Increasing the generalization capability of biomarkers through Systems Biology
Malaria Vaccines Case Study

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ANAXOMICS
Systems biology solutions

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SysMalVac

Abstract

The Problem of **high-throughput (HTP) data** for identifying **new biomarkers (BMs)** is that gene / protein combinations validated with source data usually lack **generalization capability**, leading to high numbers of **false-positive BMs**.[1]

The Solution: **Systems Biology** provides better-generalizing biomarkers by combining, in a protein/gene network, the experimental HTP and other data with all the already known information for any specific biological problem.[2] We provide an example through the application of Anaxomics's TPMS technology[2] in the context of the EU research project SysMalVac.[3]
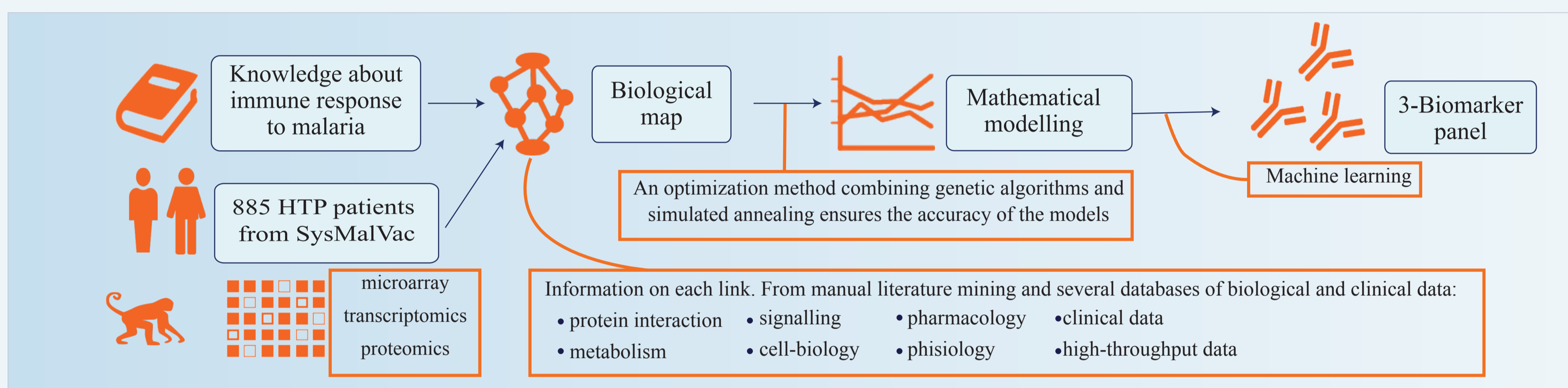
Method & Data

Case study: SysMalVac[3]
Study of the immunity generated by two malaria vaccine protocols: RTS[4] & CPS[5]

Aim
Developing a BM selection method with better generalization capability

Technology: Anaxomics's proprietary **TPMS**
Therapeutic Performance Mapping System: Systems biology applied to model and understand human physiology[2]

Knowledge about immune response to malaria → Biological map → Mathematical modelling → Machine learning → 3-Biomarker panel

885 HTP patients from SysMalVac

microarray / transcriptomics / proteomics

An optimization method combining genetic algorithms and simulated annealing ensures the accuracy of the models

Information on each link. From manual literature mining and several databases of biological and clinical data:
- protein interaction
- signalling
- pharmacology
- clinical data
- metabolism
- cell-biology
- phisiology
- high-throughput data

Results

Generalization capability (accuracy) of conventional and Anaxomics's TPMS 3-BM panel selection methods applied to the experiments of the SysMalVac project.

A. $p = 0.001328$
Leave-one-out (LOO) Accuracy
$\bar{x} = 76.89 \pm 4.07\ \%$ (SD)
$\bar{x} = 68.33 \pm 9.52\ \%$ (SD)
Conventional — Anaxomics's TPMS
Biomarker Selection Method

B. mean increment = 12.52 %.
RTS exp. 1–12, CPS exp. 1–7
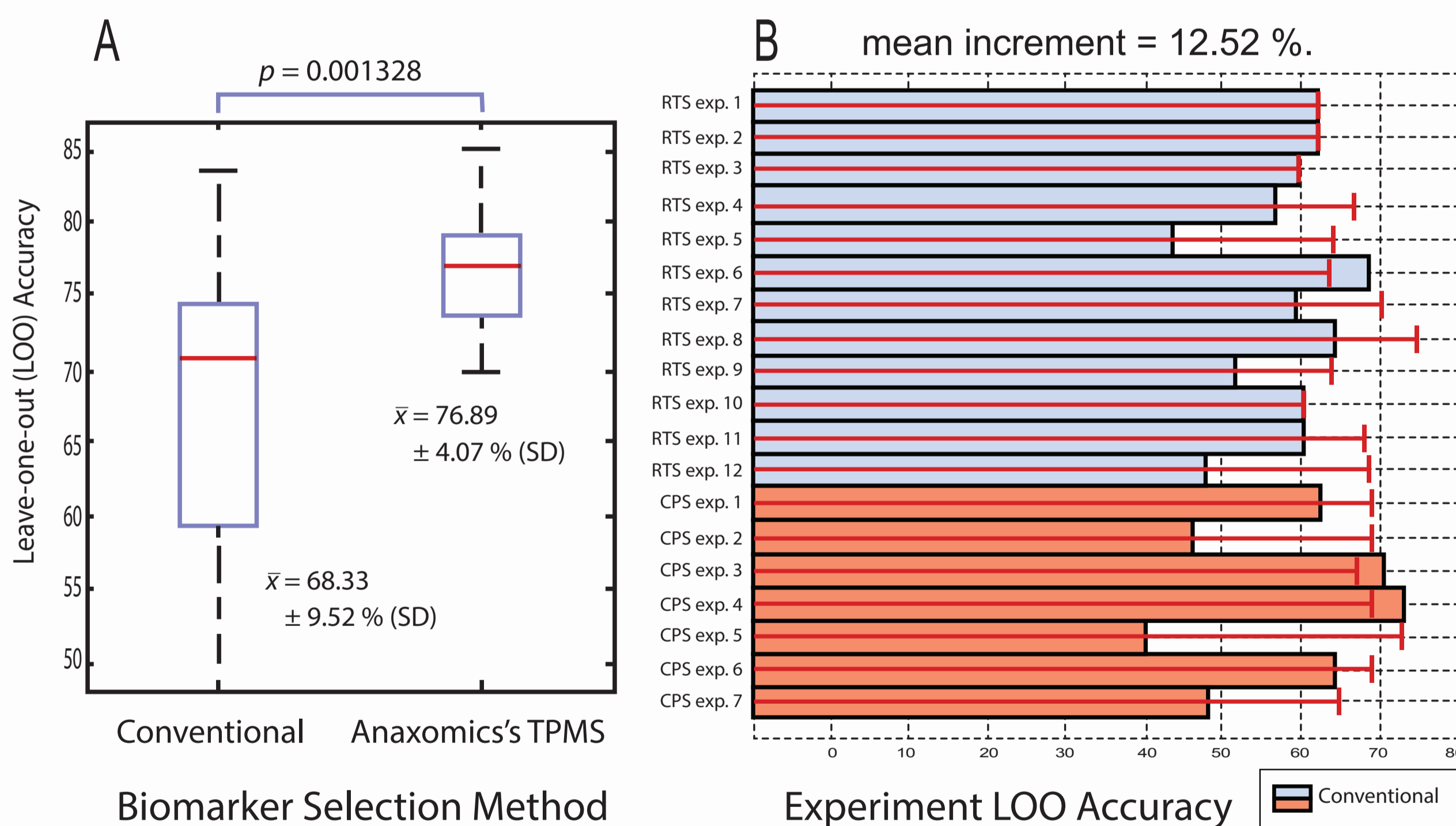Experiment LOO Accuracy
Conventional / TPMS

Fig. 1. **A.** Range, medians (red line), means and standard deviations (SD) and the p-value for a paired one-tailed T-test for the means. **B.** Generalization capability of each method for each experiment. Anaxomic's TPMS outcompetes conventional methods in most cases.

Mathematical models with > 95 % accuracy and a tool to predict (through a **3-BM signature of protection**) whether vaccination will protect an individual have been generated. It is 12.5 % **more generalizing** than conventional methods, i.e. it **predicts better** the status of new individuals (*v*. Fig. 1), partly thanks to the large quantity of considered data.

A deeper mechanistic analysis of these panels will further the understanding of malaria and the protection against it.

Conclusion

- Results underline the utility of Systems Biology (and specially Anaxomics's TPMS) for the interpretation of high-throughput data in BM identification, with a better generalization capability than conventional methods.

- Potential application of Anaxomics's Analytical Tool to other only partially efficacious vaccines.

- Present BM panel will allow the identification of individuals at risk of under- or non-protection after malaria vaccination:
  - allows applying alternative prevention methods.
  - critical for the management and final eradication of malaria.

References

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For more information

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