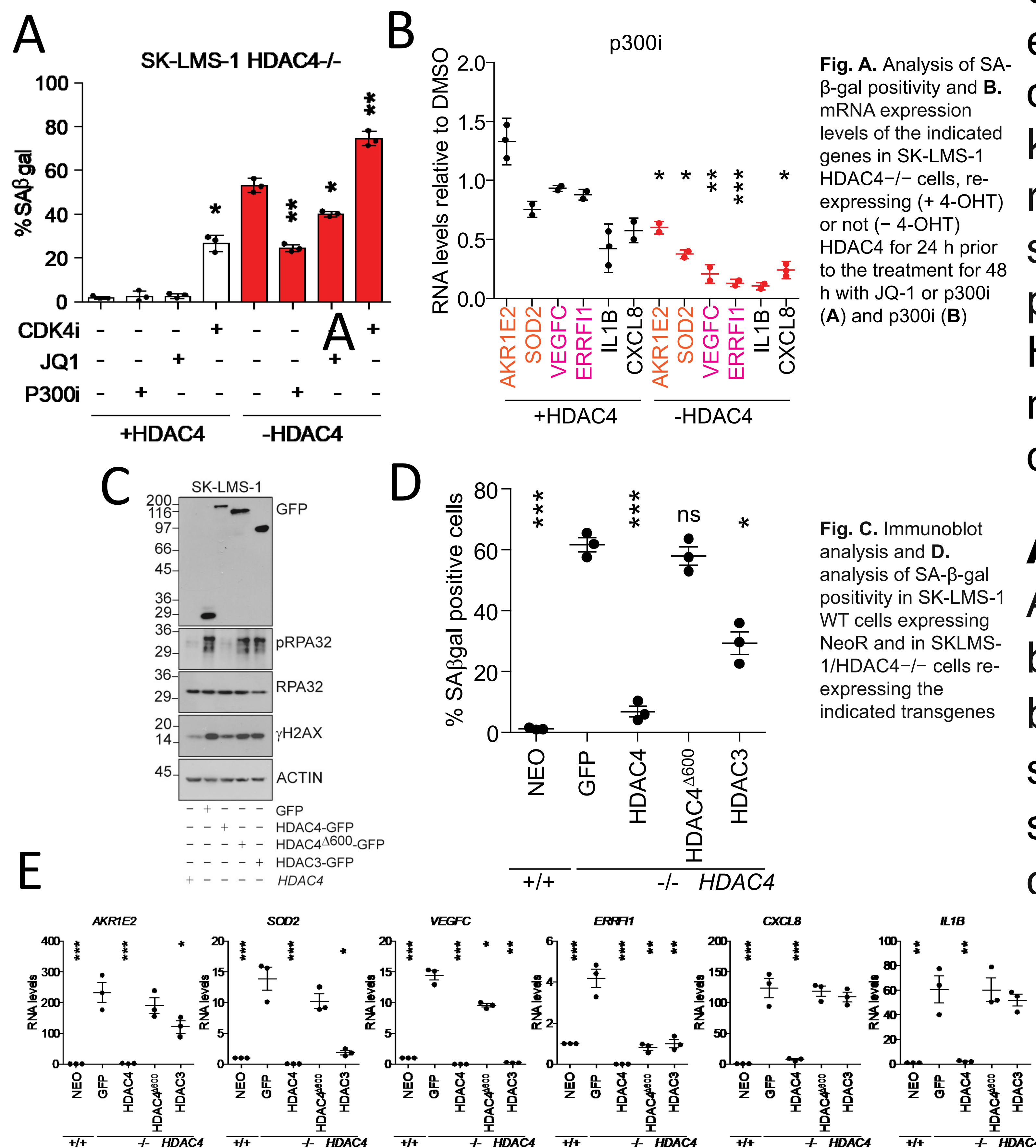
Taken together, the results presented in this thesis highly contribute to enhancing our understanding of the epigenetic role of HDAC4 in regulating the chromatin state of senescent cells. In particular, the project highlights the key role of HDAC4 as an epigenetic reader involved in the regulation of senescence-associated enhancer (TEs) and super-enhancers (SEs) that supervise the senescence program. Moreover, with our work we aim to identify the HDAC4-associated partners that are recruit as high molecular weight complexes at TEs and SEs chromatin distal regulative elements.

## APPLICATIONS:

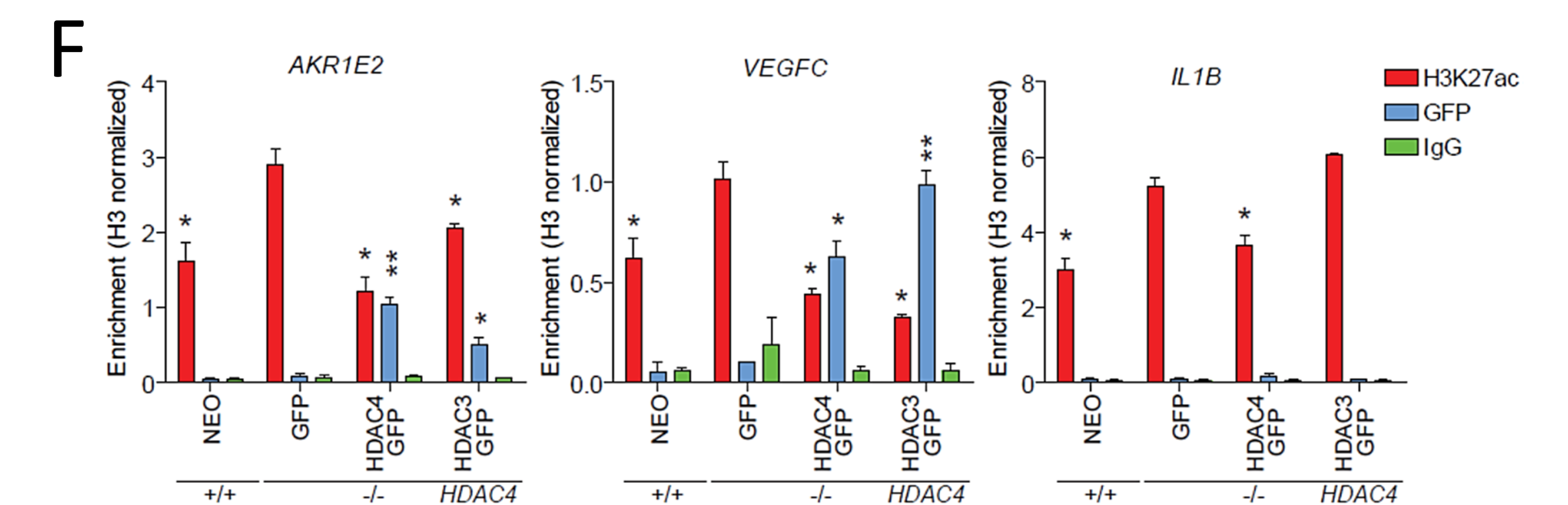
An exciting new prospect arising from these findings could be the identification of novel therapeutic approaches based on specific inhibitor for HDAC4 to induce a senescence response and enhance a proinflammatory state (SASP response) to target different age-related diseases including cancer.

## RESULTS:

The epigenome of senescent cells undergoes a deep redistribution of H3K27 acetylation. The class IIa Histone Deacetylases (HDAC4,5,7,9) are recruited on chromatin for the rapid de novo deacetylation of H3K27ac loci as part of large repressive complexes through their binding of class I HDACs. We found that HDAC4 is post-transcriptionally downregulated during aging and senescence. Moreover, HDAC4 knock-out (KO) triggers premature senescence in cancer cells through the activation of TEs and SEs supervising the senescence program and particularly the SASP response. We also found that the depletion of HDAC4 promotes the expression of endogenous retroviruses (ERVs) leading to the activation of SASP response through the engagement of a specific family of cytosolic immunosensors. The data regarding the relationship between HDAC4 and ERVs during the senescence response and the role of ERVs deregulation in the accomplishment of senescence program are now under revision for publication.



**Fig. E.** mRNA expression levels of the indicated genes in SK-LMS-1 WT cells expressing NeoR and in SK-LMS-1/HDAC4<sup>-/-</sup> cells re-expressing the indicated transgenes



**Fig. F.** ChIP-qPCR signals, normalized to total H3, obtained for the indicated antibodies in the indicated cells.





# ANAEROBIC DIGESTION FOR WASTE MANAGEMENT AND ENVIRONMENTAL IMPACT CONTROL OF MARINE FISH FARMS WITH RENEWABLE ENERGY PRODUCTION

**Keywords:** Aquaculture, anaerobic digestion, biogas, biomethane, fish farm effluents, brackish and marine wastewater, salinity, sludges, anaerobic filter.



Fig. 1 The anaerobic bioreactor simulator

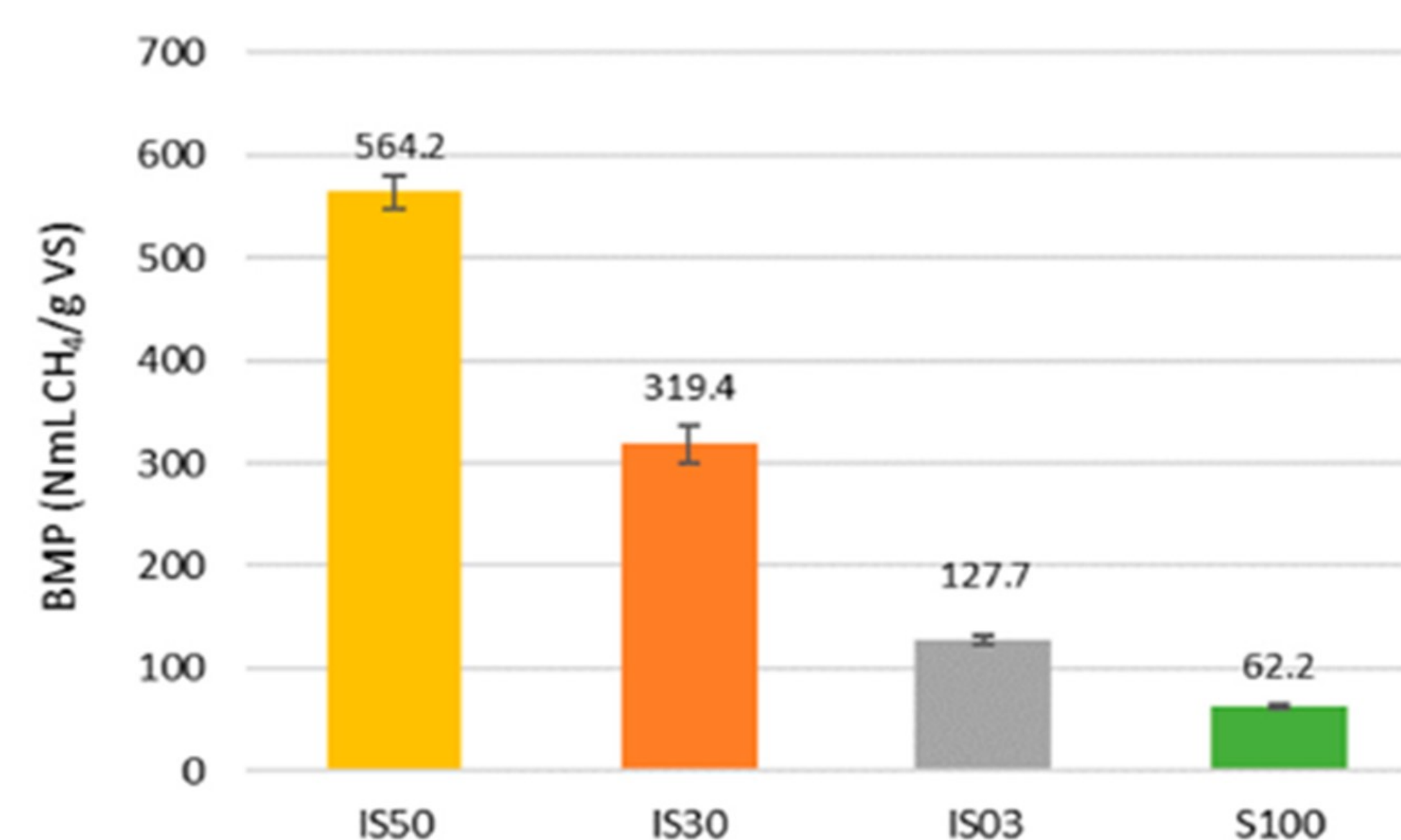


Fig. 2 The biochemical methane potentials of fish farm effluents

**AIMS:** This work focuses on improving the sustainability of marine aquaculture farming by applying the anaerobic digestion (AD) of farm effluents. Through AD of organic residues, it is possible to produce biogas and biomethane, renewable energy sources, and contemporary reducing the negative environmental impact of intensive fish farming.

**APPLICATIONS:** initially, the biochemical methane potentials (BMP) of effluents were determined in an automatic methane potential system (AMPTS, Bioprocesscontrol, Sweden), adopting a standard anaerobic inoculum and different ratios between inoculum and substrate (I/S). A second experimental phase was performed with effluents characterized by different salinity in a bioreactor simulator system (BRS, Bioprocess Control, Sweden - Fig. 1) to establish the optimal operating parameters for anaerobic process implementation on a real scale (ie. hydraulic retention time, HRT, and specific organic loading rate, OLR). Lastly, we tested a new prototype of bioreactor layout for the treatment of diluted and high-salinity aquacultural substrates consisting of an up-flow anaerobic floating filter (UAFF).

**RESULTS:** Fish farm effluents showed a considerably high methane potential (BMP): the highest I/S ratio (IS50) showed the highest BMP (564.2 NmL CH<sub>4</sub>/g VS, - Fig. 2), while decreasing BMP values were obtained corresponding to the lower amount of inoculum (319.4 and 127.7 NmL CH<sub>4</sub>/g VS, respectively for IS30 and IS03 - Fig. 2). In the continuous anaerobic process simulation, the marine effluents (salinity 35 g/L) had the lowest performance, with an average yield equal to 172.4 NmL CH<sub>4</sub>/g VS - Figure 3, compared to the brackish effluent (227.4 NmL CH<sub>4</sub>/g VS and 235.0 NmL CH<sub>4</sub>/g VS, with salinity 10-13 g/L - Fig. 3). The new prototype of UAFF reactor showed significantly higher yields compared to conventional CSTR reactor during the starting phase of anaerobic digestion, reaching 188 NmL CH<sub>4</sub>/g VS compared to 100 NmL CH<sub>4</sub>/g VS, respectively - Fig. 4.

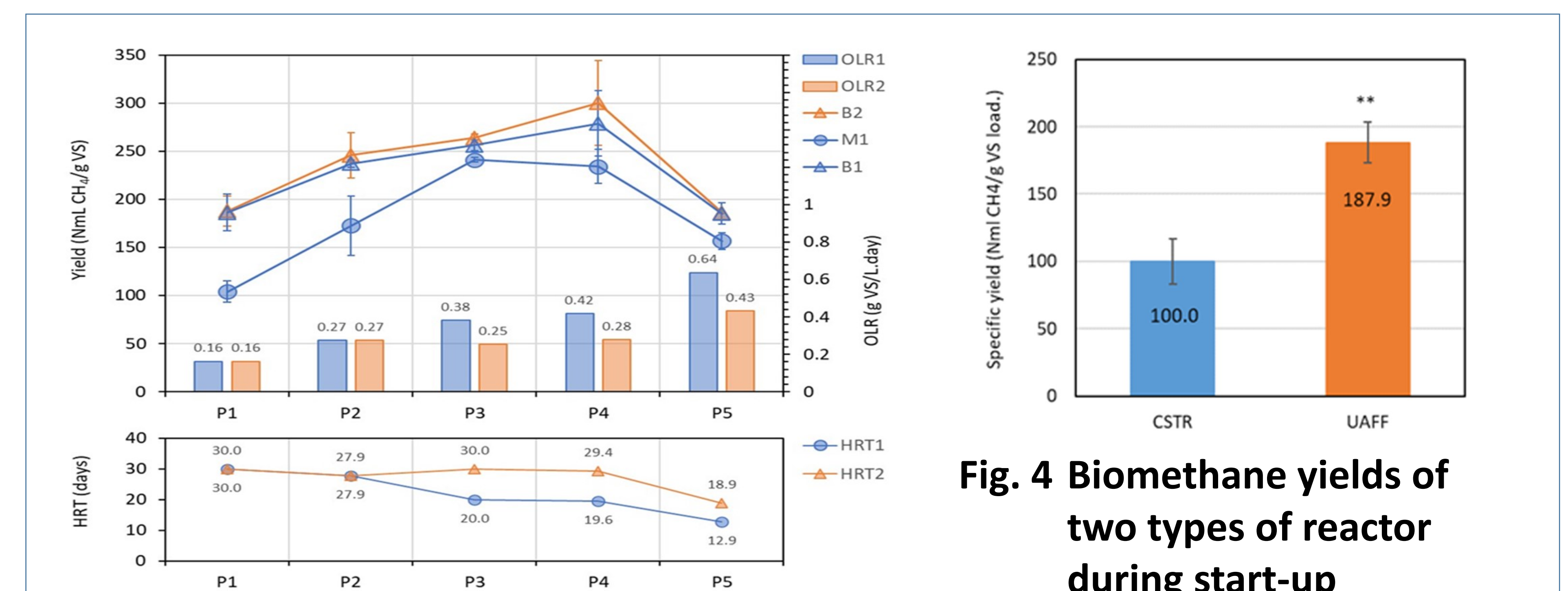
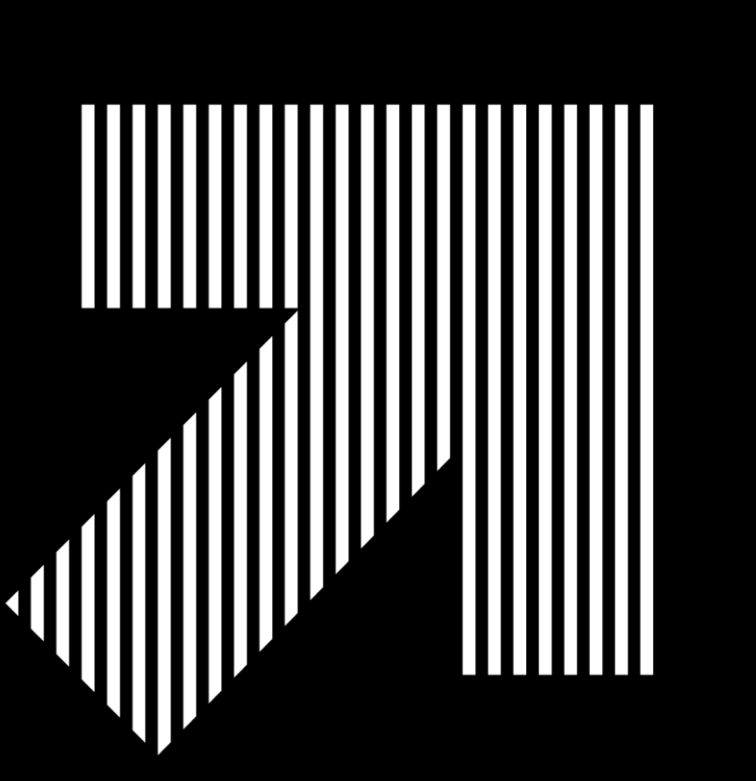


Fig. 3 Biomethane yields of marine and brackish effluents

Fig. 4 Biomethane yields of two types of reactor during start-up

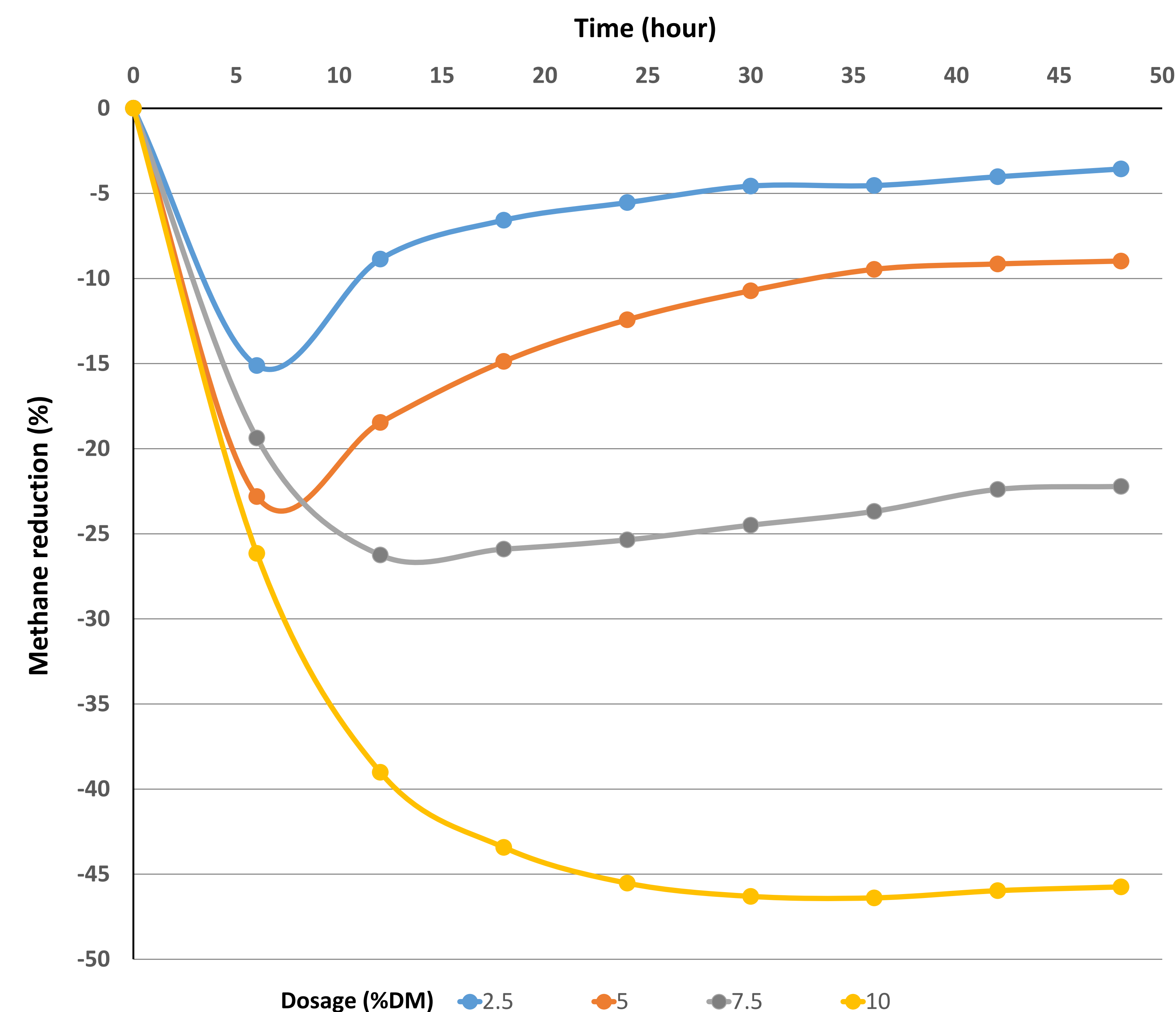




# RUMEN BATCH FERMENTATION SYSTEMS TO MEASURE METHANE YIELD

*Applications of a fully automated in vitro system for the evaluation of antimethanogenic strategies*

**KEYWORDS:** Livestock, ruminants, methane, *in vitro* techniques, sustainability.



**Effect of NaNO<sub>3</sub> dosage on methane production.** The figure reports the methane reduction as a percentage of the relative controls for the different nitrate inclusion levels achieved at different fermentation times.

## AIMS

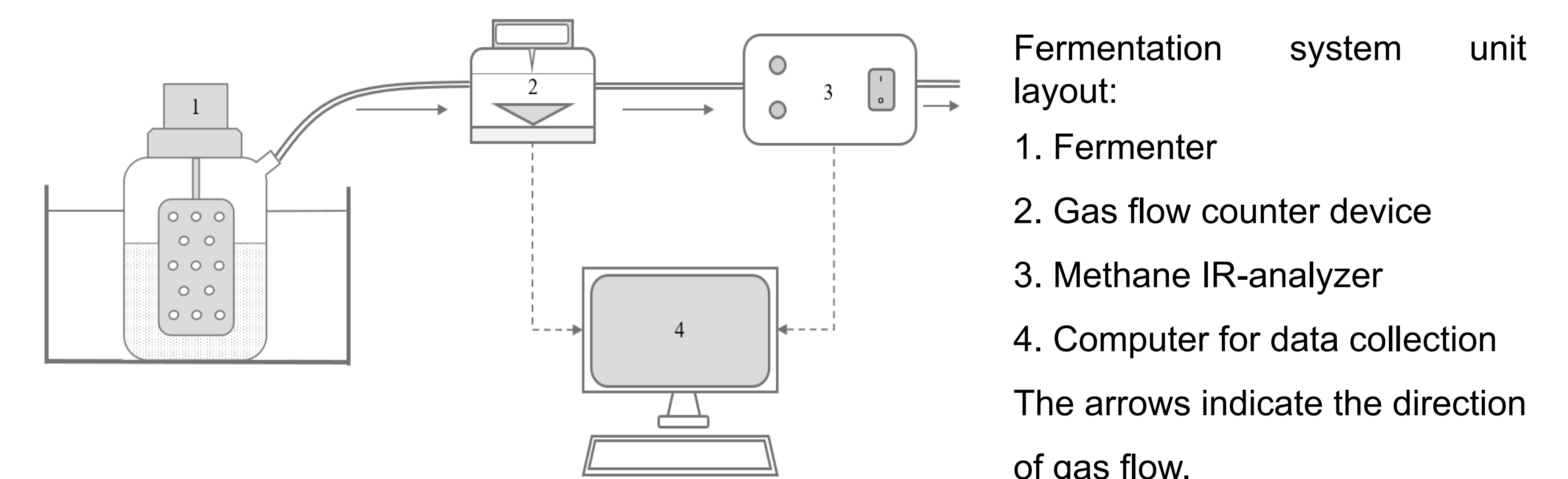
Considering the global challenges of next future, strategies to reduce the global impact of the livestock sector are fundamental to improving its sustainability. Special attention is given to methane derived from the enteric fermentation process of ruminants which accounts for 17% of global methane generated by the agricultural sector. The development of an *in vitro* equipment to study methanogenesis in ruminants represents a useful tool to meet future needs.

## APPLICATIONS

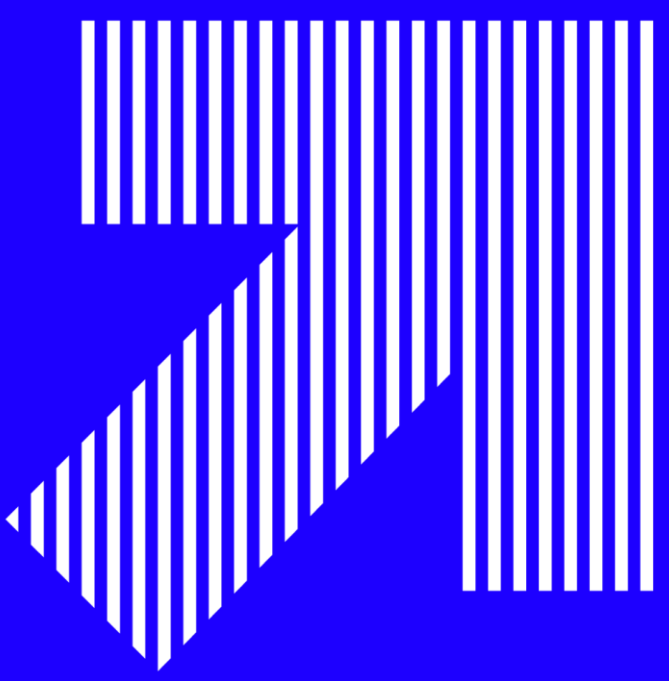
Throughout the application of our batch *in vitro* system that allows a continuous measure of methane generated during the fermentative process, it is possible to better understand the biological processes behind methanogenesis and to investigate potential strategies for its mitigation. Moreover, *in vitro* techniques represent a rapid, simpler, and less expensive alternative to *in vivo* trials promoting an improvement in animal welfare.

## RESULTS:

The outcomes achieved confirm the potential of *in vitro* techniques to study the rumen environment and its process. The equipment tested allows the continuous measurements of methane during the whole fermentation instead of an end-point measurement promoting a precise study of its kinetics and thus improving the overall accuracy of the total methane assessment. This characteristic enhances the ability to investigate the effectiveness of substances used as feed additives to reduce methane production. In particular, thanks to the methane continuous measurements was demonstrated that the antimethanogenic capacity of nitrates results be both time and dose-dependent. Without this approach, the efficacy of lower nitrate dosage was underestimated.







# Different approaches to identify genetic traits responsible for susceptibility and resistance to *Flavescence dorée* in grapevine

*Flavescence dorée*  
*Vitis vinifera*  
Susceptibility  
Resistance  
Genomics  
Transcriptomics

## AIMS:

In this PhD thesis different approaches were used with the general aim to better understand the grapevine mechanisms underpinning resistance and susceptibility to Flavescence dorée (FD) and to pave the way to the identification of genetic and genomic traits associated to FD resistance.

## APPLICATIONS:

Results obtained in the present thesis, and those that will be achieved in the future, will be useful for new breeding programs and clonal selection. Moreover, the knowledge of the molecular and metabolic mechanisms adopted by scarcely susceptible varieties and clones could help in the development, for example, of biostimulants capable to induce such defenses even in the most susceptible plants.

## RESULTS:

The study performed in a highly FD-infected vineyard showed the ability of Tocai friulano (a scarcely susceptible variety) to block and avoid the spread of the symptoms and the pathogen into the whole canopy.

The second PhD work concerns the study of a population obtained by a cross between two cultivars showing different susceptibility to FD. Genotyping by sequencing analysis was performed and the resulting SNP dataset was used both to construct a linkage map and to identify polymorphisms putatively involved in gene regulation. Parallely, the observation and the analysis of different FD symptoms in infected plants belonging to the progeny led to the identification of valuable phenotypic traits that could be used during phenotype evaluation aimed to QTL identifications.

Finally, the existence of differences in FD susceptibility among three Chardonnay clones was used to find out genetic variants distinguishing the less susceptible clone from the other two.



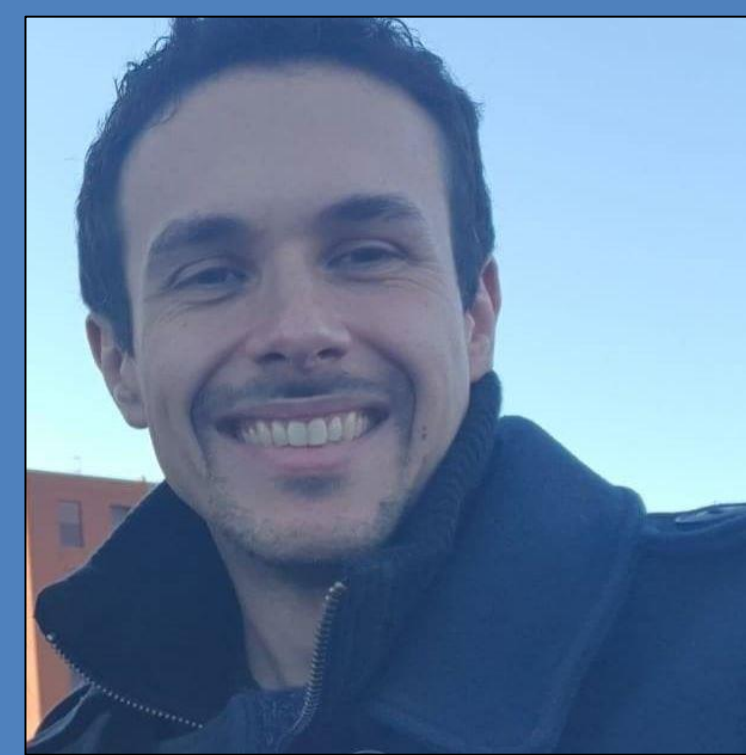


# ASSESSING THE IMPACT OF BEARS, WOLVES AND JACKALS ON EXTENSIVE LIVESTOCK PRACTICES IN NORTH-EASTERN ITALY

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## INTRODUCTION

In Friuli Venezia Giulia (north-eastern Italy) the main carnivores which may come into conflict with human activities are the brown bear (*Ursus arctos*), the grey wolf (*Canis lupus*) and the golden jackal (*Canis aureus*).

Within the region:

- From one to seven bears are genetically identified each year.
- Seven wolf packs are estimated to be present, at the very least.
- About 25-35 golden jackal packs are estimated to be present, at the very least.

Research questions:

- Is there a difference in terms of predatory pressure among predators?
- Is there a difference in terms of the overall number of predated individuals, also taking into consideration the affected livestock species and responsible predator?
- Is there a difference in terms of number of predatory events among seasons?
- Is there a variation in terms of compensations (€) recorded per year and considering each predator?
- Is there a difference in terms of number of predatory events between farms that use and don't use prevention measures?

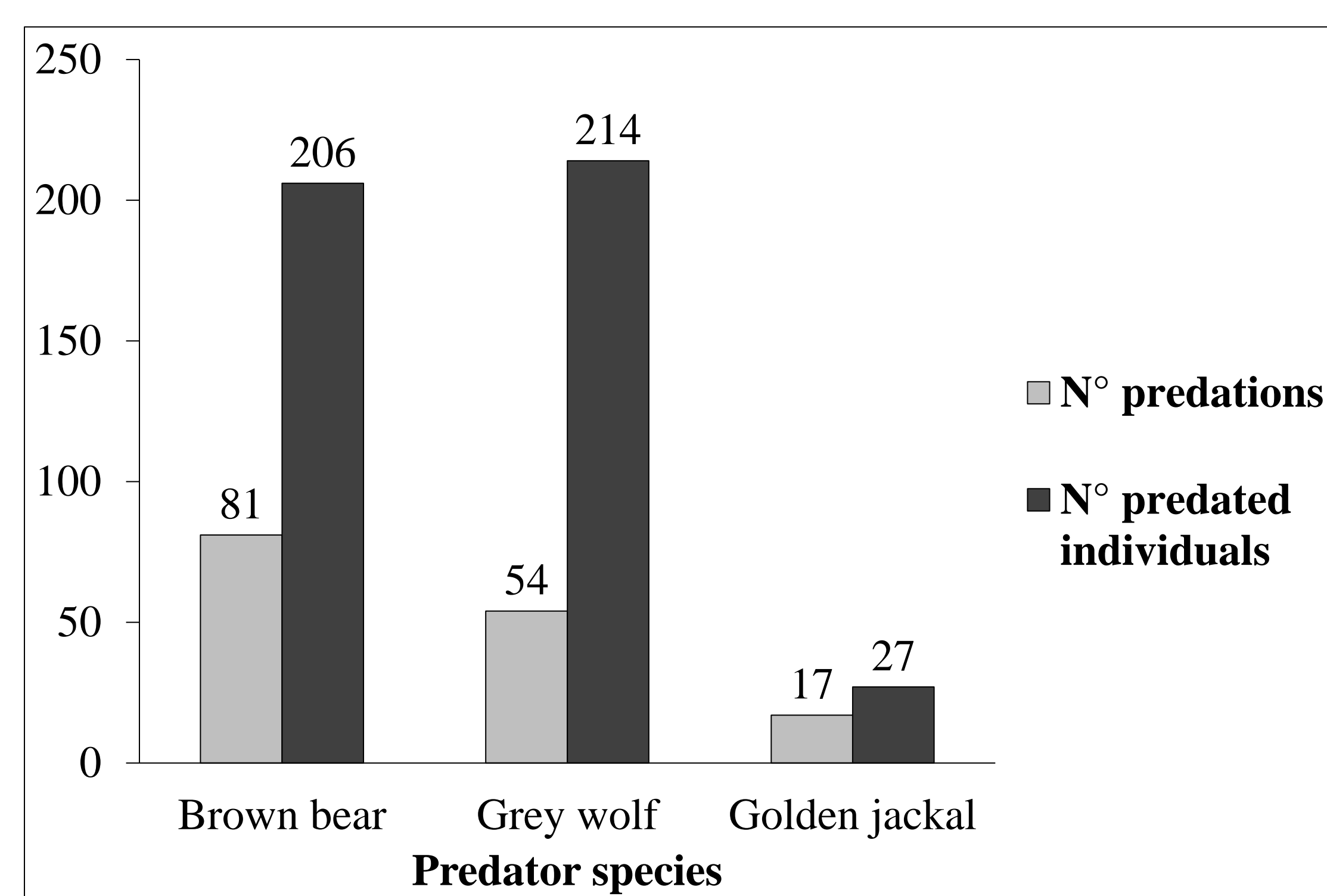
## METHODS

Data on carnivore predations (from 2009 to 2021) were collected by the regional wildlife technicians in collaboration with the researchers of the University of Udine and the members of the Regional Forestry Service.

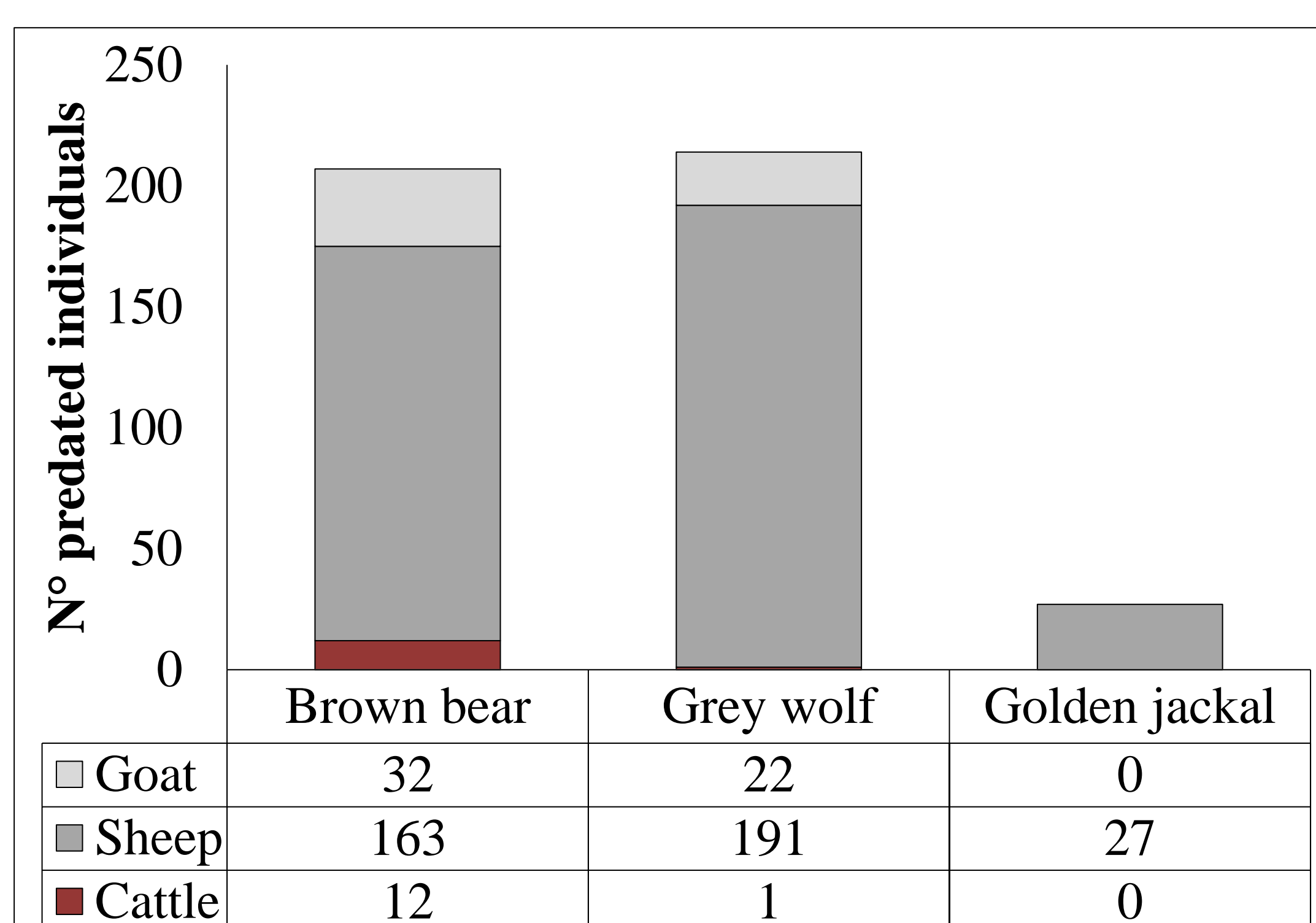
To answer questions (i), (ii), (iii) and (v), both the chi-square and Fisher's exact test (in the case of contingency tables showing values < 5) were used. The eventual difference among more than two categories was subsequently explored through the *pairwise nominal independent function* (*pnif*). To answer the question (iv) we used linear regression models.

## RESULTS AND CONCLUSIONS

We found a significant difference ( $\chi^2 = 61.12$ ,  $p < 0.001$ ) in terms of number of predatory events among predators: bears (n = 81, 53.29%), wolves (n = 54, 35.53%), jackals (n = 17, 11.18%) and in terms of number of predated individuals per predator ( $\chi^2 = 225.08$ ,  $p < 0.001$ ). However, in the latter case the only significant differences (*pnif*,  $p < 0.001$ ) were recorded comparing bears (n = 206, 46.08%) and jackals (n = 27, 6.04%), as well as wolves (n = 214, 47.88%) and jackals (**Fig. 1**). For what concerns bears, sheep (n = 163, 78.74%) were significantly (*pnif*,  $p < 0.001$ ) more predated than both goats (n = 32; 15.46%) and cattle (n = 12, 5.80%); and the same significance was observed for wolves: sheep (n = 191, 89.25%), goats (n = 22, 10.28%), cattle (n = 1, 0.47%). Regarding jackals, only predations at the detriment of sheep were observed (n = 27, 100%) (**Fig. 2**).

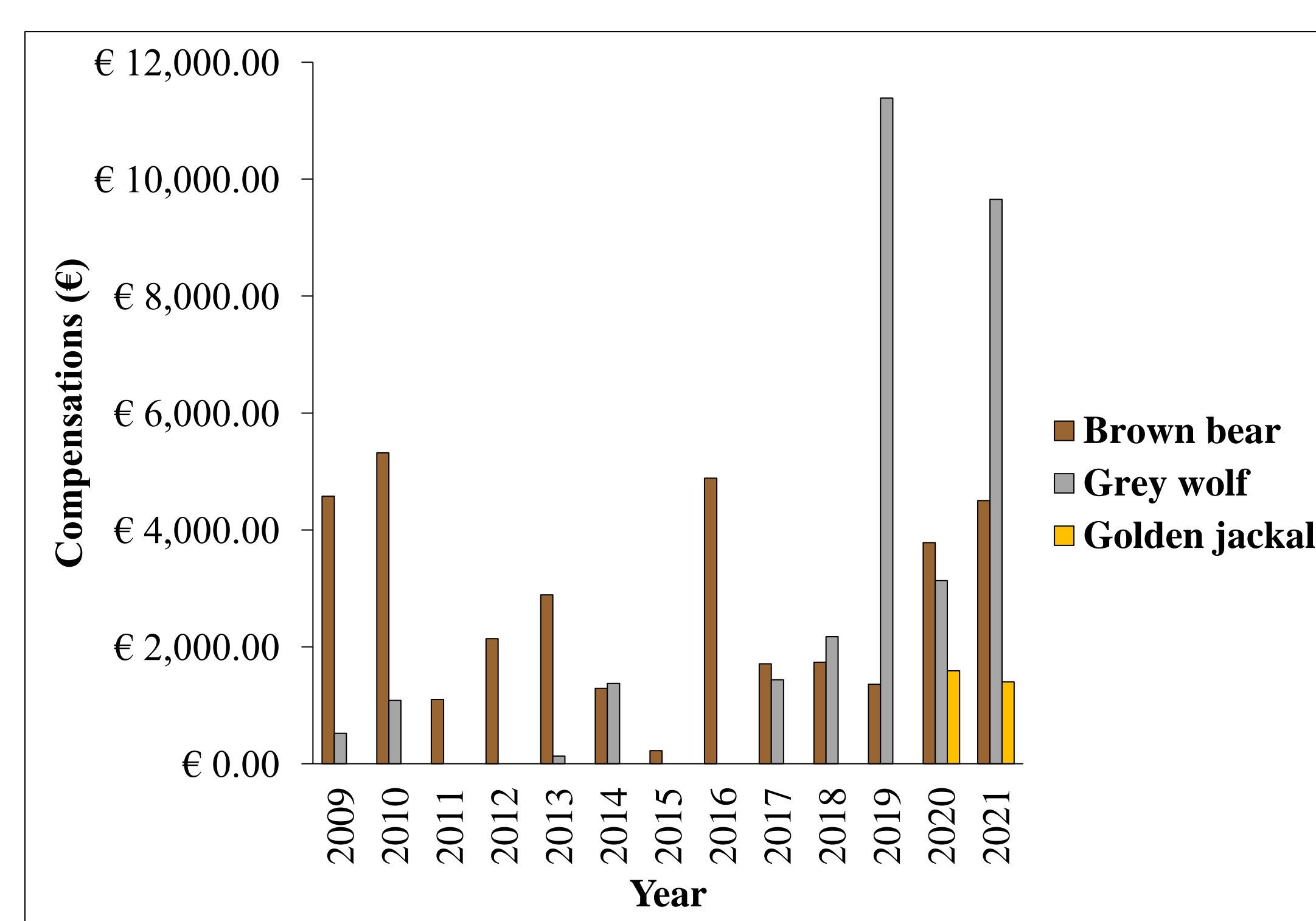


**Figure 1.** Difference in terms of number of predations and number of predated individuals per carnivore species.



**Figure 2.** Difference in terms of number of predated livestock species by each predator.

A significant difference ( $\chi^2 = 57.75$ ,  $p < 0.001$ ) in terms of number of predations was recorded among seasons: autumn (n = 25, 16.45%), winter (n = 12, 7.89%), spring (n = 53, 34.87%), summer (n = 62, 40.79%), with the only exception of spring vs summer (*pnif*,  $p = 0.34$ ). A significantly higher ( $\chi^2 = 16.12$ ,  $p < 0.001$ ) number of predations was observed in farms which did not use prevention measures (n = 94, 61.84%) compared to those that used them (n = 58, 38.16%). For what concerns bears, no significant variations (LM,  $R^2 = 0.008$ ,  $p = 0.77$ ) in terms of compensations was observed among years. Conversely, a significant high variation (LM,  $R^2 = 0.45$ ,  $p = 0.01$ ) was observed for wolves (**Fig. 3**).



**Figure 3.** Trend of compensations (€) per each predator from 2009 to 2021.

The higher number of individuals predated by wolves underlies the impact that wolves may have on livestock practices, especially in the light of its recent re-appearance in the region. Sheep confirmed to be easier to predate because of their smaller size and poor anti-predatory strategies. The higher number of predations recorded during the warm seasons match the transhumance period, during which animals are moved at higher elevations to feed in open pastures and, therefore, are more likely subjected to carnivore attacks.

The high number of predations recorded in farms that did not use prevention measures, suggests that the latter may effectively deter predators. Regarding bears, we did not observe significant variations in terms of compensations per year. However, data variability reported by the  $R^2$  did not allow us to elaborate strong inferences. Conversely, for wolves, higher compensations were registered especially in the latest years. As for jackals, compensations were given starting from 2018 when the species was included in the list of 'potentially damaging carnivores' for human activities.

**Acknowledgments.** The authors are very grateful to Dr. Umberto Fattori, Drs. Giuliana Nadalin, Dr. Luca Cristofoli and all the members of the Friuli Venezia Giulia Region for sharing their data.





# Role of different N sources on Iron and Nitrogen interplay in tomato plants

Arianna Lodovici<sup>1\*</sup>, Sara Buoso<sup>1</sup>, Begoña Miras-Moreno<sup>2</sup>, Erika Martinelli<sup>2</sup>, Luigi Lucini<sup>2</sup>, Nicola Tomasi<sup>1</sup>, Roberto Pinton<sup>1</sup>, Laura Zanin<sup>1</sup>

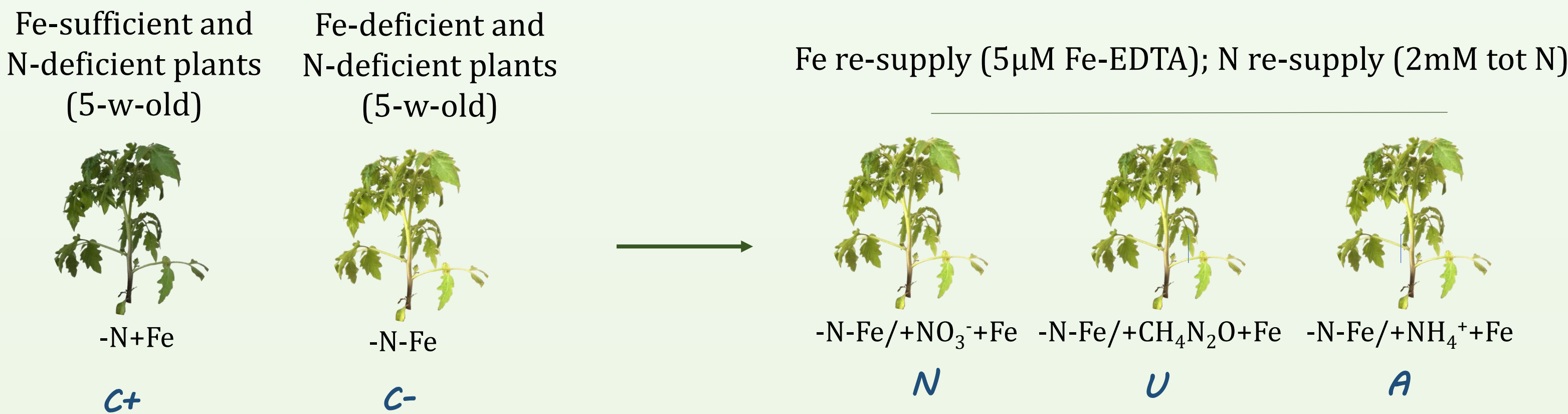
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<sup>2</sup>Department for Sustainable Food Process, Research Centre for Nutrigenomics and Proteomics, Università Cattolica del Sacro Cuore, Piacenza, Italy

## Introduction and aim

Iron (Fe) is one of the most abundant metal on the Earth’s crust, but it is poorly bioavailable under aerobic and calcareous conditions. Nitrogen (N) is the most required macronutrient by plants, and it has the peculiarity to be acquired by plants in multiple forms. Iron and N availability are two widespread limiting factors for plant growth in agricultural fields as they are involved in innumerable physiological processes in living organisms and thus their poor bioavailability in soils frequently exerts a strong constraint on crop yield. Aim of the present work is to investigate the effects of different nitrogen sources (nitrate, N; ammonium, A; urea, U; 2mM total N supplied) on tomato plant capability to acquire Fe and the resulting changes in transcription and metabolism.

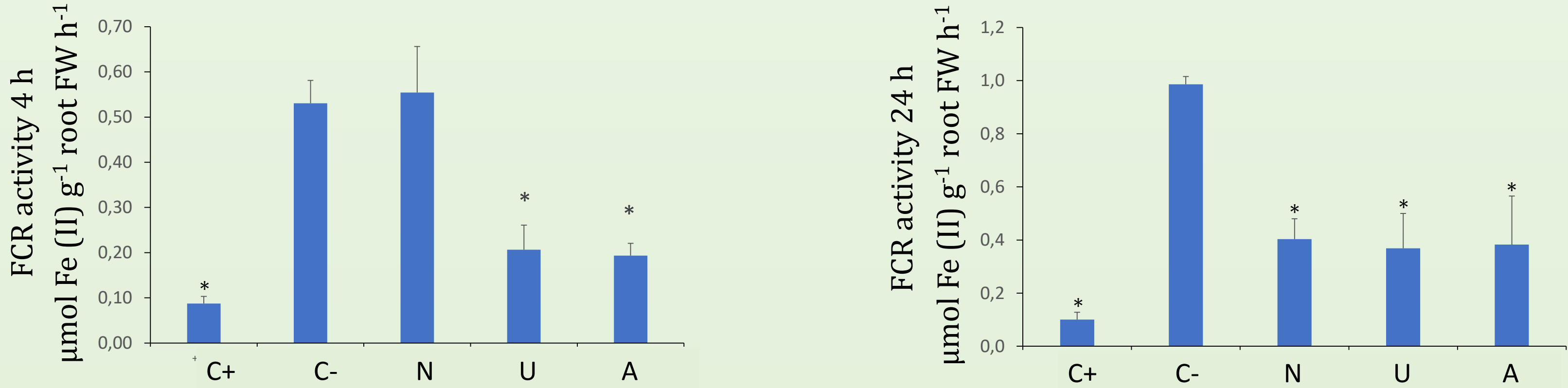
## Experimental setting



- Ionomic analysis
- Metabolomic analysis
- Transcriptional analysis
- Morphometric measurements
- Fe<sup>III</sup>-chelate reductase activity (FCR) evaluation

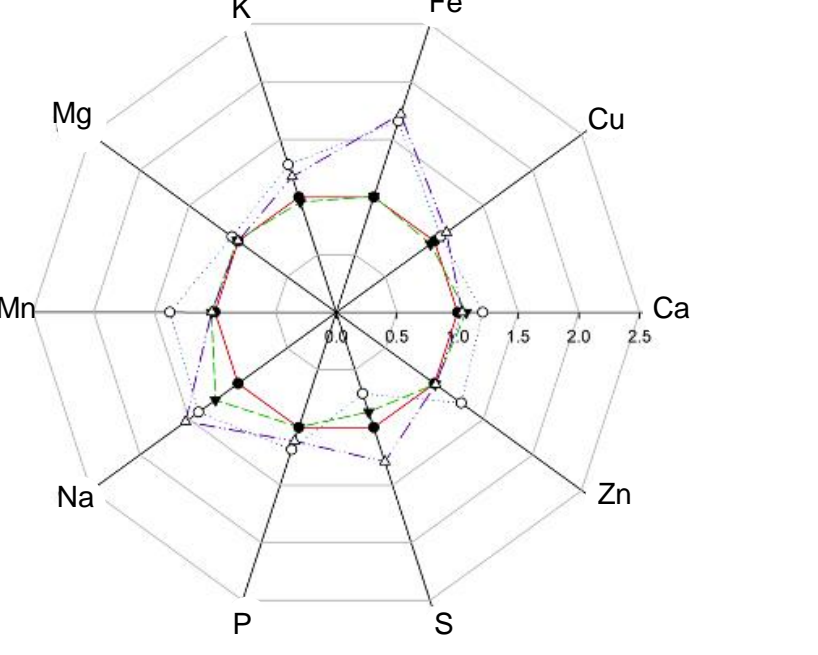
## Results

**Fe<sup>III</sup>-chelate reductase activity evaluation (FCR)** → Already 4 hours of Fe supply, the FCR activity of Fe-deficient plants slowed down if reduced nitrogen-forms were applied (U or A). While Fe resupply did not limit the FCR activity when N was applied (\*referred to significant difference between each thesis vs -N-Fe; One way ANOVA, Holm-Sidak p<0.05, N=3).

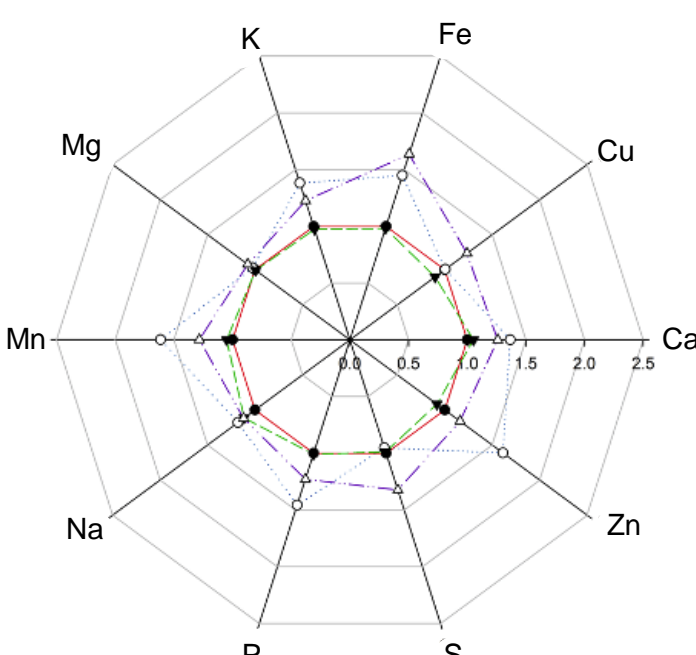


**Ionomic analysis** → Performed by ICP-OES and CHN-IRMS (C, Ca, Cd, Co, Cu, Fe, K, Mg, Mn, Mo, N, Na, P, S, Zn)

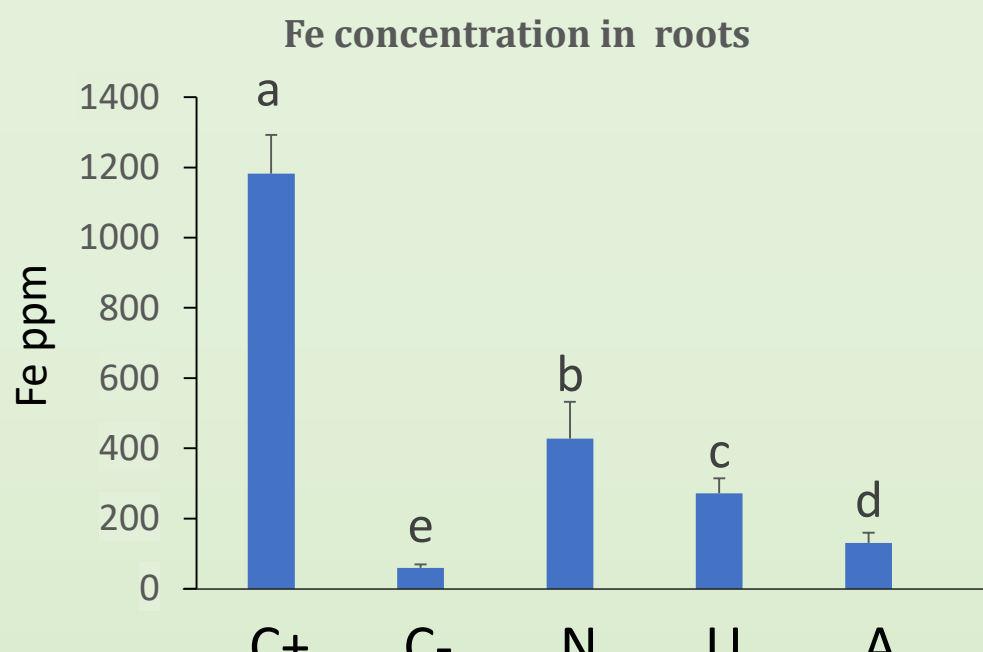
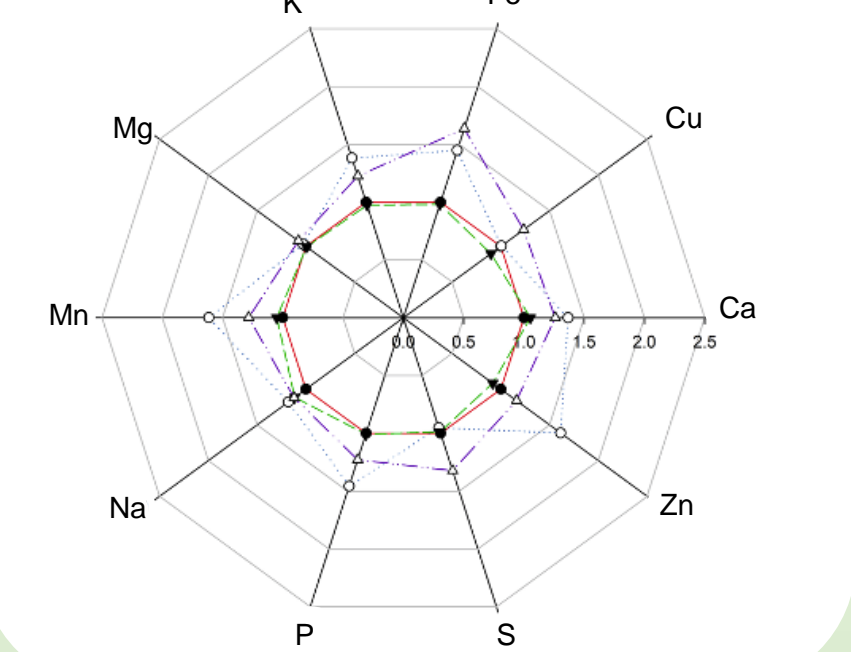
Young leaves (YL)



Old leaves (OL)



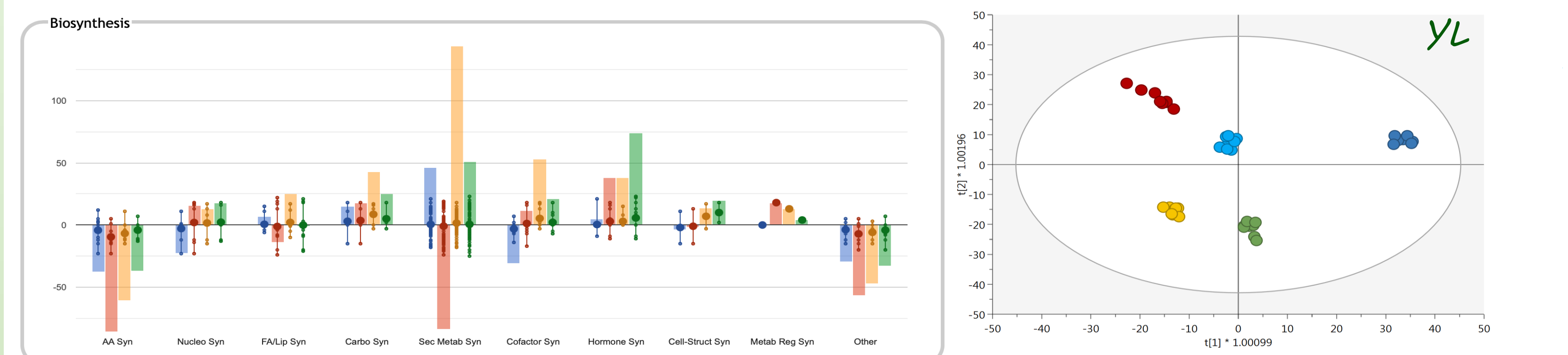
Roots (R)



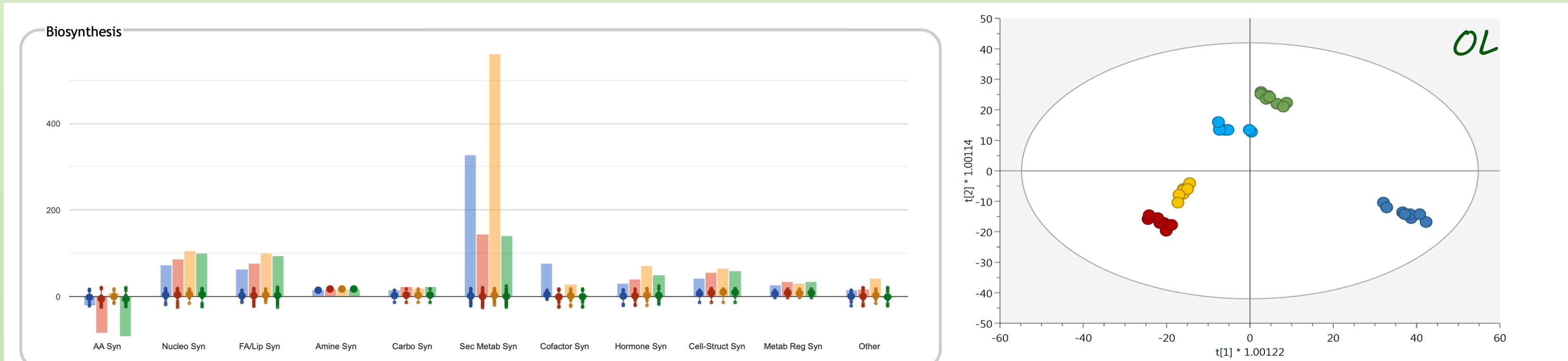
- N: increase of Mn and Zn concentration in YL and OL, of P in OL, and of Fe and Mg in R in comparison to A, U or C-.
- A: increase of S concentration in OL in comparison to N, U or C-.
- U: increase of Na concentration in OL, YL and R in comparison to C-

**Metabolomic analysis** → Biosynthetic pathways modulation and Orthogonal Projections to latent structures discriminant analysis (OPLS-DA)

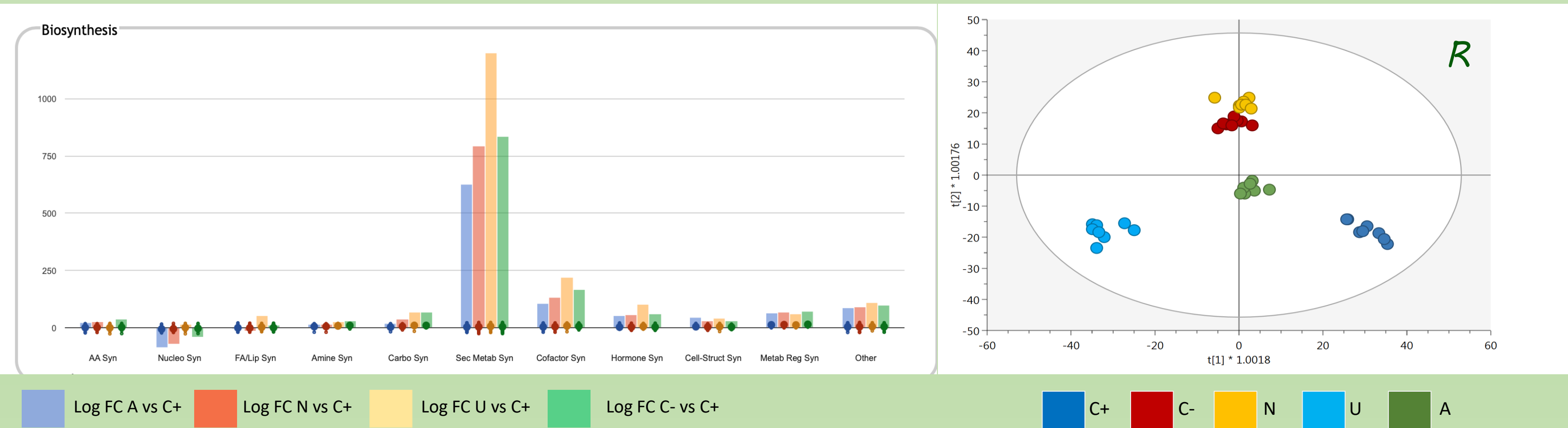
Young leaves



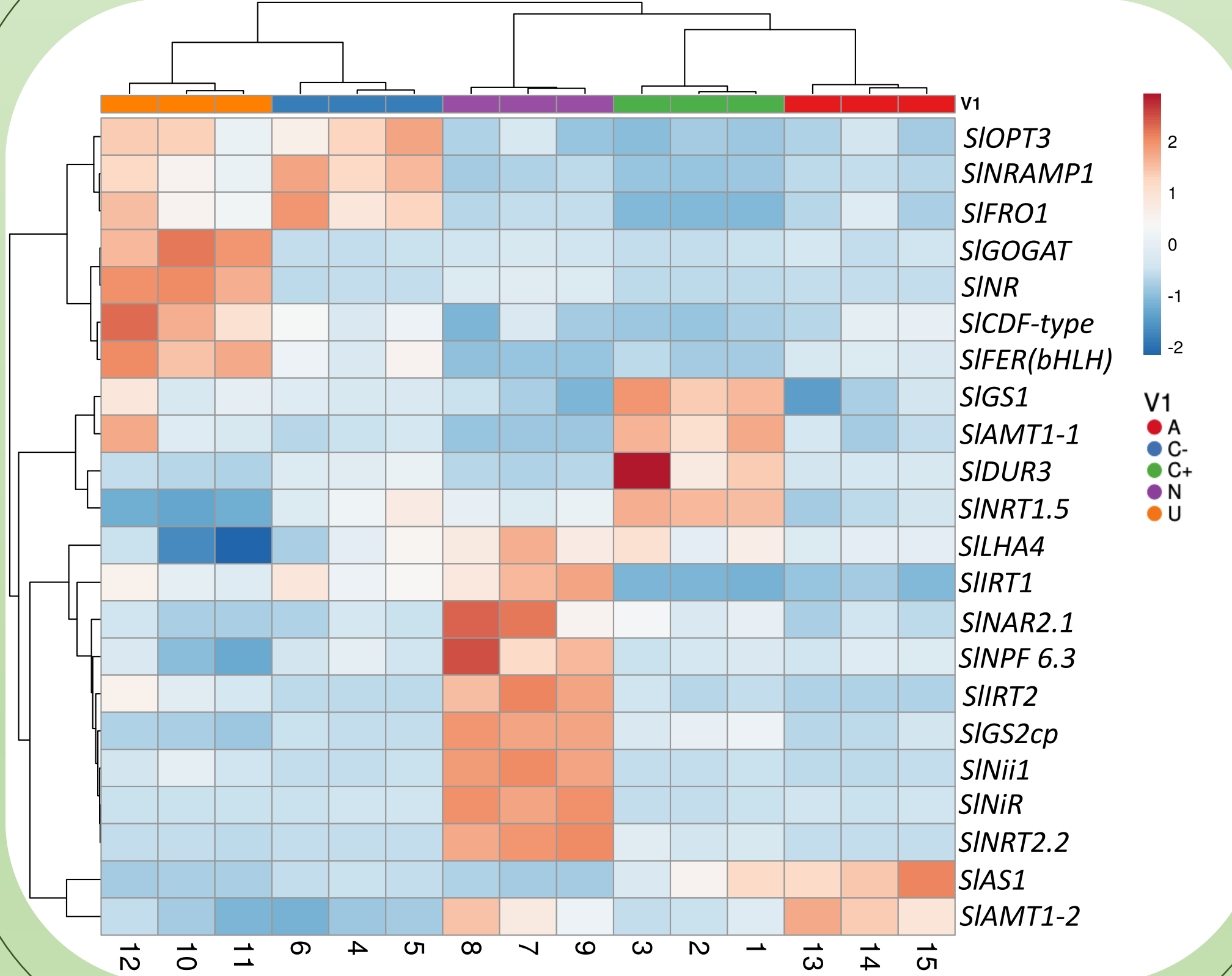
Old leaves



Roots



Gene expression analysis in roots



## Conclusions

Ionomic profiles were influenced by applied nitrogen form, in general, mineral nutrients content was more modulated in Fe-deficient plants treated with N rather than reductive nitrogen forms or C-, while U seems to led to a higher accumulation of nutritional elements in Fe-sufficient ones in comparison to N, A or C+. FCR results were further supported by gene expression analysis results, that showed an increased expression of transporter genes that may explain the observed higher micronutrients content in plants treated with N in comparison to other nitrogen forms or C-. Moreover, metabolomic profiles were influenced by nitrogen treatment, and overall, nitrogen supply seems to promote the biosynthesis of secondary metabolites in all the considered vegetal organs. Obtained results and the ongoing molecular analyses will help to better define the interactions between nitrogen sources and iron acquisition that could give clues on how to improve the use efficiency of nitrogen and Fe in crops.





# Hempseed By-Product in Diets of Italian Simmental Cull Dairy Cows and Its Effects on Animal Performance and Meat Quality .

**Keywords:** Hempseed cake;  
Cannabis sativa L.  
Cull cows; fatty acids profile;  
carcass traits.

**AIMS:** This research work was centered on the valorization of the Hemp sativa by-product obtained during the mechanical extraction, the Hempseed cake is rich in polyunsaturated fatty acids, so its use in the diets of cull cows could probably improve meat value and contribute to pursuing the objectives of a circular economy. The aim of this study was to investigate the effects of adding hempseed cake to the diet of IS cull dairy cows on performances and meat quality.

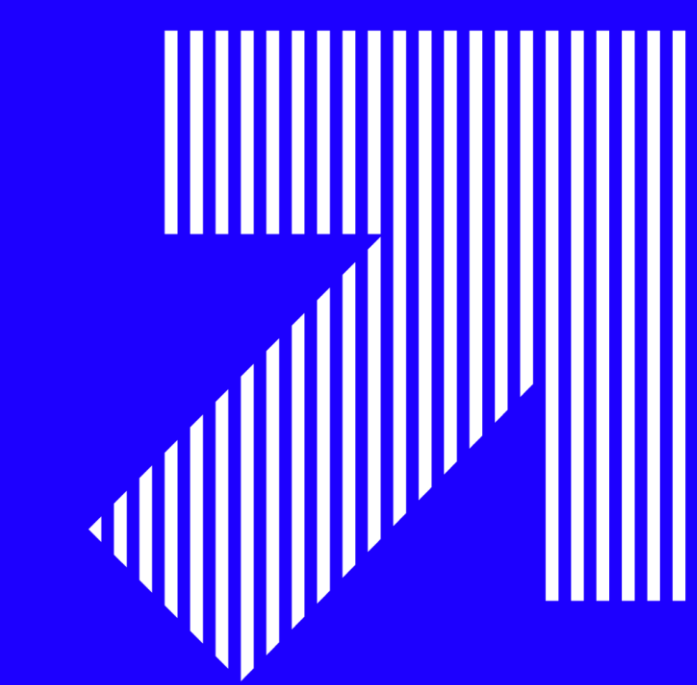
**APPLICATIONS:** The multiparous Italian Simmental cull dairy cows were divided into three dietary groups: hay-based (H, n = 10), corn silage-based (CS, n = 8) and pasture-based (Pa, n = 8) diets. The animals were equally divided into two treatments based on the protein source of the concentrate: hempseed cake (HEMP) or soybeans meal (SB). At the beginning of the trial, HEMP and SB groups had similar initial body weight ( $609.6 \pm 13.87$  kg), age ( $86.8 \pm 6.60$  months) and body condition score ( $3.14 \pm 0.087$  points).

**RESULTS:** Hempseed cake can replace soybean in the diet of cull cows up to 5% DM, without affecting in vivo performance, carcass characteristics and meat quality in terms of color, cooking loss and shear force. The fatty acids composition of intramuscular fat was similar between experimental groups, with the exception of the desirable fatty acids (DFA) level, which was lower in the animals fed with hempseed cake.

This study showed that hempseed cake can replace soybean meal, thus improving the circular economy.







# Hyperbaric Storage as an innovative technology to extend stability and functionality of food

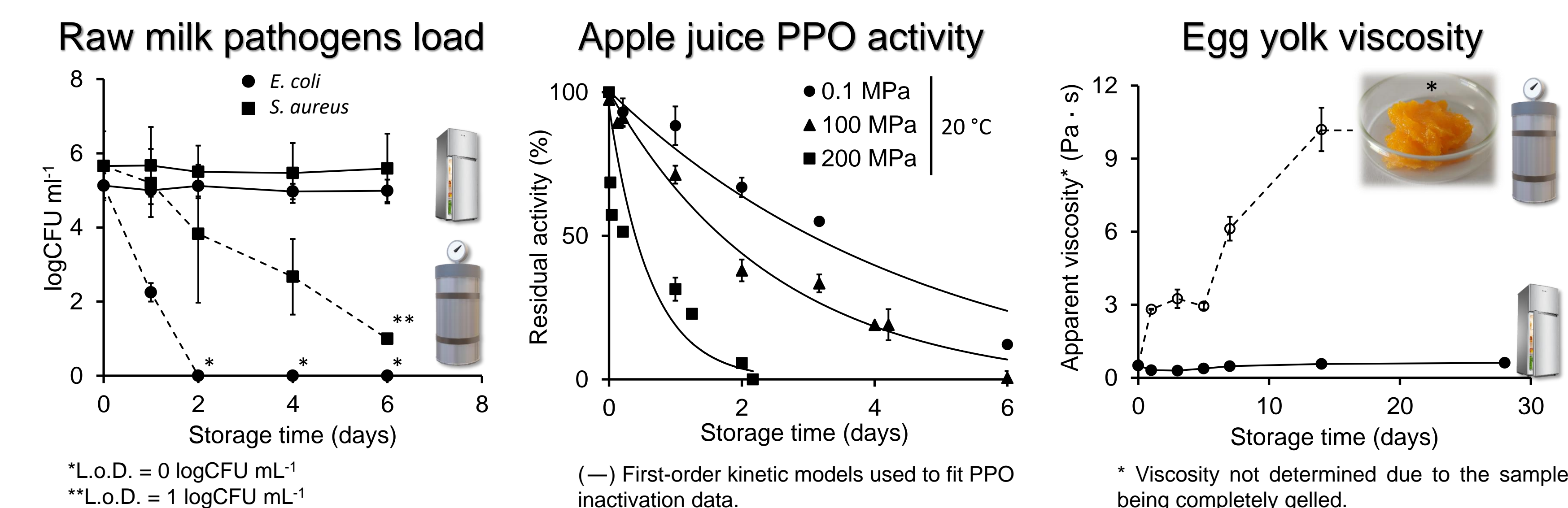
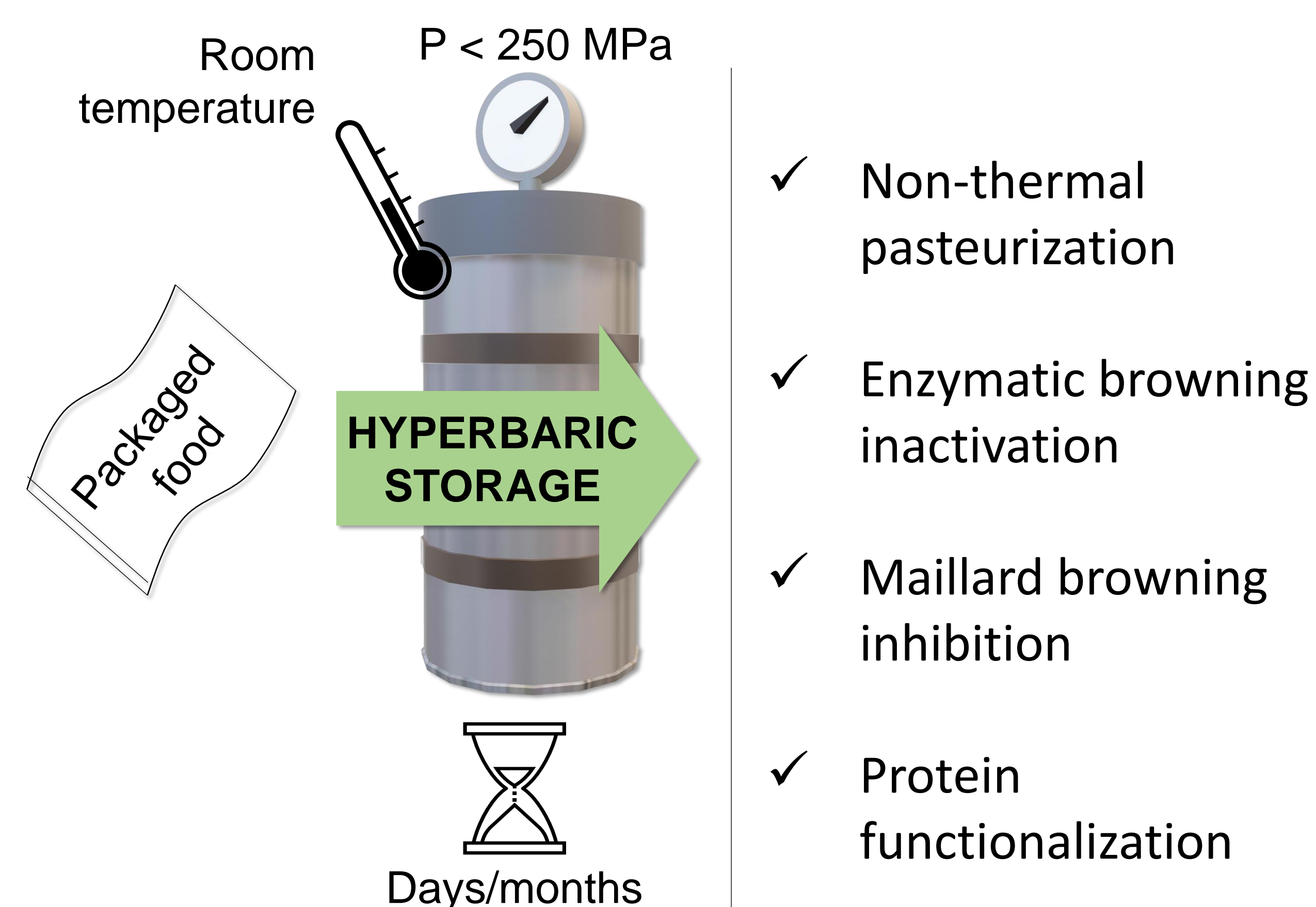
*In this Thesis, moderate hydrostatic pressure was used to concomitantly stabilize and functionalize food during storage at room temperature*



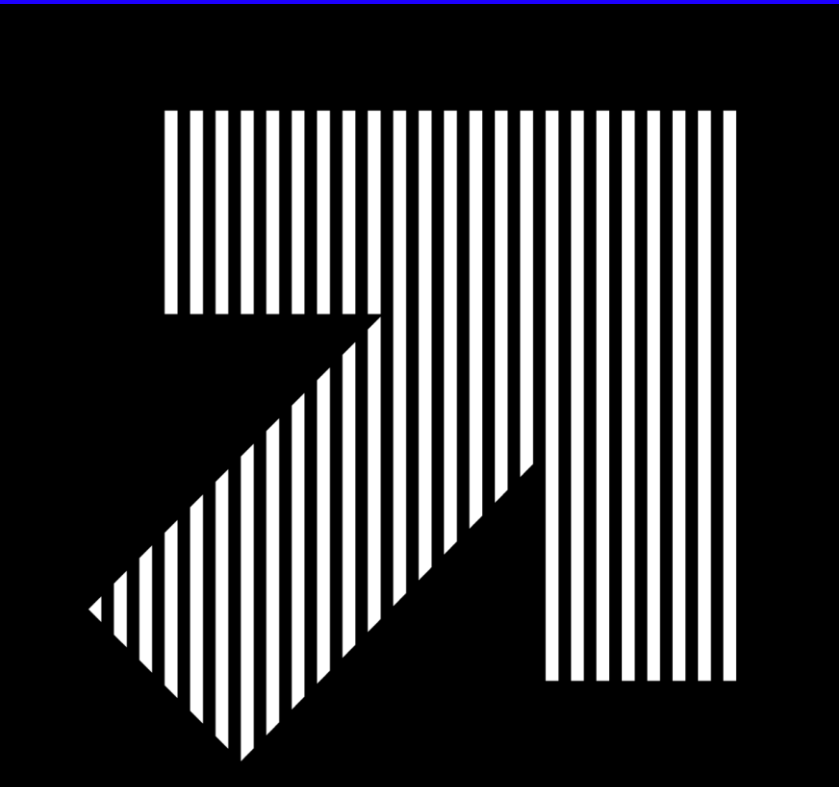
**AIMS:** This Ph.D Thesis was structured as a multi-aspect study on hyperbaric storage (HS). The attention was focused on: (i) the identification of packaging solutions feasible for HS; (ii) the capability of HS to obtain microbiological, enzymatic and chemical stabilization of food; (iii) the modification of the structure of proteins by HS to improve the technological functionality of food.

**RESULTS:** In the first part of the Thesis, the feasibility of food packaging materials for HS was tested considering single-layer (PET, PLA) and multi-layer (PA/PE, PP/EVOH/PE) solutions. Multi-layer films resulted adequate for HS and were thus used in the subsequent experiments. In the second part, the capability of HS to microbiologically, enzymatically and chemically stabilize food was demonstrated by achieving raw skim milk pasteurization, apple juice polyphenoloxidase (PPO) inactivation, and glucose-glycine Maillard reaction inhibition, respectively. The third and last part of the work was focused on the use of HS to steer food techno-functionality. By modifying protein structure, HS was capable to improve milk and egg white foaming and egg yolk rheological properties.

**APPLICATIONS:** The results achieved in this Thesis demonstrate the multi-tasking character of HS, which is concomitantly capable to stabilize and improve techno-functionality of food. The technology has thus the potential to evolve from storage technology solely to a non-conventional treatment improving food quality in a number of different ways. However, several gaps need to be filled to make HS viable for industry, with particular reference to the development of economically sustainable working units.

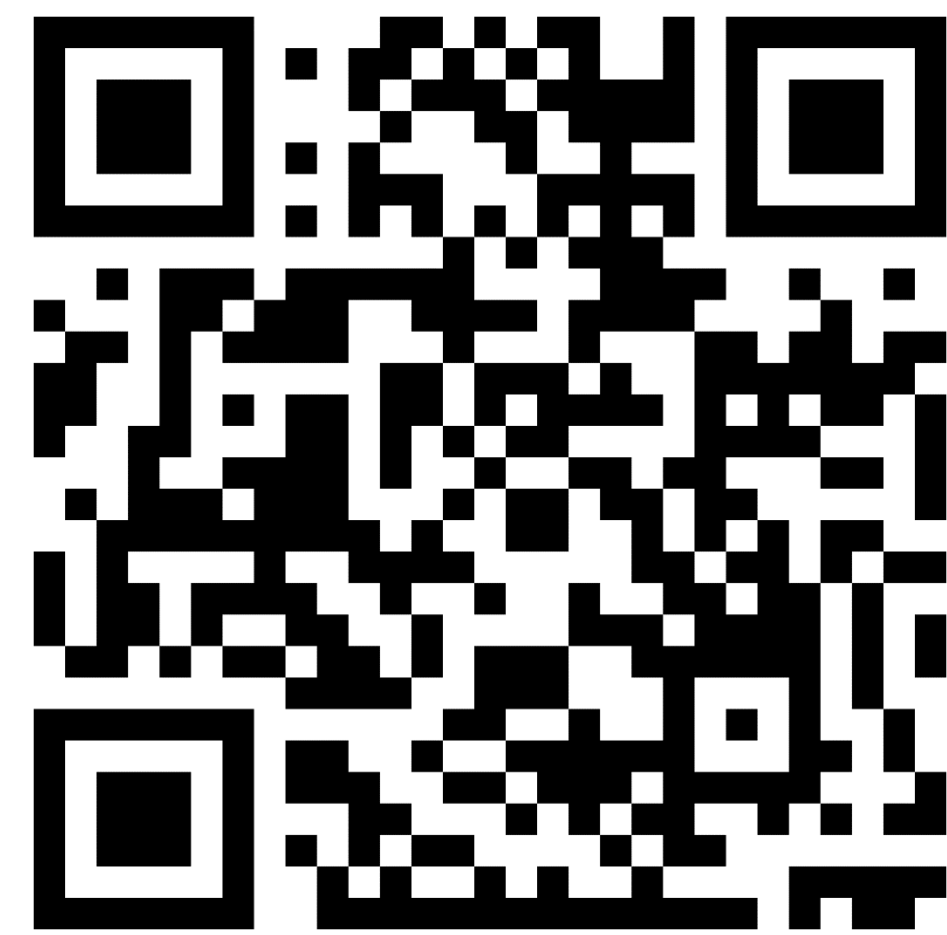






# Whole Genome Sequencing of ancient bacteria

## Draft Genome Sequences of Eight Bacilli Isolated from an Ancient Roman Amphora from IV-V century AD



- Paleomicrobiology
- Genome-sequencing
- Antibiotic-resistance
- Ancient Roman amphora
- Bacilli

The amphora and its content



### AIMS:

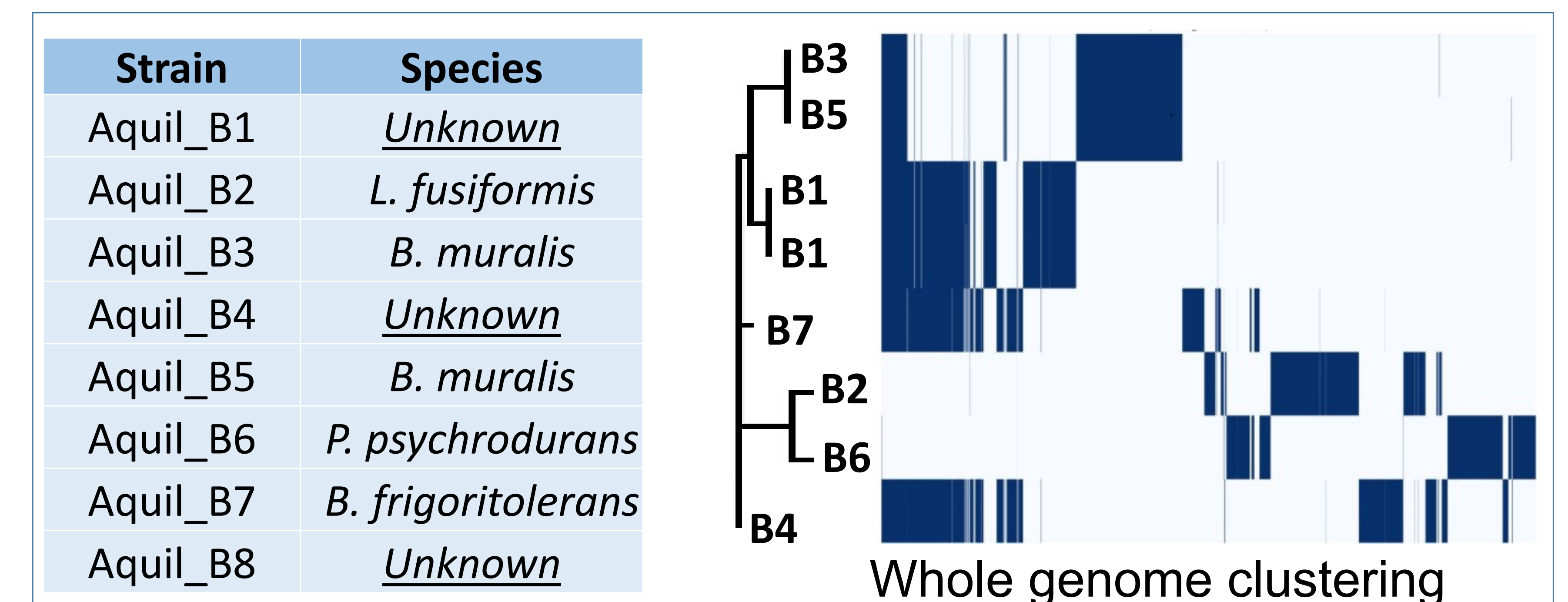
The various paleomicrobiological discoveries of recent years have made it possible to study important microbiological subjects, providing valuable informations. In this regard, the genetic characteristics of 8 bacterial strains isolated from a Roman amphora of the 4<sup>th</sup>-5<sup>th</sup> century AD, found intact and still sealed during excavations conducted in Aquileia were studied in this work. After being taxonomically identified, a comparison was then made with current genomes of the same species to identify the evolutionary differences.

### APPLICATIONS:

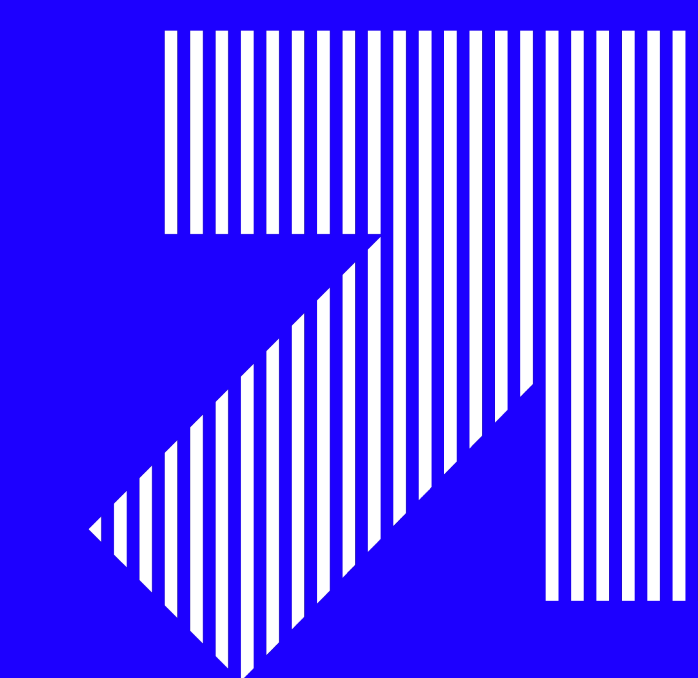
Through the compared study of these ancient genomes in respect to the modern species, it was possible to highlight the effects of evolutionary pressure on specific genetic features, for example the analysis the diffusion of antibiotic resistance traits.

### RESULTS:

*Bacillus* spp. spores were found at a concentration of 7.26 LogCFU/g. Following characterization by genetic fingerprint, 8 representative strains were chosen for whole-genome sequencing. Strains were then identified comparing ANI and dDDH values with the reference strains available in the literature, but three strains showed no genetic correlation with currently deposited sequences and could be considered new species. Following the search for resistance factors through specific databases, it was possible to identify resistance factors related to vancomycin, azaleucine, phosphomycin and arsinothricin in 5 out of the 8 strains considered. These results suggest a widespread presence of factors related to resistance to antibiotic substances already in an era in which their use was not widespread.







# FORMULATION AND PROCESSING STRATEGIES FOR OBTAINING BAKERY PRODUCTS TAILORED TO THE ELDERLY'S NEEDS

*Development of pea protein-rich bread intended for the elderly*

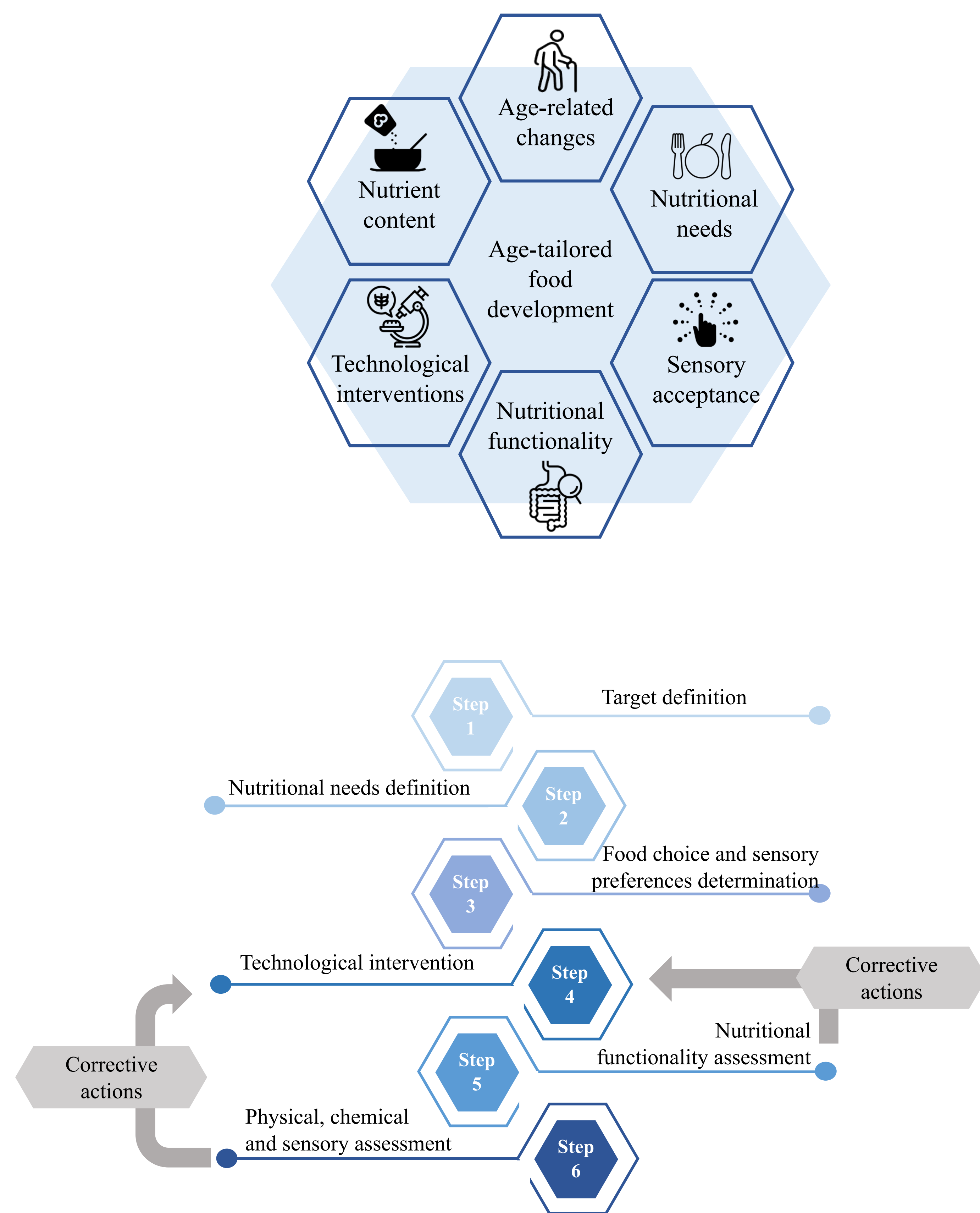


Fig. 1. Multi-step integrated approach.

## AIMS:

For the first time in history, the elderly population is growing worldwide and the number of the elderly (> 65 years) is predicted to increase to 2 billion by 2050. Nutrition plays a critical role in modulating the development of many age-related physiological changes and diseases. The aim of this Ph.D. project was to design a food (*i.e.*, bread) tailored to the elderly's needs that might fulfil nutritionally balanced diets, to promote active and healthy ageing, by applying a “multi-step integrated approach” (Fig. 1).

## APPLICATIONS:

Food consumption and dietary patterns are recognized as pivotal factors in promoting an active and healthy ageing. At this regard, the need to develop age-tailored food for the elderly is becoming increasingly pressing. Aging can bring about physiological and socio-economical changes that can impact nutritional needs and food preferences of the elderly. Tailoring foods to meet the specific nutritional needs of different age groups can help ensure that people are getting the nutrients they need to stay healthy.

## RESULTS:

A protein-enriched bread was developed by applying the approach in Fig. 1. The desirable sensory properties that an ideal bread targeting the elderly should have were identified as: homemade appearance, bread odor and flavor, and crumbly and soft texture. Based on these results and protein requirement of the elderly, bread with pea proteins, either untreated or high pressure homogenization-treated (HPH), was processed. Results showed that pea proteins led to improving the nutritional quality of the bread, and HPH processing shaped the functionalities and digestibility (Fig. 2a) of bread. The developed bread was well-accepted compared to commercial bread by the elderly (Fig. 2b). This Ph.D. thesis allowed taking a small step forward in tailoring food products able to satisfy the elderly nutritional requirements and to promote active and healthy ageing.

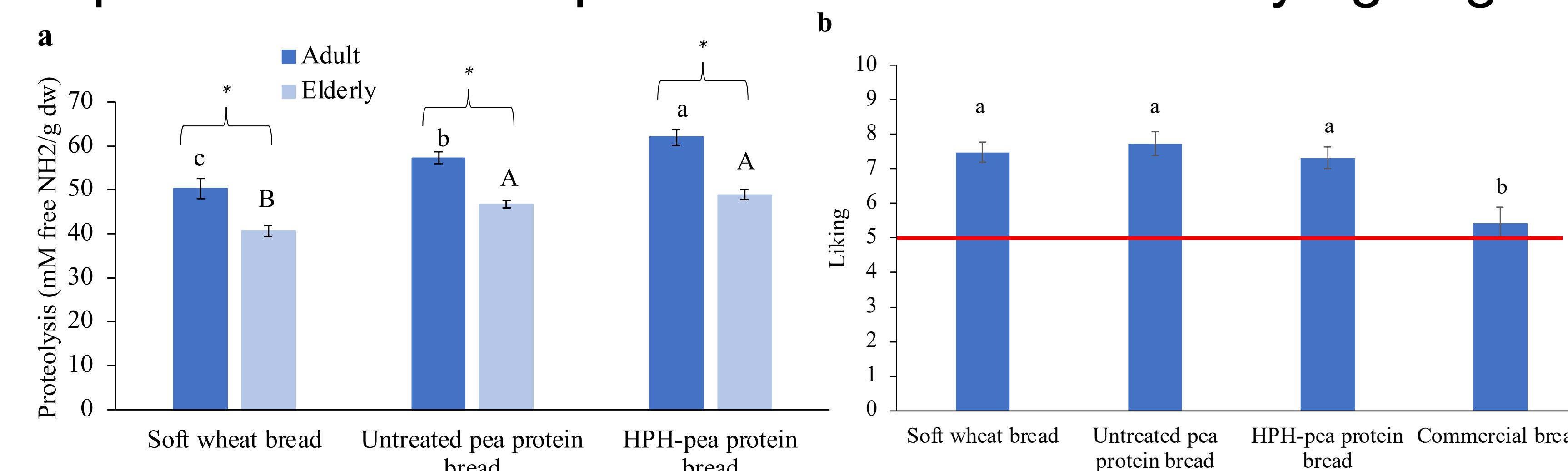


Fig. 2. Digestibility (a) and liking (b) of soft wheat, untreated and HPH-treated pea protein bread





# Investigation about new concepts of yeast derivatives for winemaking with enhanced antioxidant properties and polysaccharides content

Yeast derivatives with high content of antioxidant compounds and polysaccharides starting from non-*Saccharomyces* strains and by applying non-thermal technologies as innovative production process

## Keywords

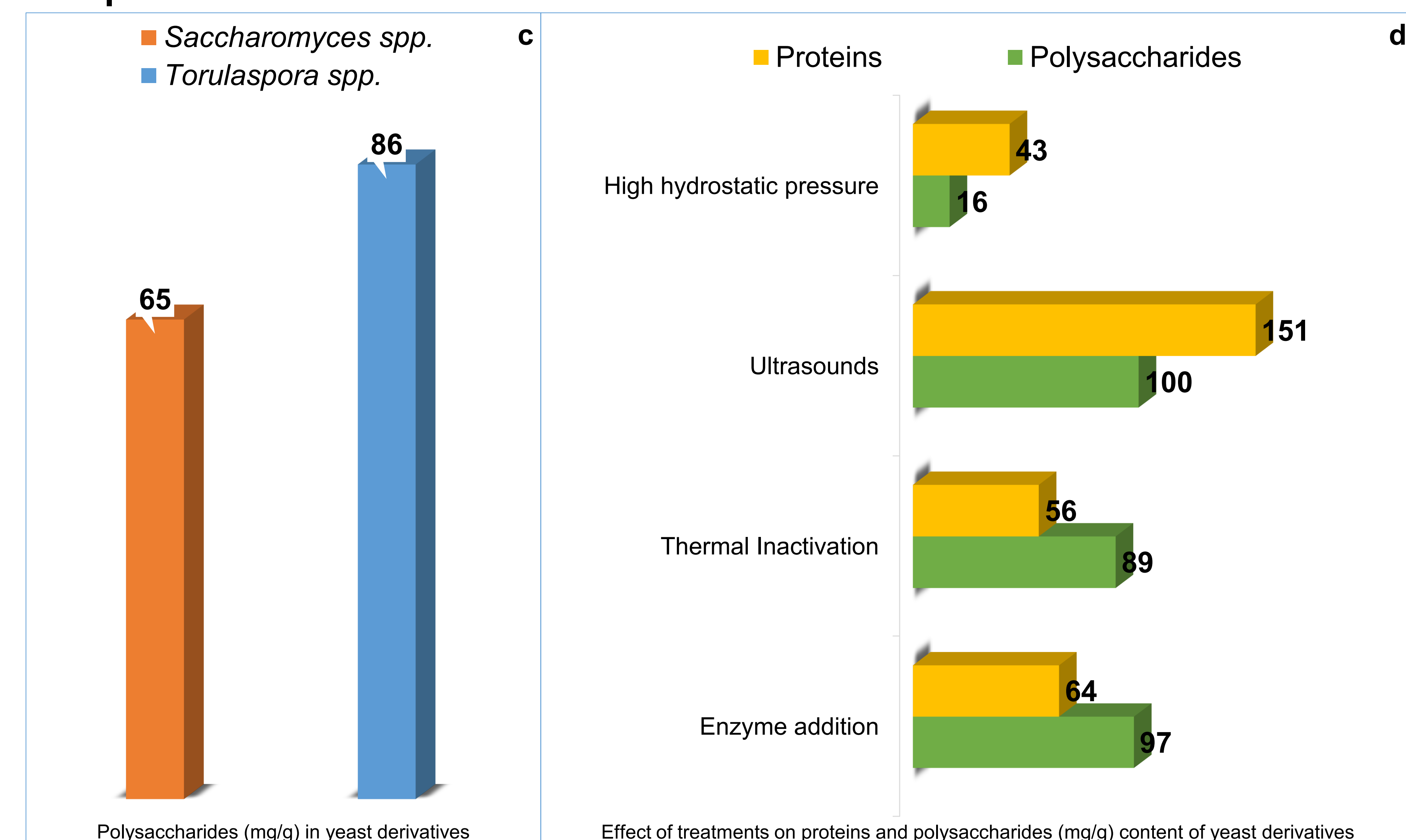
non-*Saccharomyces*; antioxidants, polysaccharides, yeast derivatives, non-thermal technologies, aging

## AIMS

Production of innovative yeast derivatives for winemaking use, with better chemical composition, high antioxidant properties and low odor impact, starting from non-*Saccharomyces* strains, by using non-thermal approach. Evaluation of different strains and processing technologies (emerging vs traditional methods) on yeast derivatives composition and on wine quality and stability during aging

## RESULTS

Both strains and technology affected the chemical composition of yeast derivatives. *Hanseniaspora* spp. (a) and high-pressure treatment (b) released considerable amount of glutathione, whereas high content of soluble molecules, polysaccharides and proteins, were found in derivatives obtained by *Torulaspora* spp. (c) or by ultrasounds (d). During aging, the addition of yeast derivatives determined a good protective effect against oxidation, comparable to sulfur dioxide; the volatile profile was more complex in wines added with derivatives obtained by ultrasound or with lees obtained by *Hanseniaspora* spp. treated by high-pressure. In general, ultrasounds gave results similar to enzyme addition, whereas high-pressure was comparable to thermal inactivation.



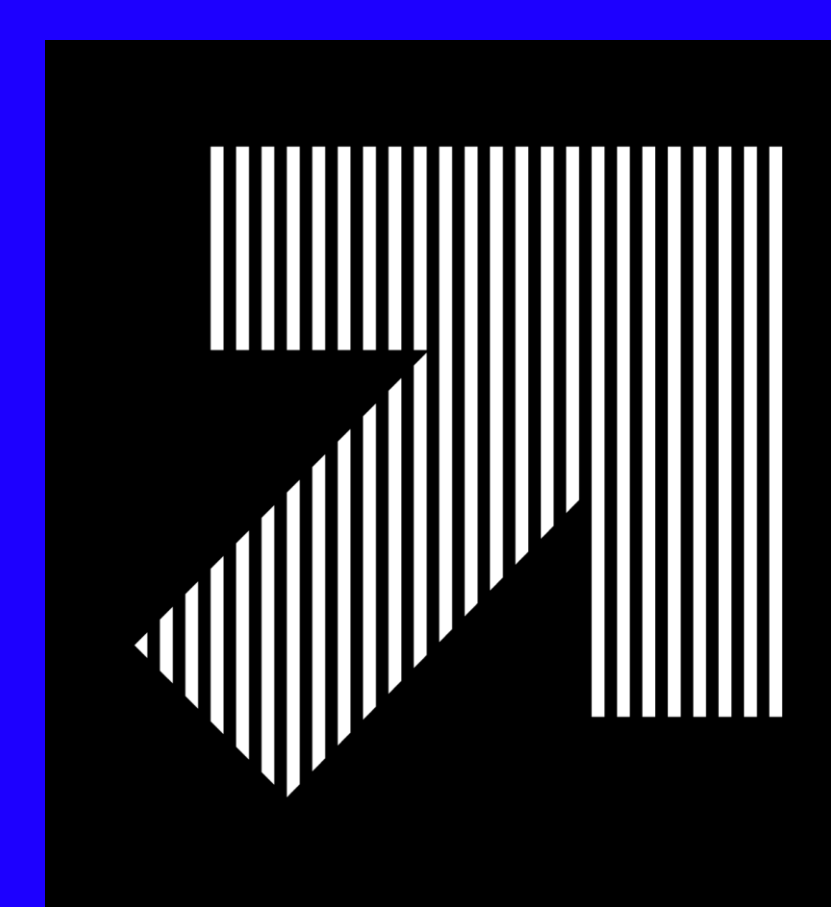
## APPLICATIONS

Use of *non-Saccharomyces* strains for producing yeast derivatives, with high content of antioxidants and polysaccharides.

Emerging technologies as low-cost and low-energy alternatives to traditional methods for producing yeast derivatives.

In relation to composition, by combining strain and appropriate technology, different products with different applications may be obtained, *i.e.*, fermentation and wine quality enhancers.





# IL QUADRO SOCIOLINGUISTICO E GLI INTERPRETI NEI CAMPI DI CONCENTRAMENTO FASCISTI PER CIVILI JUGOSLAVI (1941-1943)

*La società, le lingue ed il ruolo degli interpreti nei campi di concentramento voluti dal fascismo per gli abitanti della Jugoslavia occupata*

GONARS	ARBE
VISCO	BUCCARI
TREVISO	MELADA
PADOVA	COLFIORITO
ANGHIARI	MAMULA

## OBIETTIVI:

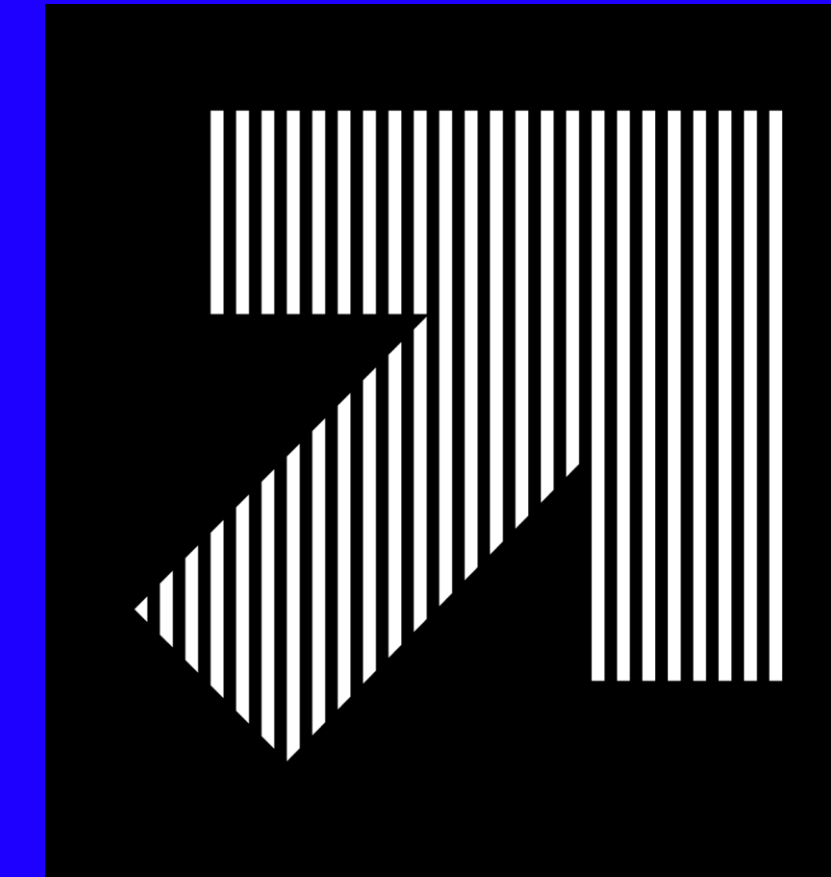
La tesi affronta l'argomento dei campi di concentramento fascisti per civili jugoslavi, strutture create dal regime fascista e rimaste in funzione tra il 1941 e il 1943, che videro l'internamento di circa 100.000 persone. Il focus principale riguarda la situazione sociolinguistica e la figura dell'interprete, argomenti finora mai trattati in maniera ampia e di cui la ricerca si occupa per la prima volta. I materiali analizzati sono in italiano, sloveno, croato e serbo. Si tratta di memorie scritte e orali di ex internati, di testi e disegni prodotti nei campi, di relazioni e documenti interni al Regio Esercito ed alla Chiesa Cattolica. Il lavoro intende contribuire ad una maggiore elaborazione critica dei crimini compiuti dal fascismo ai danni della popolazione civile durante l'occupazione della Jugoslavia.

## RISULTATI:

La ricerca evidenzia una quotidianità dominata da fame, violenza e incertezza. Gli internati, privi di prospettive e divisi su base nazionale, sociale, politica e religiosa, sviluppano un uso della lingua ricco di italianismi e di toponimi ed etnonimi ironici e sarcastici, il *lageržargon*. Gli interpreti, scelti tra i soldati bilingui o tra gli stessi internati, si ritrovano a dover mediare in una situazione di forte squilibrio, nella quale le autorità hanno potere di vita o di morte sui prigionieri.







# INTENSIFICATORI SINTAGMATICI DELL'ITALIANO CONTEMPORANEO. PROPRIETÀ SEMANTICHE E DISTRIBUZIONALI.

Parole sintagmatiche;  
espressioni idiomatiche;  
*multi-words expressions*;  
intensificazione; corpora;  
semantica

## AIMS:

Il lavoro di tesi ha come obiettivo l'analisi semantica e distribuzionale di alcuni modificatori sintagmatici dell'italiano che veicolano intensificazione. Tali strutture presentano al loro interno un item lessicale afferente alle aree semantiche della morte, della paura e della pazzia. Lo studio contribuisce all'analisi sul comportamento delle parole sintagmatiche dalla semantica idiomatica, campo di studio poco indagato per l'italiano.

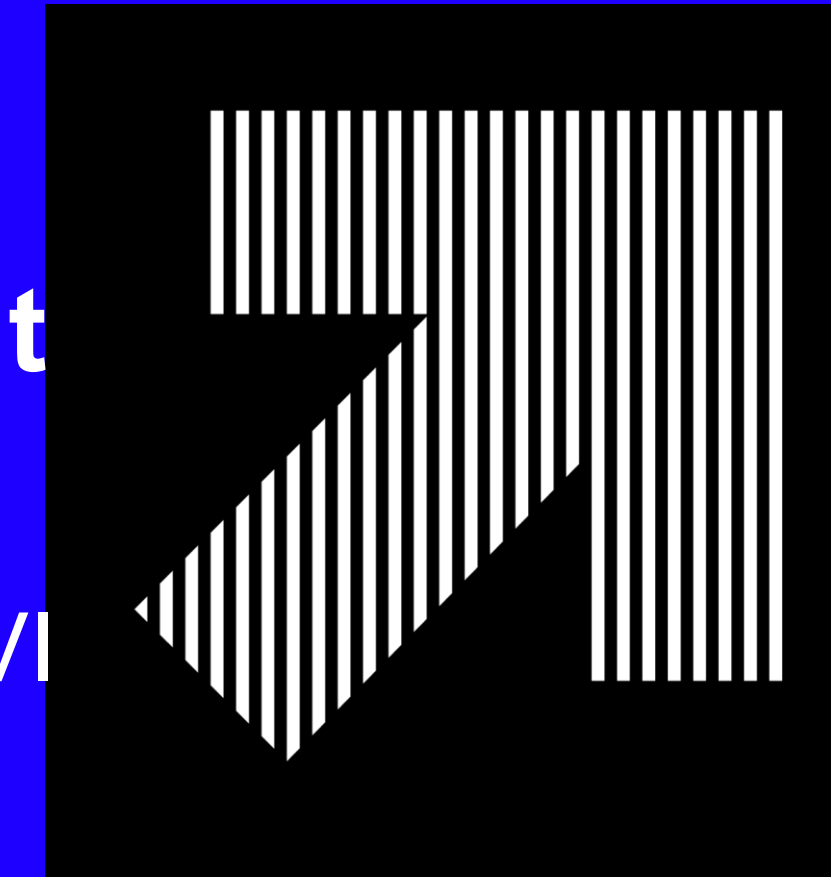
## APPLICATIONS:

I risultati, assieme ai dati estratti dal corpus dell'italiano online ItTenTen20, contribuiscono alla ricerca sulle parole sintagmatiche in italiano. Le analisi semantiche qui contenute contribuiscono inoltre alla riflessione sul comportamento distribuzionale delle espressioni idiomatiche. I risultati mostrano una convergenza fra tratti distribuzionali e specializzazioni semantiche dei pattern di riferimento. Il database può essere utilizzato come benchmark per lavori futuri sul tema.

## RESULTS:

I risultati del lavoro contribuiscono a tracciare un quadro dell'uso dei seguenti intensificatori sintagmatici: *da morire*, *a morte*, *da paura*, *come* + DET + *matto/pazzo*, *da matti/da pazzi*, *da impazzire*. Si è tentato di verificare se questi modificatori rappresentassero un network Costruzionale all'interno del quale si verificassero delle regolarità formali e semantiche. Abbiamo notato come queste strutture modifichino preferenzialmente verbi, tranne il sintagma *da paura* che co-occorre con più frequenza con nomi. Le classi semantiche dei verbi più modificate sono quelle dei verbi di movimento e dei verbi psicologici. I sintagmi in co-occorrenza con queste classi di verbi vengono usati come intensificatori puri, ovvero senza contributo referenziale apportato dall'item lessicale al loro interno.





## Arte contemporanea, supermusei e città in Italia tra anni Ottanta e Duemila

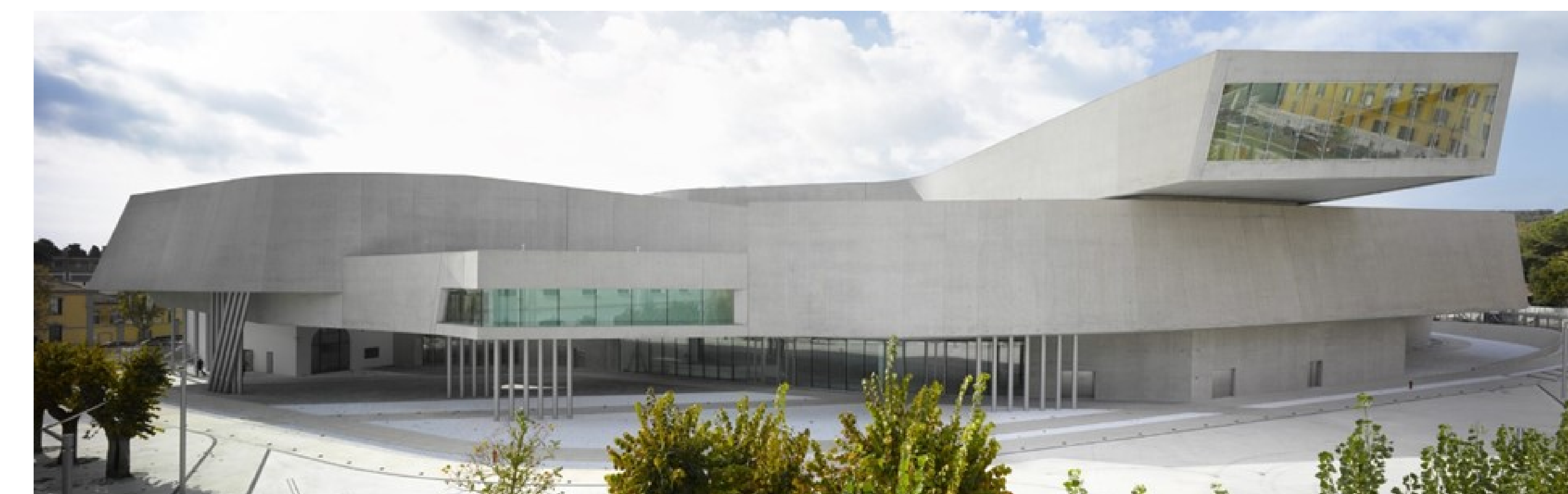
*Il MART di Rovereto, Casa Cavazzini a Udine, il MAXXI di Roma, Museion di Bolzano*

Musei  
Arte Pubblica  
Spazio Urbano  
Anni Novanta

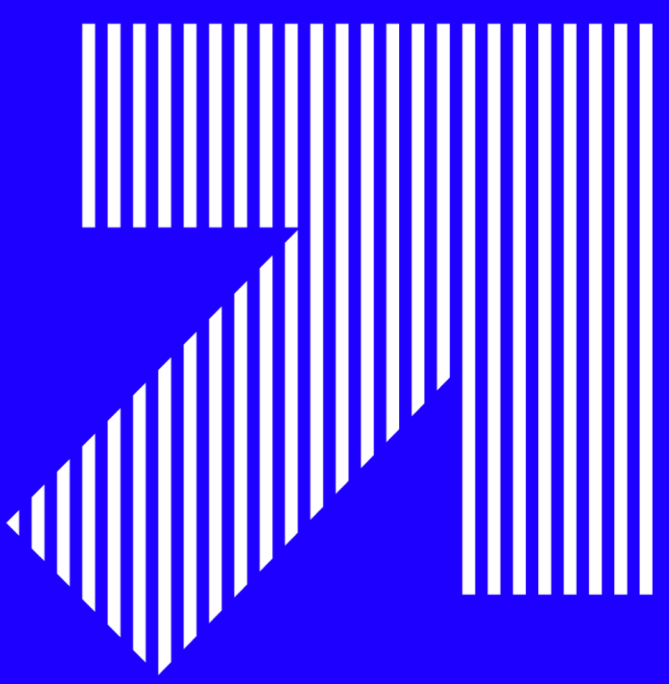
Questo lavoro di ricerca si è proposto di indagare la nascita dei primi musei d'arte moderna e contemporanea in Italia tra gli anni Novanta e Duemila, nell'epoca in cui si diffusero i cosiddetti supermusei. Il tema principale su cui si è focalizzato la tesi è la modalità con cui i diversi protagonisti sulla scena museale hanno voluto stabilire, almeno nelle intenzioni iniziali, un rapporto stretto e nuovo tra le loro istituzioni e con le città di insediamento. Si è perciò approfondito il rapporto tra i musei e gli artisti, in particolar modo riguardo a commissioni d'arte appositamente pensate per lo spazio urbano.

Per questo motivo si è inteso delineare le caratteristiche del contesto museale internazionale, concentrandosi soprattutto sul periodo di vent'anni intercorso tra l'apertura al pubblico del Centre Pompidou nel 1977 e quella del Museo Guggenheim di Bilbao nel 1997. Quindi è stato preso in considerazione anche il fenomeno dei giardini museali all'aperto nonché la serie di iniziative di arte nello spazio pubblico portate avanti dalle istituzioni museali, con una netta influenza anche sulla relazione tra museo e città.

Il cuore del lavoro è stata però l'indagine di quattro casi-studio: due supermusei, il MART a Rovereto e il MAXXI a Roma, e due musei di dimensione locale, il Museion a Bolzano e Casa Cavazzini a Udine. Le quattro istituzioni hanno avuto in comune l'essere state individuate come perni di un rinnovamento cittadino, sia in senso urbano che in senso culturale e artistico. Se il MART e il MAXXI sono divenuti sia a livello architettonico che a livello simbolico dei nuovi punti di riferimento per le città e il territorio, venendo a colmare una lacuna museale italiana nei confronti dell'arte contemporanea, musei locali come Museion e Casa Cavazzini, nelle loro sedi rinnovate, hanno reso possibile nelle città italiane una crescita di interesse nei confronti dell'arte a noi più recente, che si è sempre più voluta integrare nella vita quotidiana e nell'identità collettiva.







# SEMANTICS FOR VISION AND LANGUAGE UNDERSTANDING

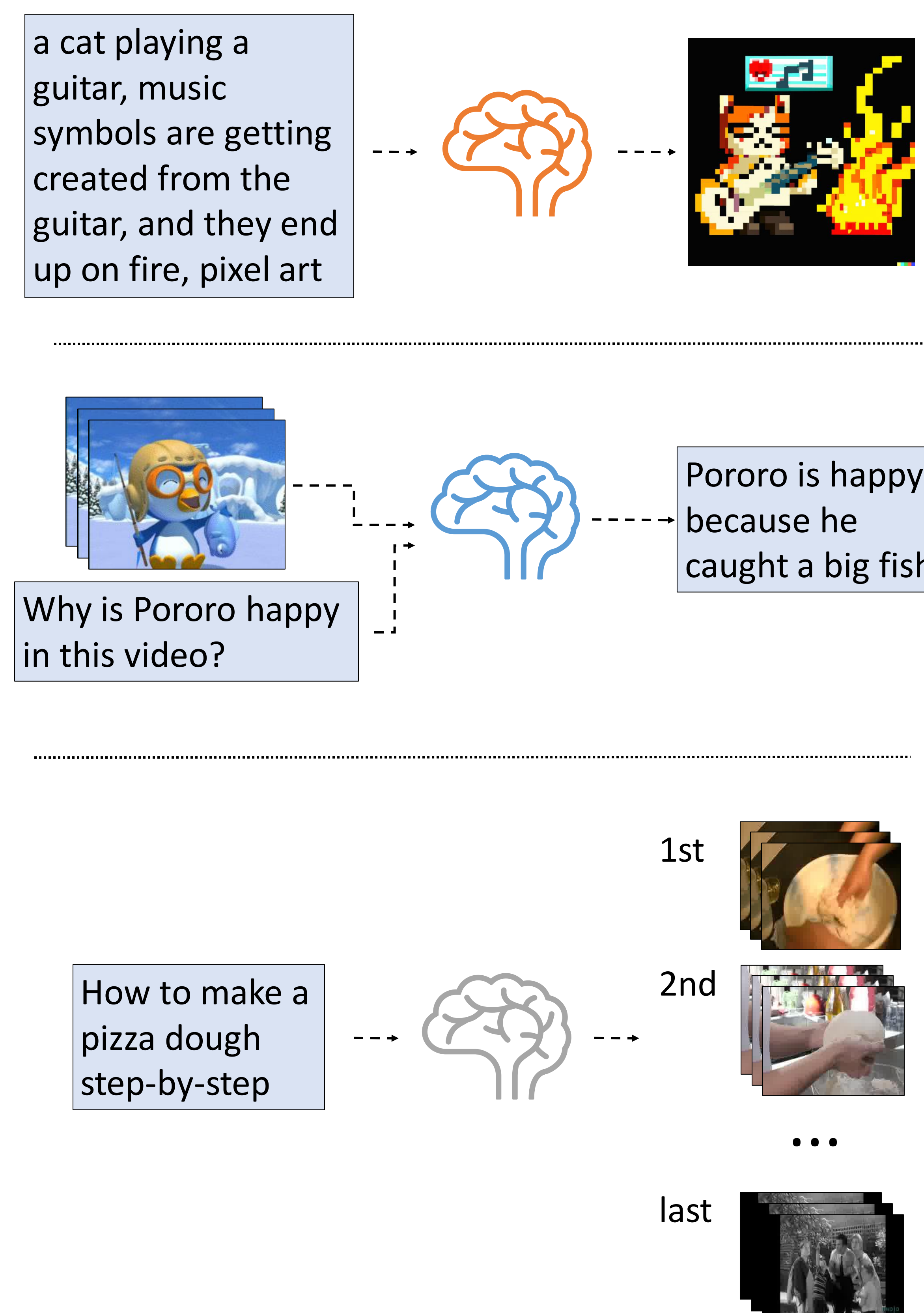
Our proposed techniques involve the semantic analysis of multi-modal inputs and their relations, and have shown promising results in addressing the generalization gap without requiring additional annotated examples, indicating the potential for advancing cross-modal understanding.

## AIMS:

Deep learning has enabled numerous scientific breakthroughs, such as protein structure prediction and self-driving cars, by effectively addressing the generalization gap. However, these achievements often rely on training with billions of annotated examples, which entails an expensive annotation process and is impractical in domains such as medicine. In this thesis, we aimed to bridge this gap by pursuing two approaches: automatic generation of new annotations and customization of the training objective.

## APPLICATIONS:

The techniques developed in this thesis involve semantic analysis of textual inputs and their relations to visual inputs. They were tested on a variety of multimedia problems, such as video question answering, multi-instance text-video retrieval, and text-to-image synthesis. Moreover, they can be readily adapted to other problems involving multi-modal and cross-modal understanding, such as video/image captioning and visual dialog.



## RESULTS:

Our proposed techniques for addressing the generalization gap were validated on multiple problems.

### ➤ *Text-to-Image Synthesis:*

we proposed and validated a pipeline to generate images without human-provided annotations.

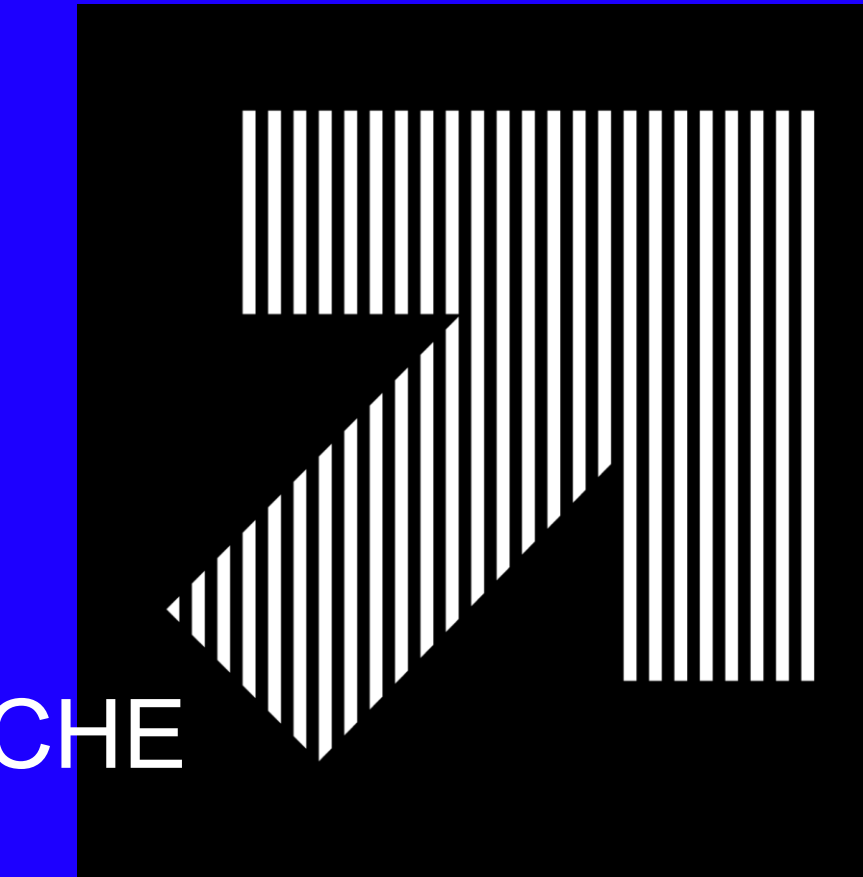
### ➤ *Video Question Answering:*

using the already available annotations, we designed three data augmentation techniques and a multi-task learning framework, obtaining better accuracy across two public benchmarks.

### ➤ *Text-Video Retrieval:*

we proposed a feature-space multimodal data augmentation technique and two customized loss functions, leading to state-of-the-art results across multiple public benchmarks, including 1° place at a worldwide challenge (EPIC-Kitchens-100).

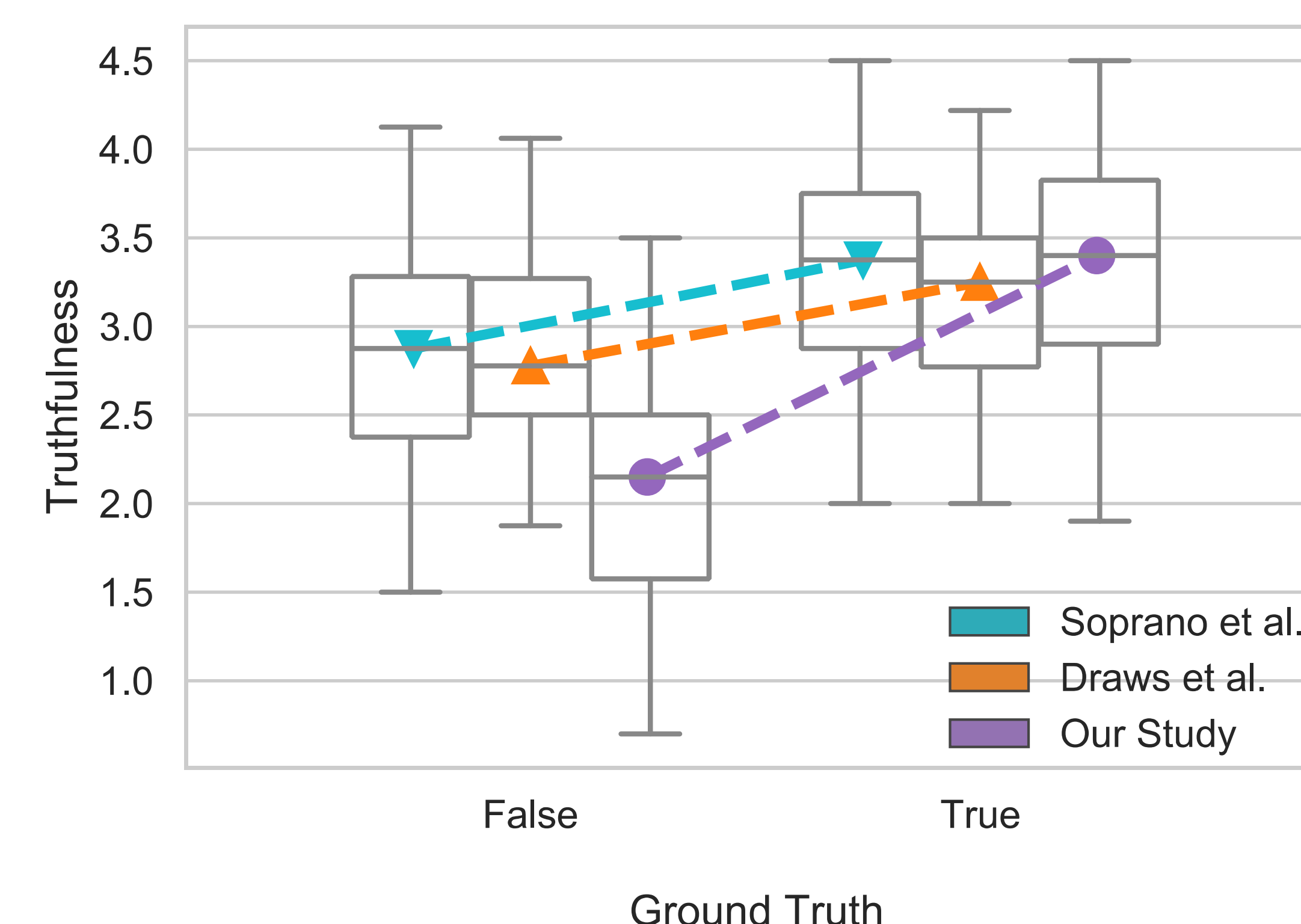
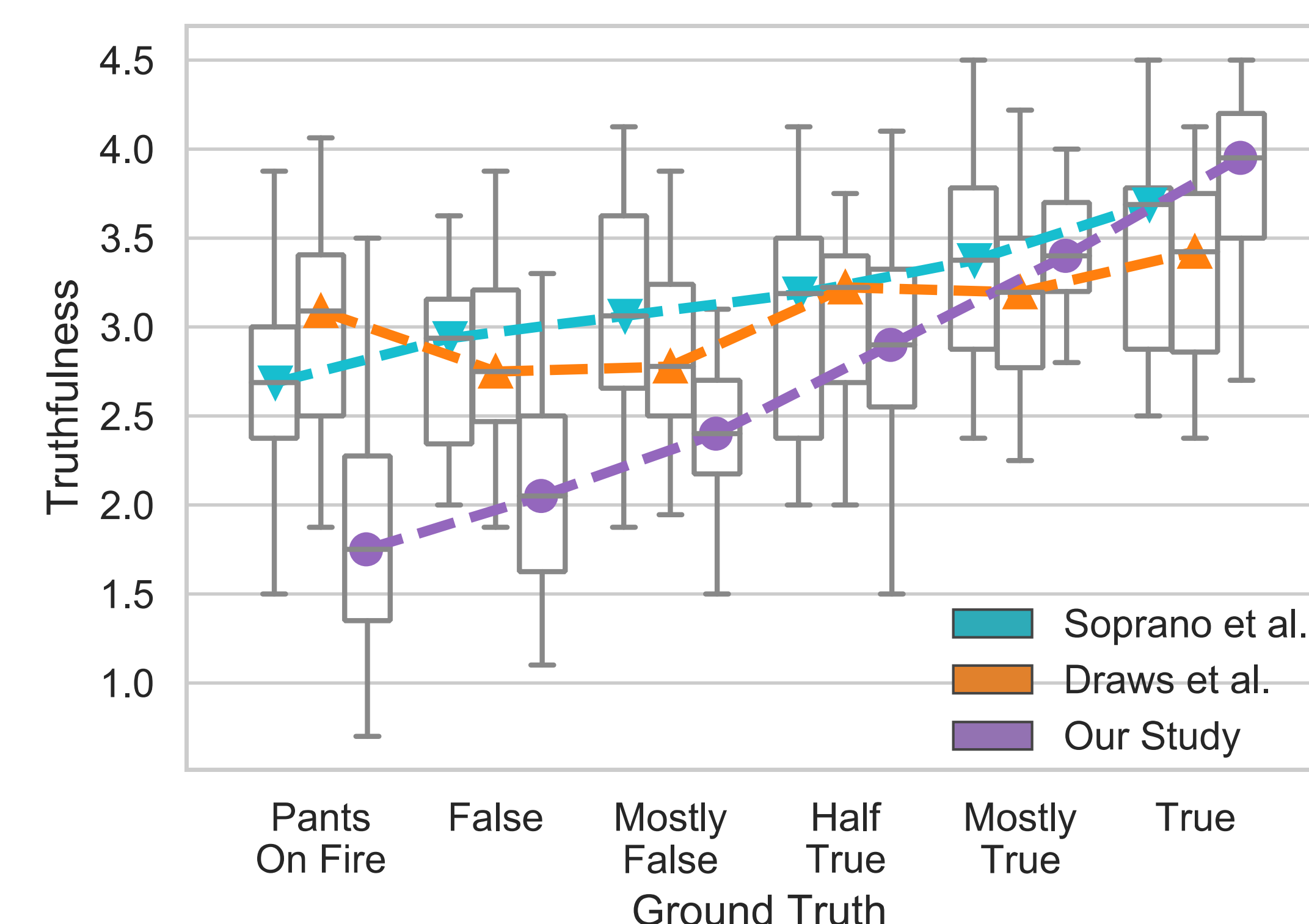




# IN CROWD VERITAS

*Leveraging Human Intelligence To Fight Misinformation*

- Crowdsourcing, Misinformation
- Cognitive Biases, Machine Learning



*Agreement with expert fact-checkers judgments for multiple experiments*

## AIMS: (500 caratteri max)

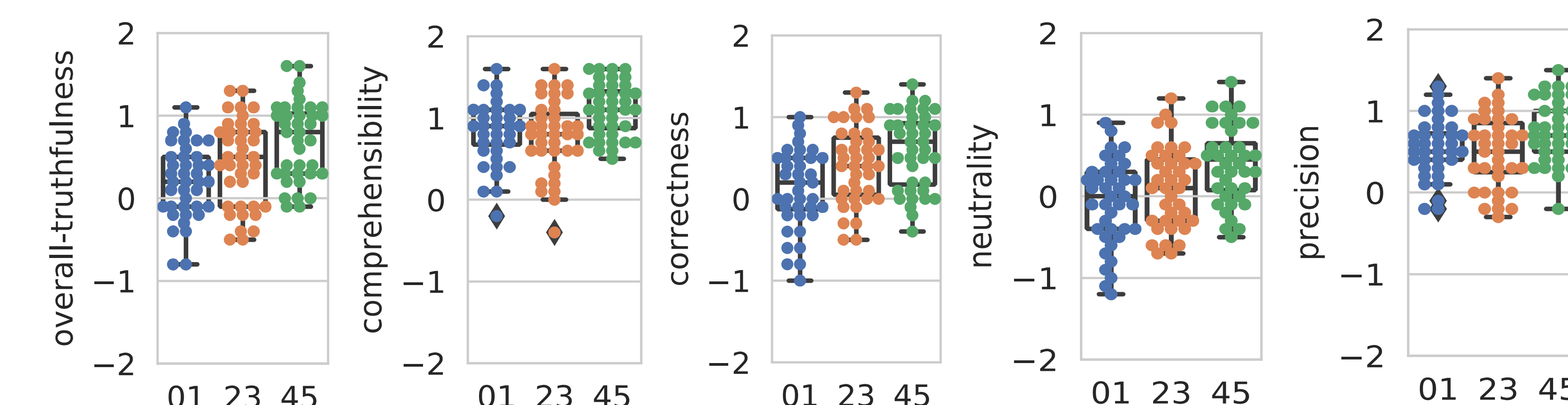
The spread of online misinformation has important effects on the stability of democracy. The sheer size of digital content on the web and social media has made it difficult to perform timely fact-checking at scale. In recent years, crowdsourcing has become a popular method for collecting to collect reliable truthfulness judgments to scale up the manual fact-checking effort. This thesis investigates whether human assessors can detect and objectively categorize such online (mis)information.

## APPLICATIONS: (500 caratteri max)

Researchers and practitioners can rely on non-expert humans to perform the fact-checking process, since they can address the misinformation spreading problem, also for recent information items. The study of the cognitive biases that might manifest while performing the fact-checking process can lead to building a more robust and bias-free pipeline. Jointly predicting truthfulness judgments and generating explanations makes automated fact-checking systems more transparent and fosters greater trust in them.

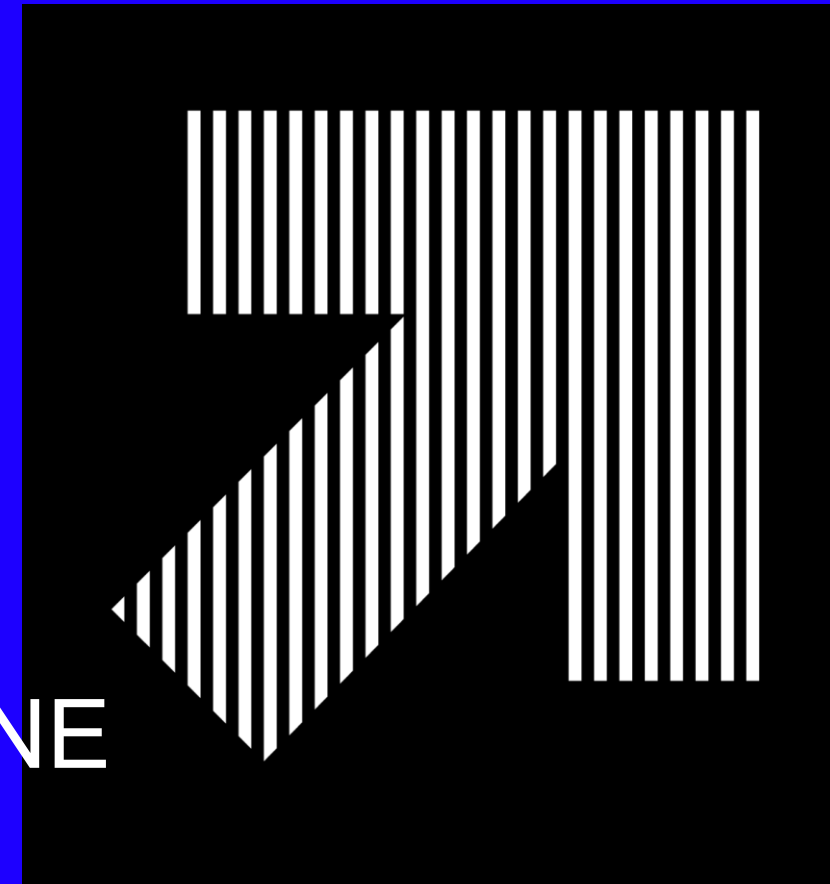
## RESULTS: (800 caratteri max)

The data obtained from non-expert humans about the truthfulness of statements said by public figures correlate well with expert fact-checker judgments. The results show that the background of the non-expert humans has an impact and that they can also address recent (mis)information, for instance, about the COVID-19 pandemic. A list of cognitive biases that may affect the fact-checking process is proposed, together with a classification and a list of countermeasures. A machine learning-based architecture that makes a truthfulness prediction and jointly provides a human-readable explanation is also proposed. The evaluation of such explanations reveals that they make people more accurate in detecting misinformation and more skeptical of information encountered online.



*Correlation with the ground truth for multiple dimensions of truthfulness.*

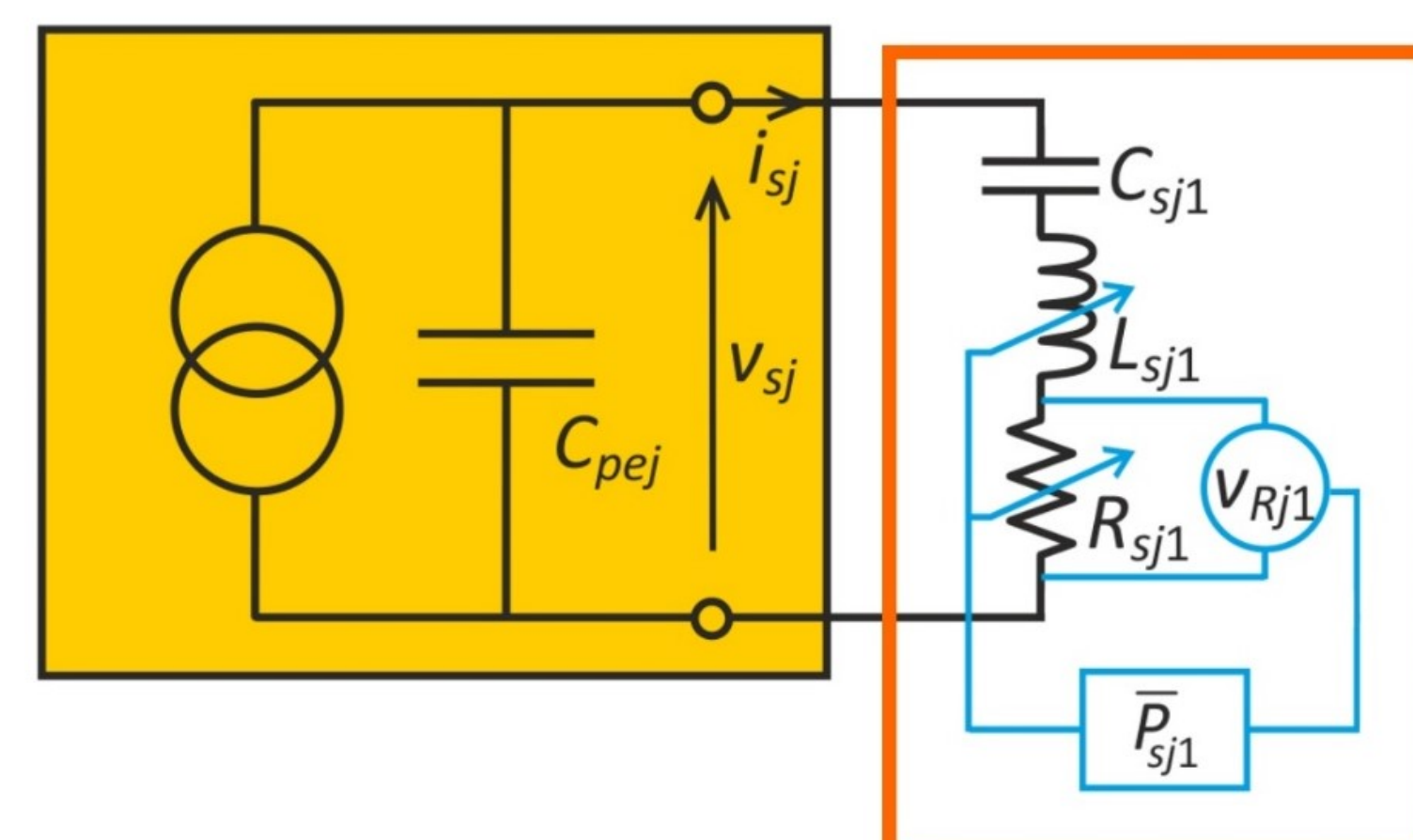
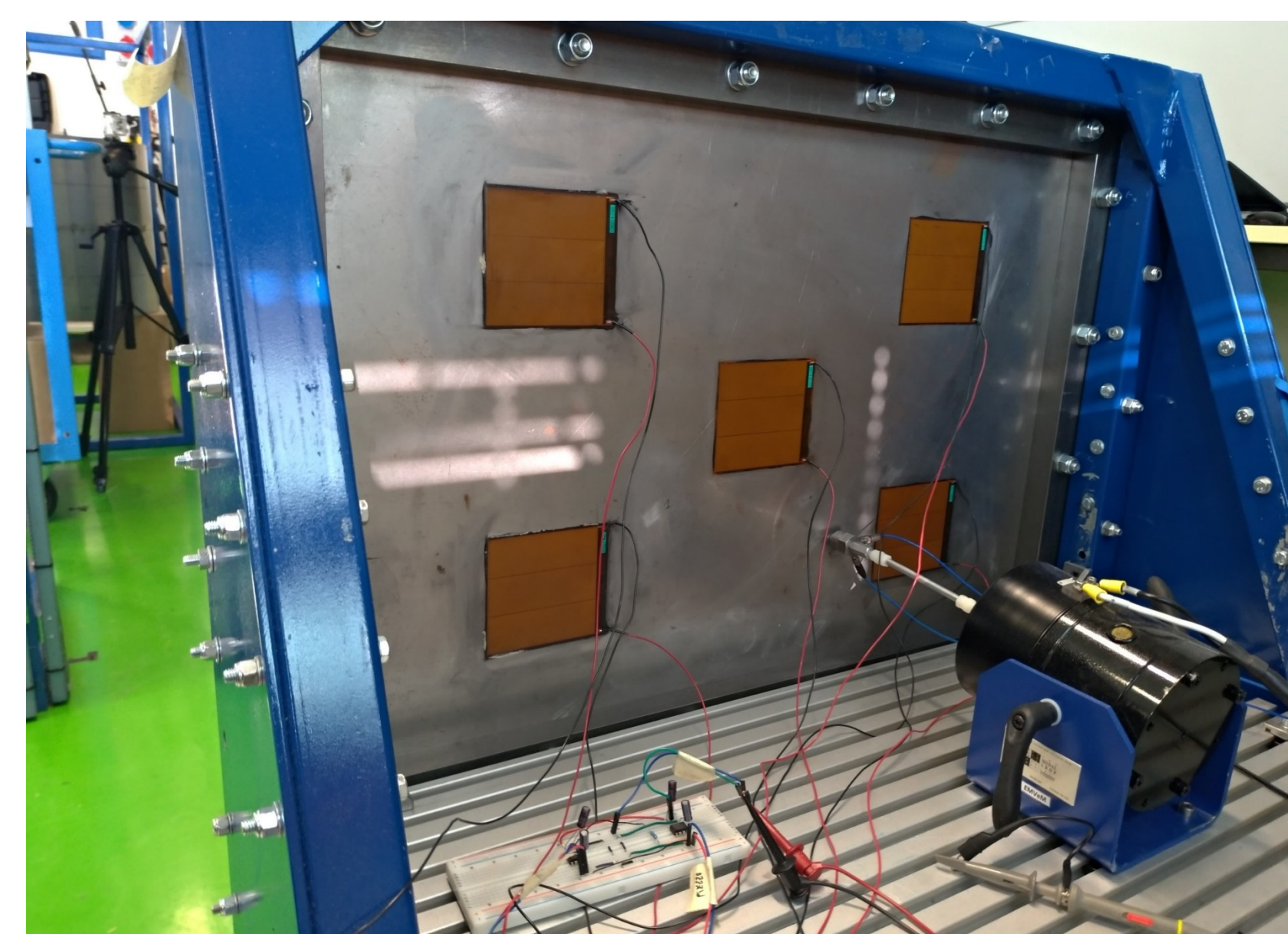




# PIEZOELECTRIC UNITS WITH SELF-TUNING MULTIRESONANT SHUNTS FOR VIBRATION ABSORPTION

*Piezoelectric patches connected to RLC shunts with self-tuning based on extremum seeking algorithm set to maximise electric power dissipation to achieve vibration absorption*

Semi-active control;  
 Power maximisation;  
 Adaptive absorber;  
 Broadband control;  
 Extremum seeking.



## AIMS:

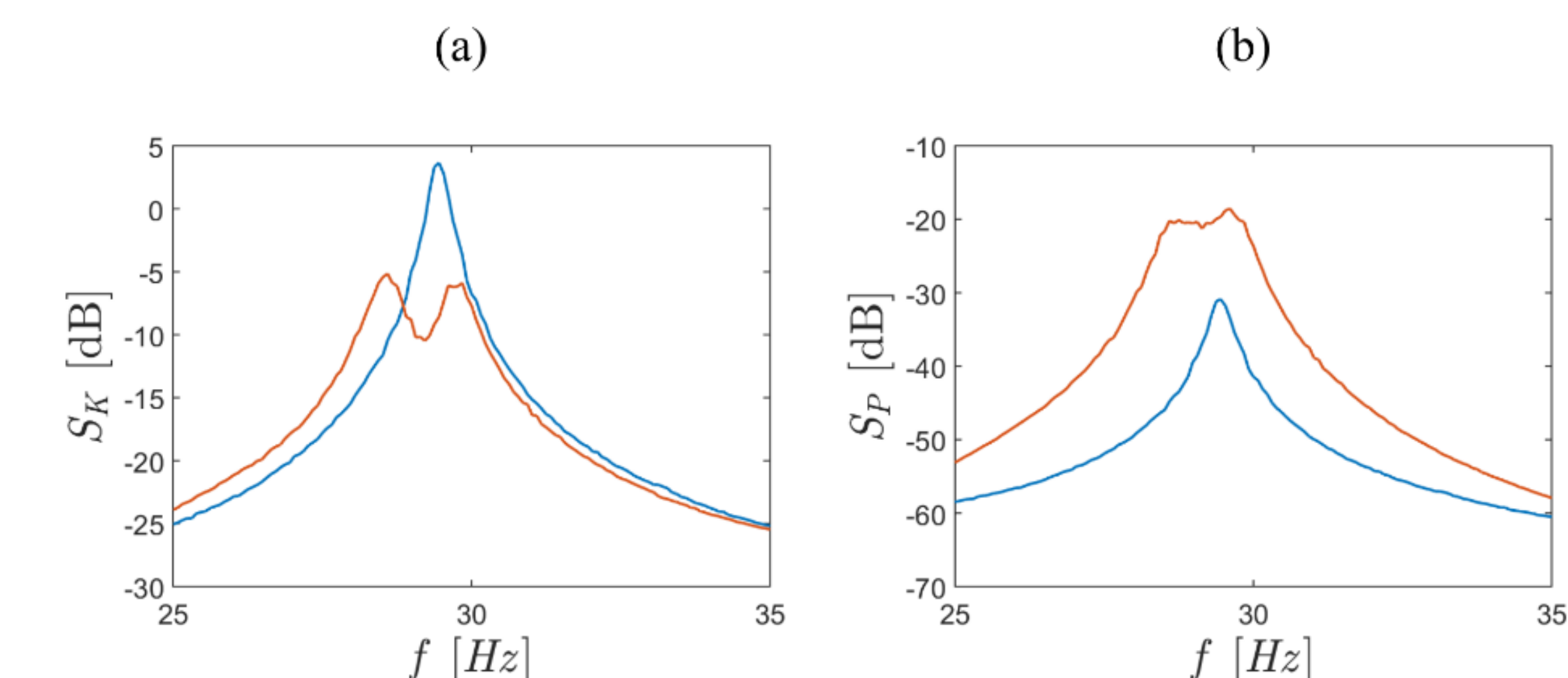
The overall goal of this research is to control the low frequency flexural response due to stochastic broadband disturbances on thin panel structures. To achieve this, the development of a modular control unit formed by a piezoelectric patch connected to a self-tuning shunt is addressed. The self-tuning approach is carried locally and is set to maximise the active electric power of the resonant shunt. Moreover, the proposed extremum seeking on-line tuning strategy can adapt for exogenous changes on the structure.

## APPLICATIONS:

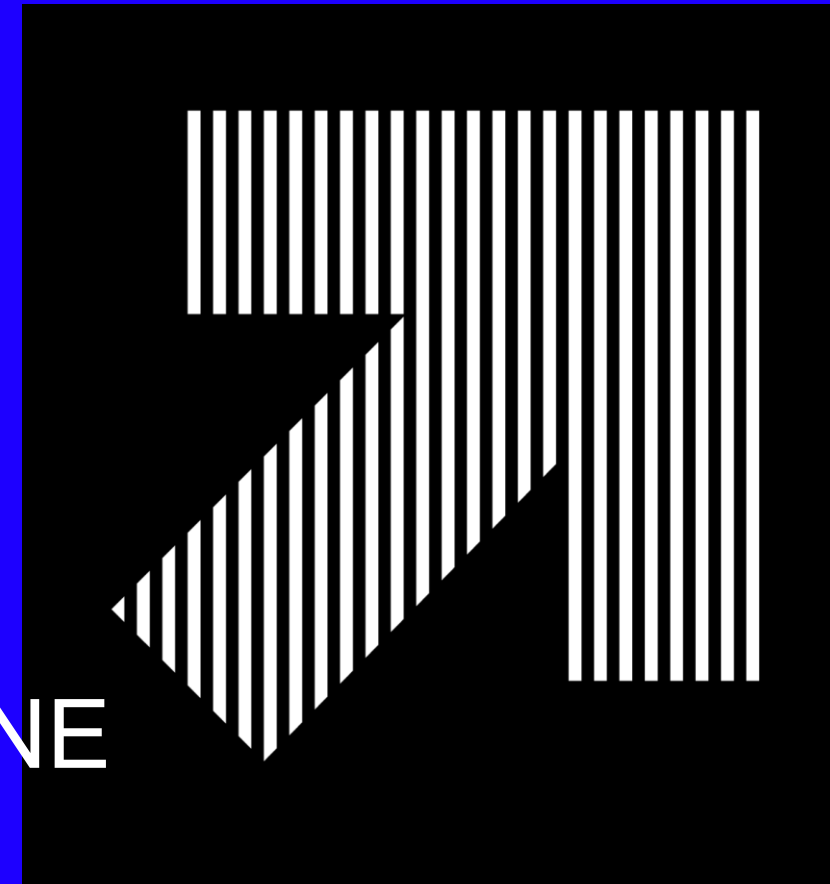
The results presented in this thesis contribute to achieve a decentralised vibro-acoustic control for lightweight structures. The maximisation of the power dissipated by the shunt instead the minimisation of kinetic energy of the overall structure allows for a more convenient approach for real world implementations of vibro-acoustic control approaches. In addition, the adaptive qualities of the proposed extremum seeking online tuning can retain performance even with time-varying structures.

## RESULTS:

The initial analysis of the resonant shunt parameters indicates that the maximisation of the proposed local cost function based on the power dissipated by the shunt is equivalent to the minimisation of the overall kinetic energy of the panel. This is based on the fact of the shunt values that achieves the maximum electric power dissipation and minimum kinetic energy are the same. For the tuning procedure, an approach called two-step is proposed. In this approach, the inductance of the system is tuned first and then the resistance value is set. To perform the tuning, an extremum seeking method is utilised for it can search for the shunt values that maximises the dissipated power. Experimental results shows that the resonant responses of the first resonant mode were reduced by 12dB with the implementation of the proposed unit.







# ISO/IEC 27001: AN EMPIRICAL MULTI-METHOD RESEARCH

## AIMS:

This research project pursued the following objectives:

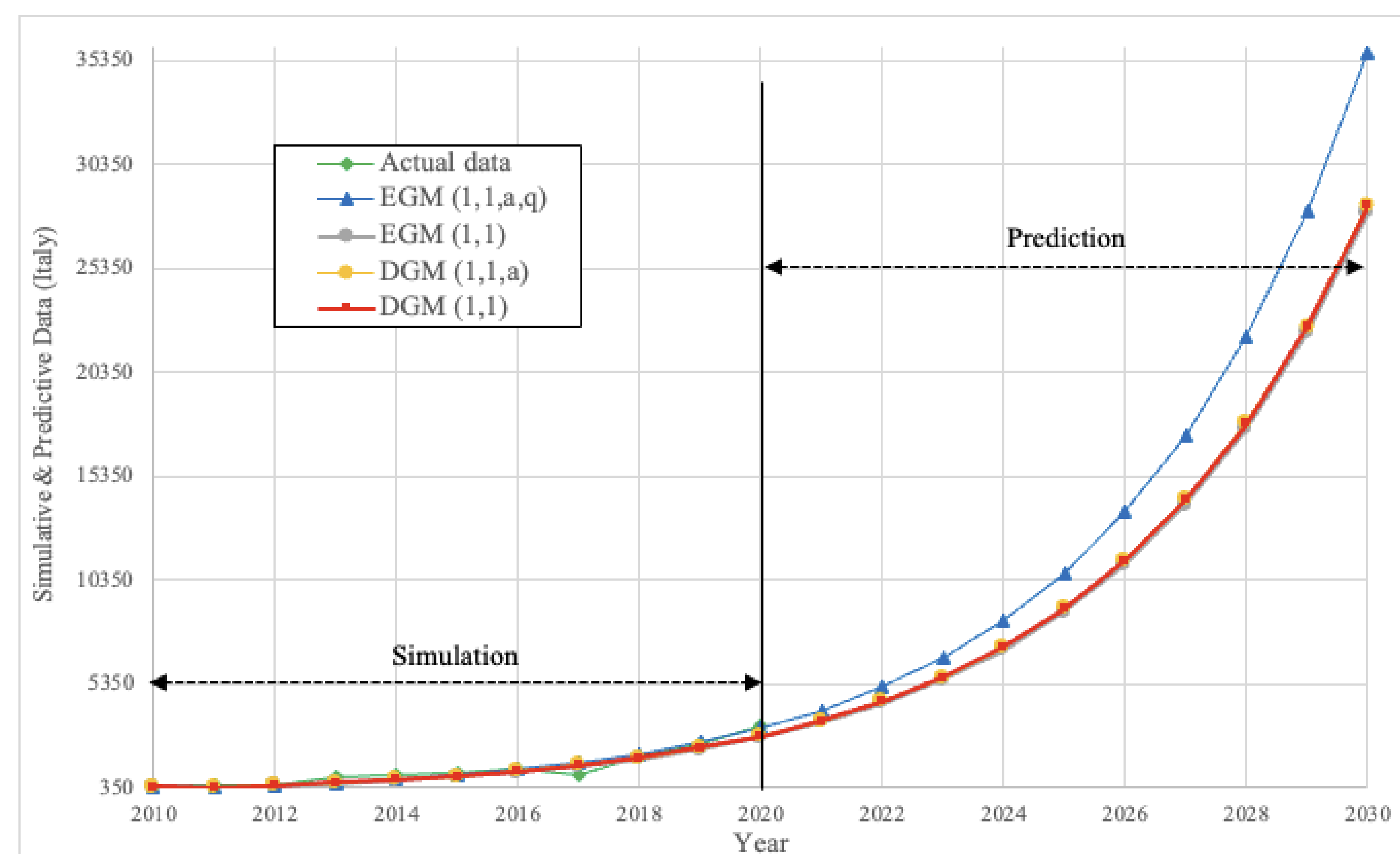
- 1) Highlight the most relevant information security challenges in the context of Industry 4.0
- 2) Provide a comprehensive synthesis of the academic body of knowledge on ISO/IEC 27001 (i.e., the most renowned international management standard for information security)
- 3) Investigate the diffusion patterns of ISO/IEC 27001
- 4) Shed light on the performance implications of ISO/IEC 27001 adoption

## RESULTS:

Four main findings emerged:

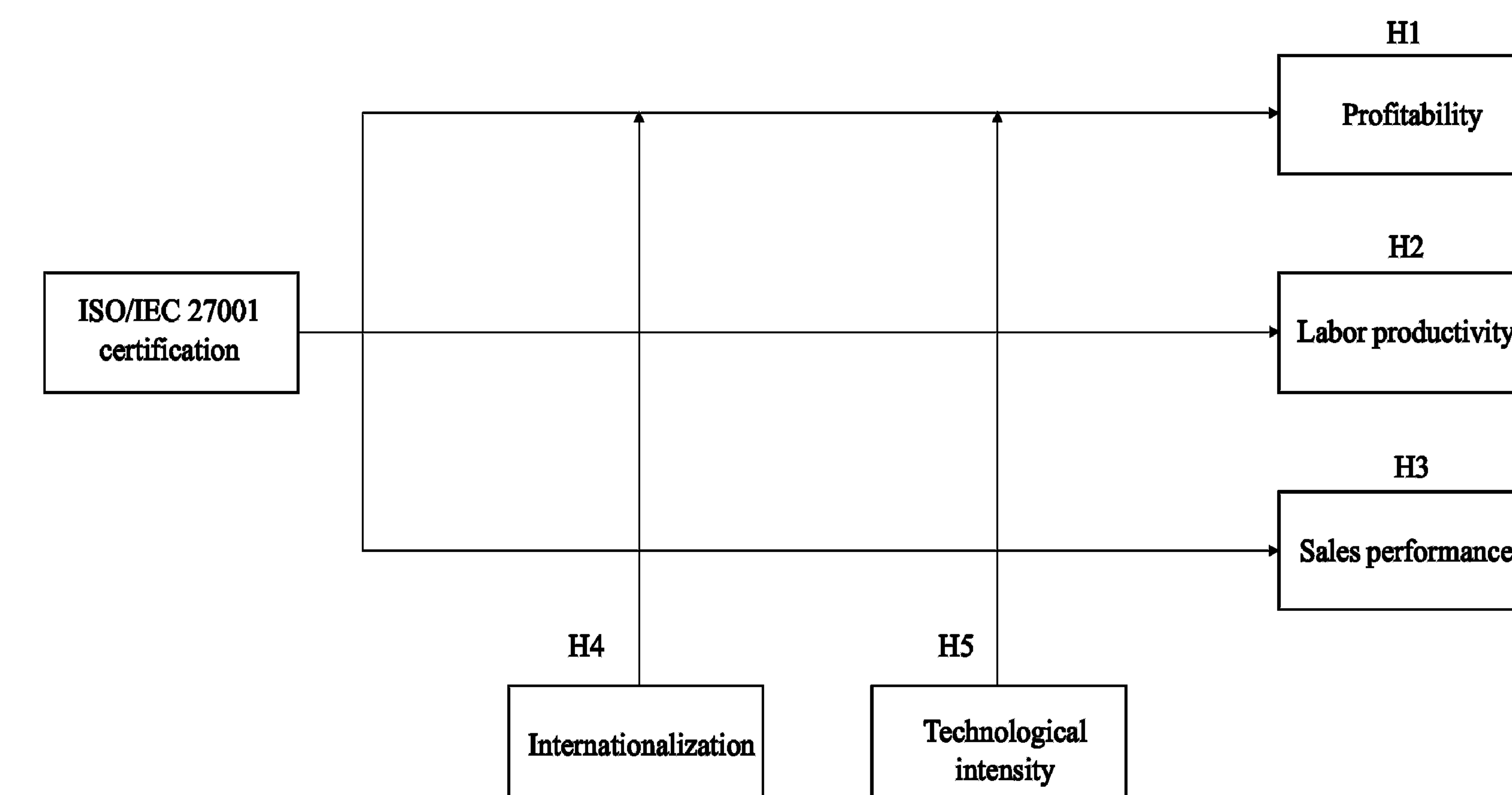
- 1) Information security is not a purely technical topic but requires, above all, managerial approaches/solutions
- 2) Extant research on ISO/IEC 27001 exhibits a paucity of empirical studies on the ISO/IEC 27001 and a limited debate addressing the topic from a managerial point of view
- 3) A generalized growing trend in the number of ISO/IEC 27001 issued certificates is likely to be expected in the years to come with China that will become the leading country in terms of certified organizations.
- 4) ISO/IEC 27001 adoption is associated with improvements in profitability, labour productivity, and (partially) sales performance. The impact appears affected by the level of internationalization of the certified firm, while the technological intensity of the industry has no effect

INFORMATION SECURITY,  
 CYBERSECURITY, ISO/IEC 27001, ISO  
 27001, INFORMATION SYSTEMS,  
 INTERNATIONAL MANAGEMENT  
 STANDARDS

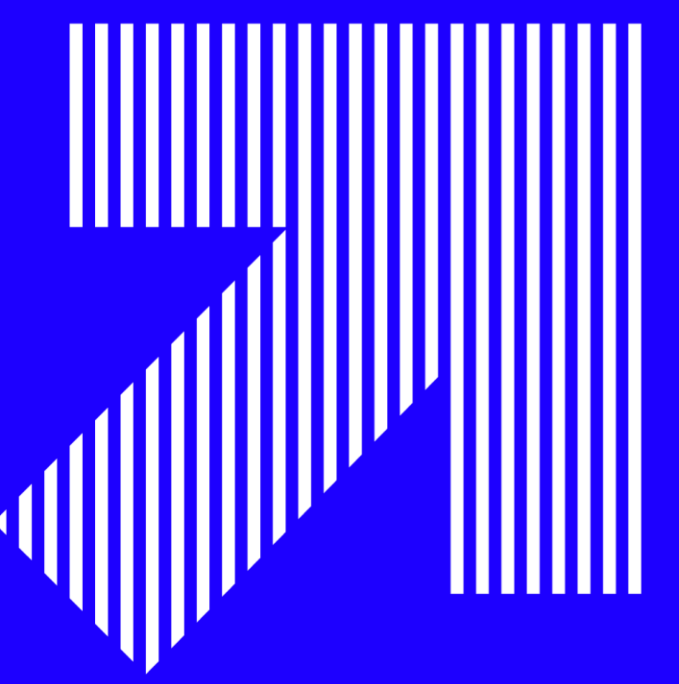


## APPLICATIONS:

Overall, this project provided several contributions to both theory and practice. From a theoretical point of view, it highlighted the need for managerial disciplines to start addressing information security-related aspects. From a practical point of view, it showed the relevance and usefulness of ISO/IEC 27001. In particular, the value of the standard is not only related to the fulfilment of customer requests and/or to what can be communicated to external stakeholders but resides, also, in significant implications for a firm's internal processes



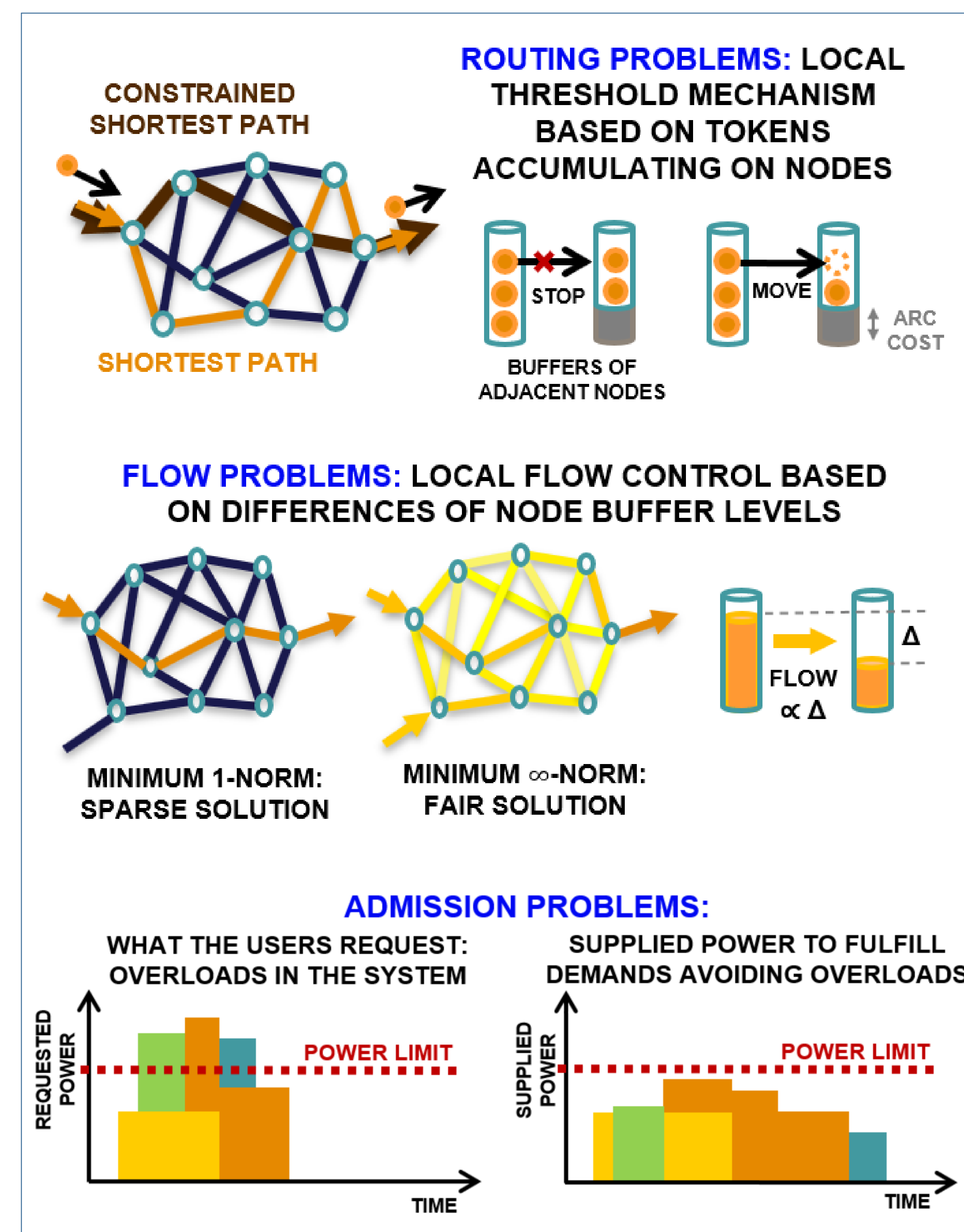




# A DECENTRALIZED APPROACH FOR ADMISSION, ROUTING AND FLOW PROBLEMS

Local information can be used to get a global behavior: for admission problems, heuristic solutions might be evaluated on the basis of historical data, while for routing and flow problems global optimality results can be guaranteed.

**KEYWORDS:** decentralized control, agent-based control, shortest path flow, p-norm minimization, delay minimization



## AIMS:

Online control of large dynamic networks is challenging as little environment data are usually available, decentralized strategies relying only on local data are used, and faults can occur. Three problems have been studied: *admission problems* about the scheduling of requests of a resource from a supplier with limited capacity, *routing problems* of tokens injected in a network to find a leaving path, and *flow problems* where flows are controlled to meet a demand and asymptotically minimize their p-norm.

## APPLICATIONS:

The considered problems have applications in the context of smart homes and smart grids. Typically, in *admission problems*, energy is requested from power networks, either by appliances to function or by electric vehicles for battery charging. *Routing problems* can refer to packet transmission in unknown networks, where packets both carry information and are also routing agents, for instance, in sensor networks. *Flow problems* apply to data transmission, transportation, energy, and fluid networks.

## RESULTS:

For *admission problems*, an optimal control framework for delay minimization, supporting many supply strategies, provides optimal solutions and lower bounds. Centralized and decentralized online heuristics are studied and evaluated offline using recorded data. For *routing problems*, a decentralized routing policy makes the injected tokens eventually discover the shortest outgoing paths, despite some are lost in the initial exploring phase. An enhanced policy avoids this issue. Constraints on the maximum number of transitions can be imposed. For *flow problems*, a decentralized control stabilizes the flow to the optimal desired one if  $1 < p < \infty$ . As  $p \rightarrow 1$  and  $p \rightarrow \infty$ , suboptimal 1 and  $\infty$ -norm solutions emerge, respectively. Unknown dynamics and buffer level control can be supported.

## PUBLICATIONS:

- Rosset F., Casagrande D., Jafarpisheh B., Montessoro P. L., and Blanchini F., "Optimal Control Approach to Scheduling Power Supply Facilities: Theory and Heuristics", IEEE Trans. Control Netw. Syst., 2022
- Rosset F., Blanchini F., and Pesenti R., "An agent-based decentralized threshold policy finding the constrained shortest", 2022 (submitted)
- Blanchini F., Devia C. A., Giordano G., Pesenti R., and Rosset F., "Fair and sparse solutions in network-decentralised flow control", IEEE Control Syst. Lett., 2022



# Joint modelling of regional electricity net-demand in Great Britain

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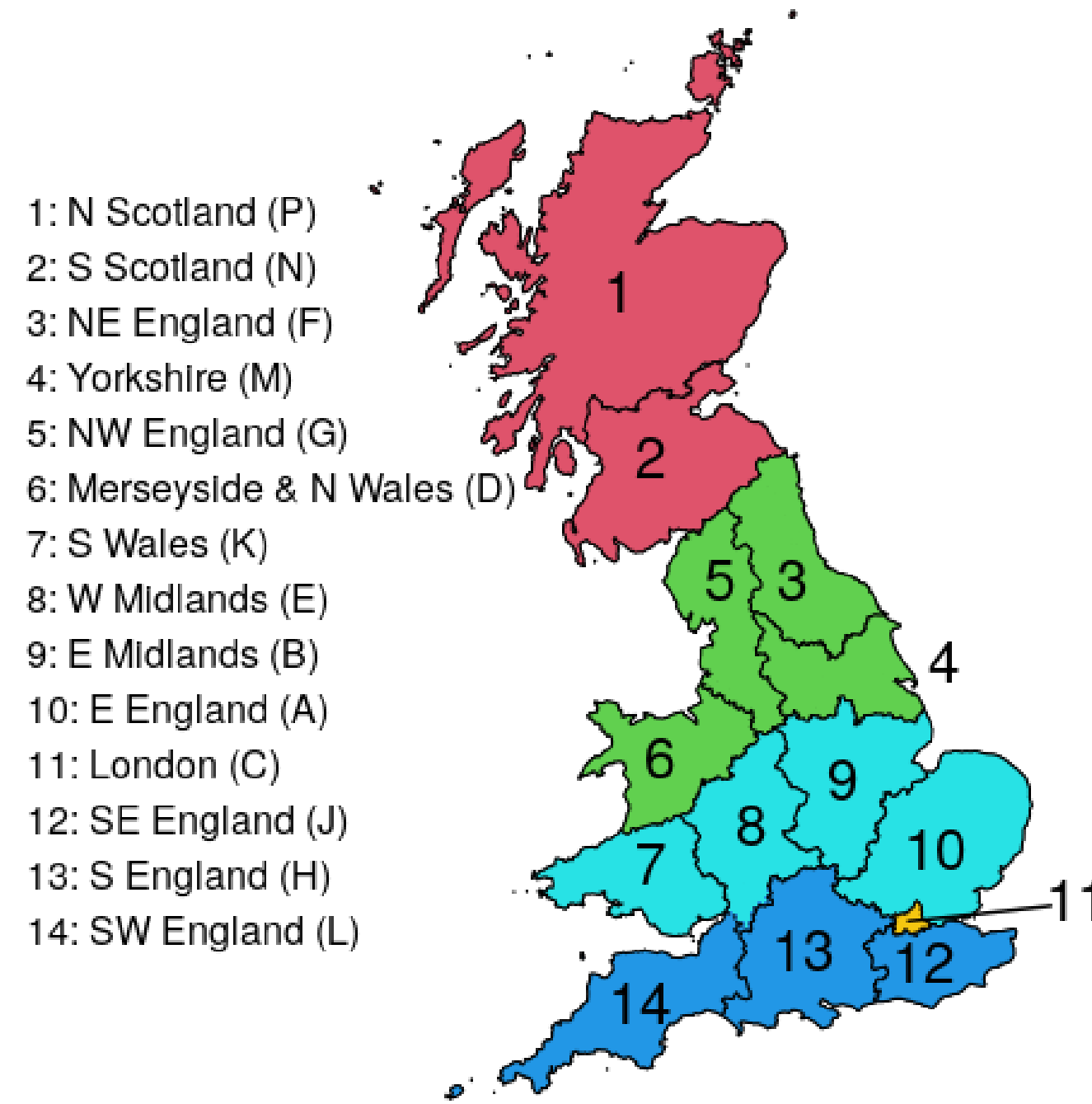
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## Motivation

Short-term forecasts of electricity net-demand are essential inputs to predict and manage power flows on electricity networks. We focus on the joint forecasting of net-demand across the 14 Grid Supply Point (GSP) regions comprising Great Britain's transmission system. The net-demand variability within each region, and the dependencies between regions, vary with temporal, socio-economical and weather-related factors. Motivated by the need for spatially coherent, probabilistic short-term net-demand forecasts to support energy system operations, we account for the varying nature of the covariance matrix structure.



## Multivariate Gaussian Additive Model

Consider independent  $\mathbf{y}_i = (y_{i1}, \dots, y_{id})^\top \sim \mathcal{N}(\boldsymbol{\mu}_i, \boldsymbol{\Sigma}_i)$ ,  $i = 1, \dots, n$ . The covariates enter the model through the linear predictor vector,  $\boldsymbol{\eta}_i = (\eta_{i1}, \dots, \eta_{iq})^\top$ ,  $q = d + d(d+1)/2$ , with  $\eta_{ij} = \mathbf{X}_i^j \boldsymbol{\beta}_j$ . The mean model is specified by  $\mu_{ij} = \eta_{ij}$ ,  $j = 1, \dots, d$ , while the remaining  $\eta_{ij}$ ,  $j = d+1, \dots, q$ , specify the unconstrained entries of the covariance matrix parametrisation based on the modified Cholesky decomposition (Pourahmadi, 1999), that is

$$\boldsymbol{\Sigma}^{-1} = \mathbf{T}^\top \mathbf{D}^{-2} \mathbf{T},$$

where  $D_{jj} = C_{jj}$ ,  $j = 1, \dots, d$ , and  $\mathbf{T} = \mathbf{D} \mathbf{C}^{-1}$ , with  $\mathbf{C}$  the Cholesky factor.

## Mean model specification

Let  $y_{ij}$  be the standardised net-demand of the  $j$ -th GSP group at a 30min resolution. The data span 2014 - 2018 ( $n = 83024$ ), and include calendar, weather forecasts and other information. The mean vector elements,  $\mu_{ij} = \eta_{ij}$ , are built on Browell and Fasiolo (2021) and take the form

$$\begin{aligned} \eta_{ij} = & g_{j1}(t_i) + g_{j2}(t_i^2) + g_{j3}(dow_{ij}) + g_{j4}(shol_{ij}) + g_{j5}(y_{ij}^{24}) + g_{j6}(wsp_{ij}^{10}) \\ & + f_{j1}^{20}(doy_i) + f_{j2}^{35}(tod_i) + f_{j3}^{10}(n2ex_i) + f_{j4}^{35}(temp_{ij}) + f_{j5}^{35}(temp_{ij}^S) \\ & + f_{j6}^{10}(rain_{ij}) + wcap_i \times f_{j7}^{20}(wsp_{ij}^{100}) + f_{j8}^{35}(irr_{ij}) \\ & + f_{j9}^{30}(tod_i, dow_{ij}^+) + f_{j10}^{20}(tod_i, shol_{ij}) \\ & + f_{j11}^{5,5}(n2ex_i, tod_i) + f_{j12}^{5,5}(temp_{ij}, tod_i) + f_{j13}^{5,5}(rain_{ij}, tod_i), \end{aligned}$$

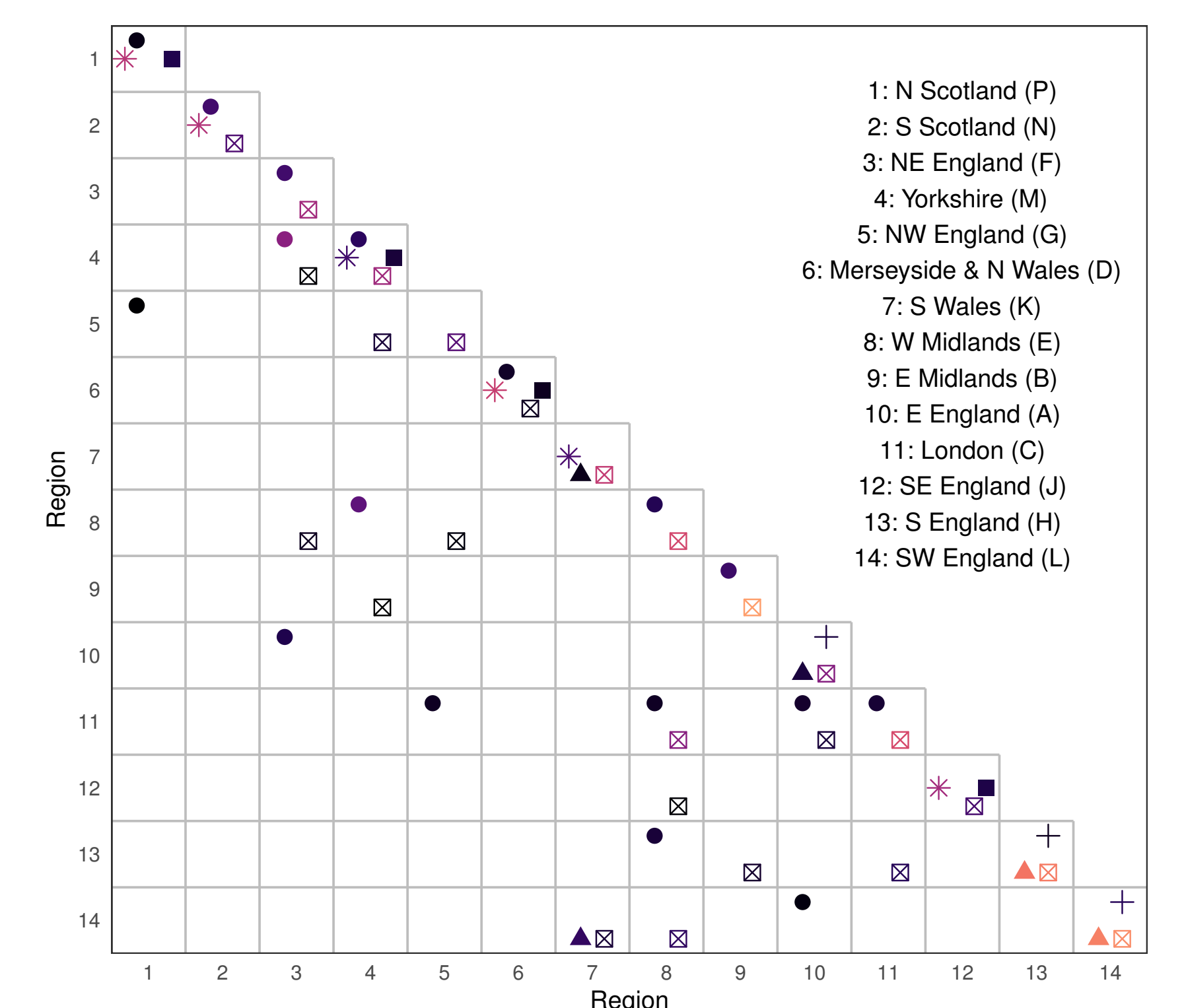
with linear effects ( $g_{jk}$ ), smooth effects and smooth-factor interactions ( $f_{jk}^t$ ), tensor-product smooths ( $f_{jk}^{s,t}$ ).

## Covariance matrix model specification

Consider the candidate effects in

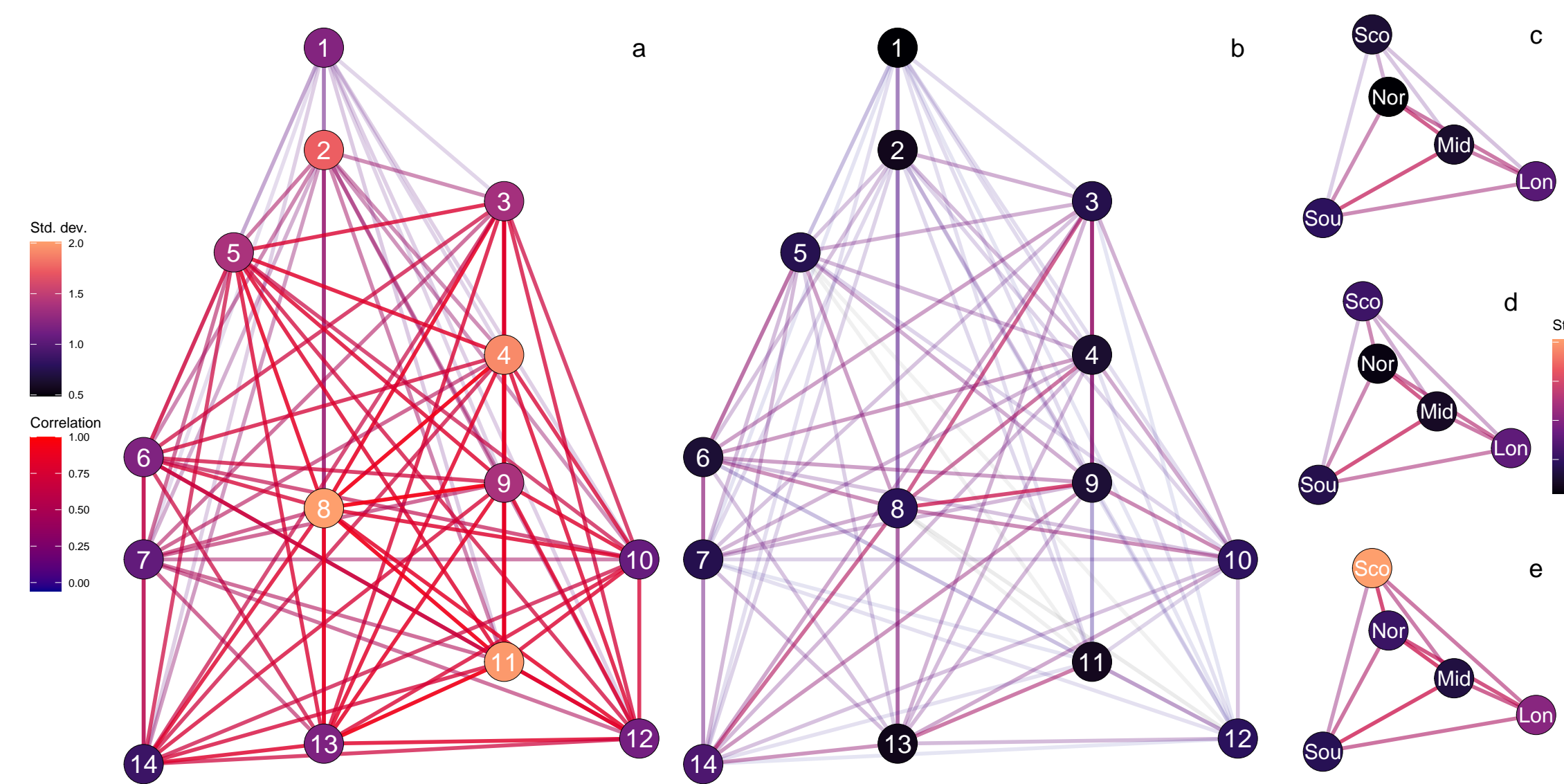
$$\begin{aligned} \eta_{ij} = & g_{j1}(t_i) + g_{j2}(t_i^2) + g_{j3}(dow_i) + f_{j1}^{10}(doy_i) \\ & + f_{j2}^{10}(tod_i) + f_{j3}^{5}(wsp_{il_j}^{100}) + f_{j4}^{5}(irr_{il_j}) \\ & + f_{j5}^{5}(temp_{il_j}) + f_{j6}^{5}(rain_{il_j}) + f_{j7}^{5}(n2ex_i), \end{aligned}$$

for  $j = 15, \dots, 119$ . The gradient boosting algorithm is run over 2014-2016 and orders the candidate effects in terms of decreasing importance. Then, by using the out-of-sample predictions and log-likelihood covering the 2017, the procedure suggests to include 60 effects for the covariance matrix model.

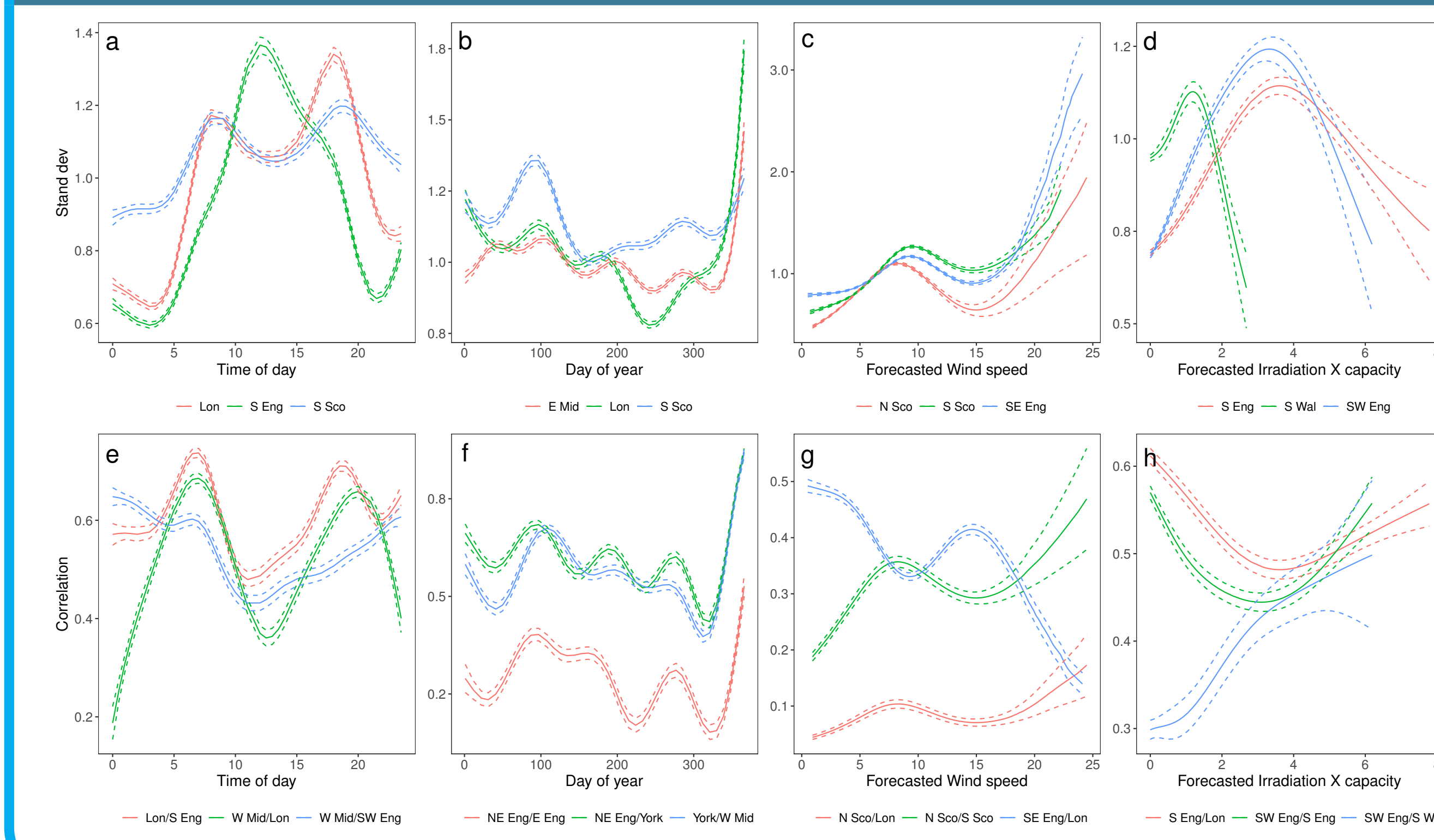


## Predicted variances and correlations

The joint distribution of net-demand is time-varying, as it is affected by daily and yearly seasonalities, as well as is strongly affected by weather.



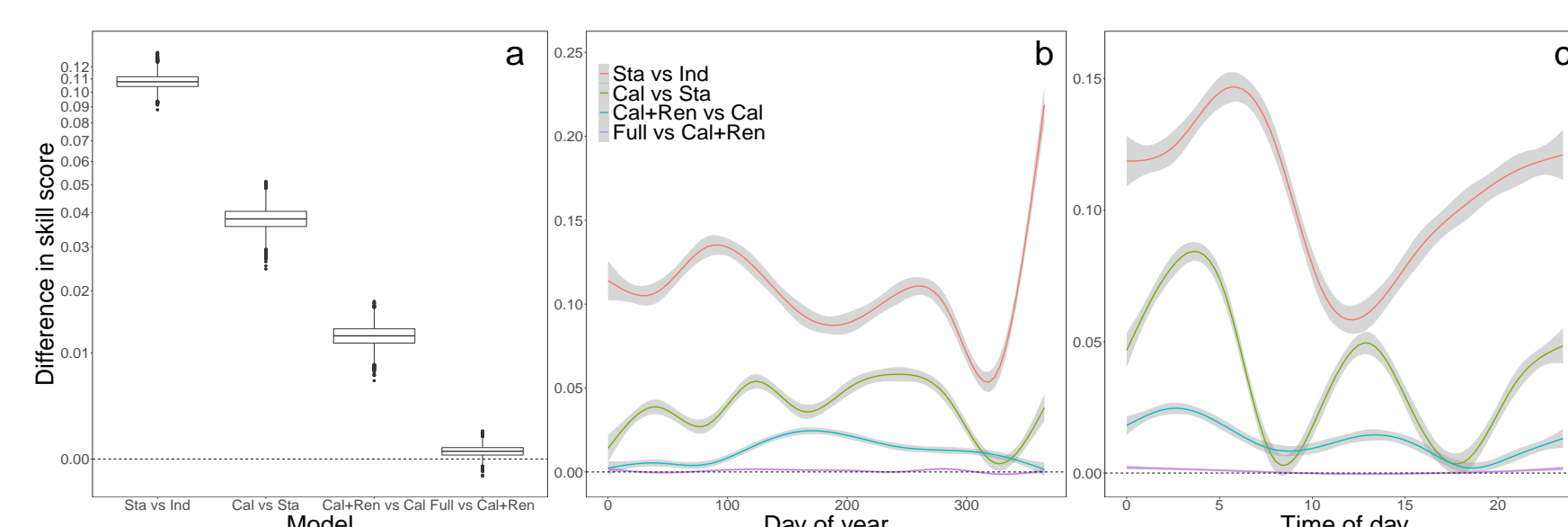
## Accumulated local effects



The covariates effect on variances and correlations is explored via ALEs (Apley and Zhu, 2020). A greater uncertainty and stronger correlations are clear around peak hours and year-end. Solar maxima, high wind speed and partial clouds result in a greater uncertainty.

## Model evaluation

The model evaluation task considers 2018 data. We include two benchmark static covariance matrix models (Static and Indep) and some alternative models which consider only calendar (Cal) and calendar with solar and wind (Cal+Ren) as candidate effects for the model selection procedure. The benefits of modelling the cross-regional dependencies and capturing calendar and renewable-generation-related effects are substantial, while only marginal improvements by further expanding the set of covariates.



	GSP regions			
	Log	Energy	Var 0.5	Var 1.0
Indep	27496	3547	43403	175076
Static	24214	3519	39928	161166
Cal	23139	3475	37411	150253
Cal+Ren	22787	<u>3470</u>	36772	147251
Full	<u>22773</u>	<u>3470</u>	<u>36693</u>	<u>146843</u>

## Take-home messages

- 1) Forecast errors exhibit spatial correlation, and this changes in time due to temporal, weather-driven and other factors.
- 2) Modelling dynamic correlations is hard, but we have developed a multivariate GAM model for doing so.
- 3) Capturing dynamic correlations between GSP groups leads to improved probabilistic joint net-demand forecasts.
- 4) Joint net-demand forecasts at GSP group level could be fed to probabilistic power flow analysis tools for improved power system operations.

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