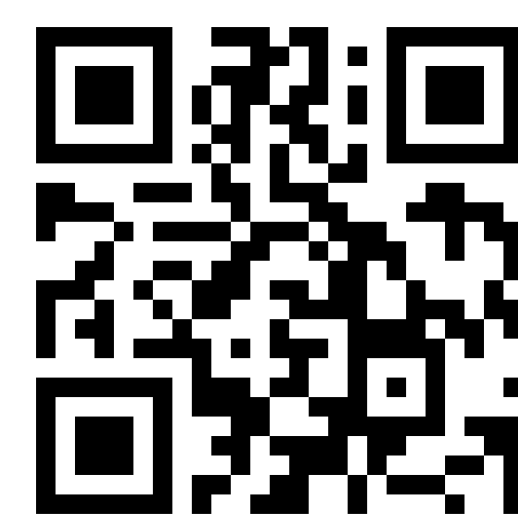


Scientific Computing Infrastructure for Systems Toxicology

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(Part of Philip Morris International group of companies)

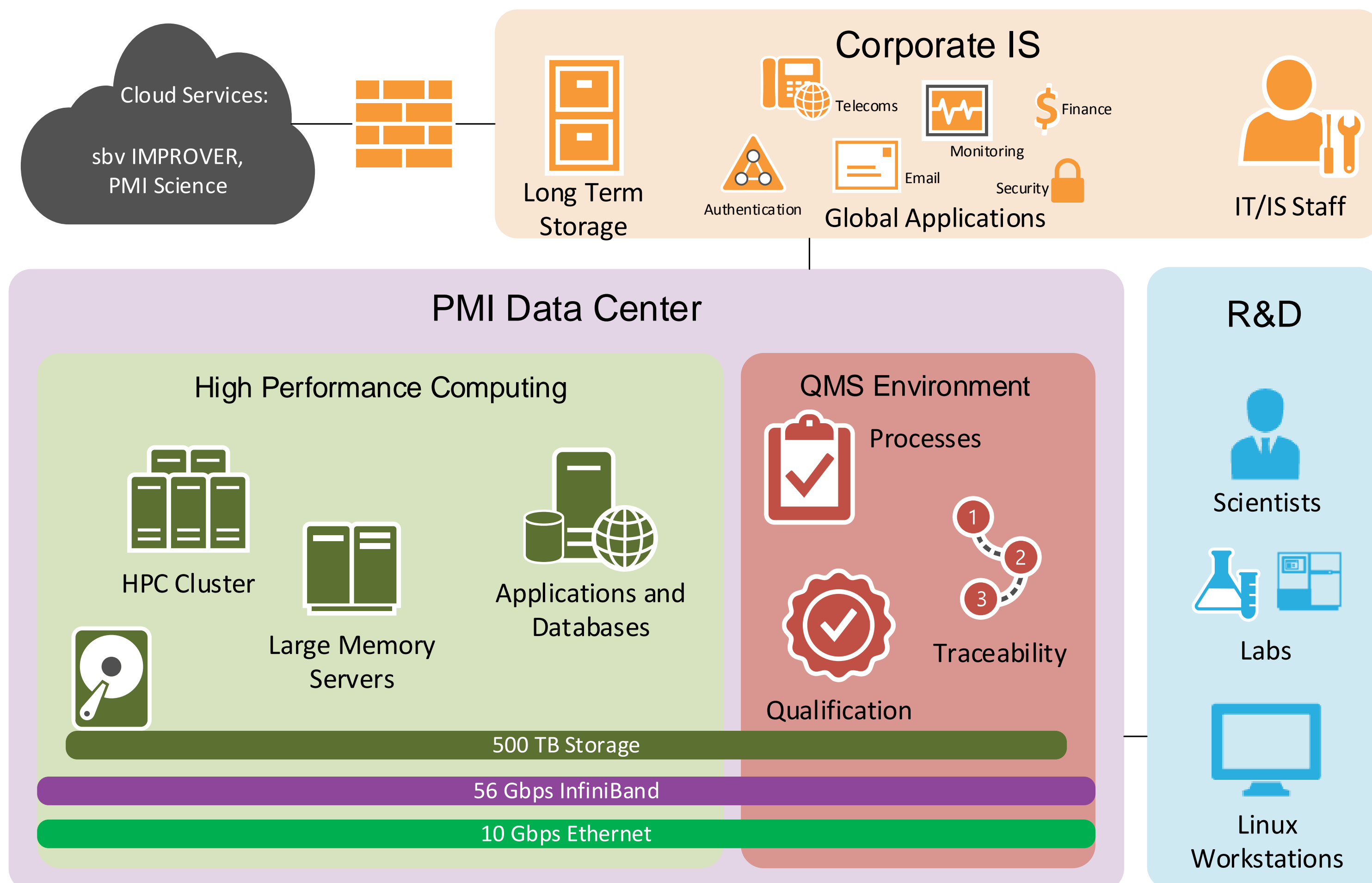


<https://www.pmiscience.com>

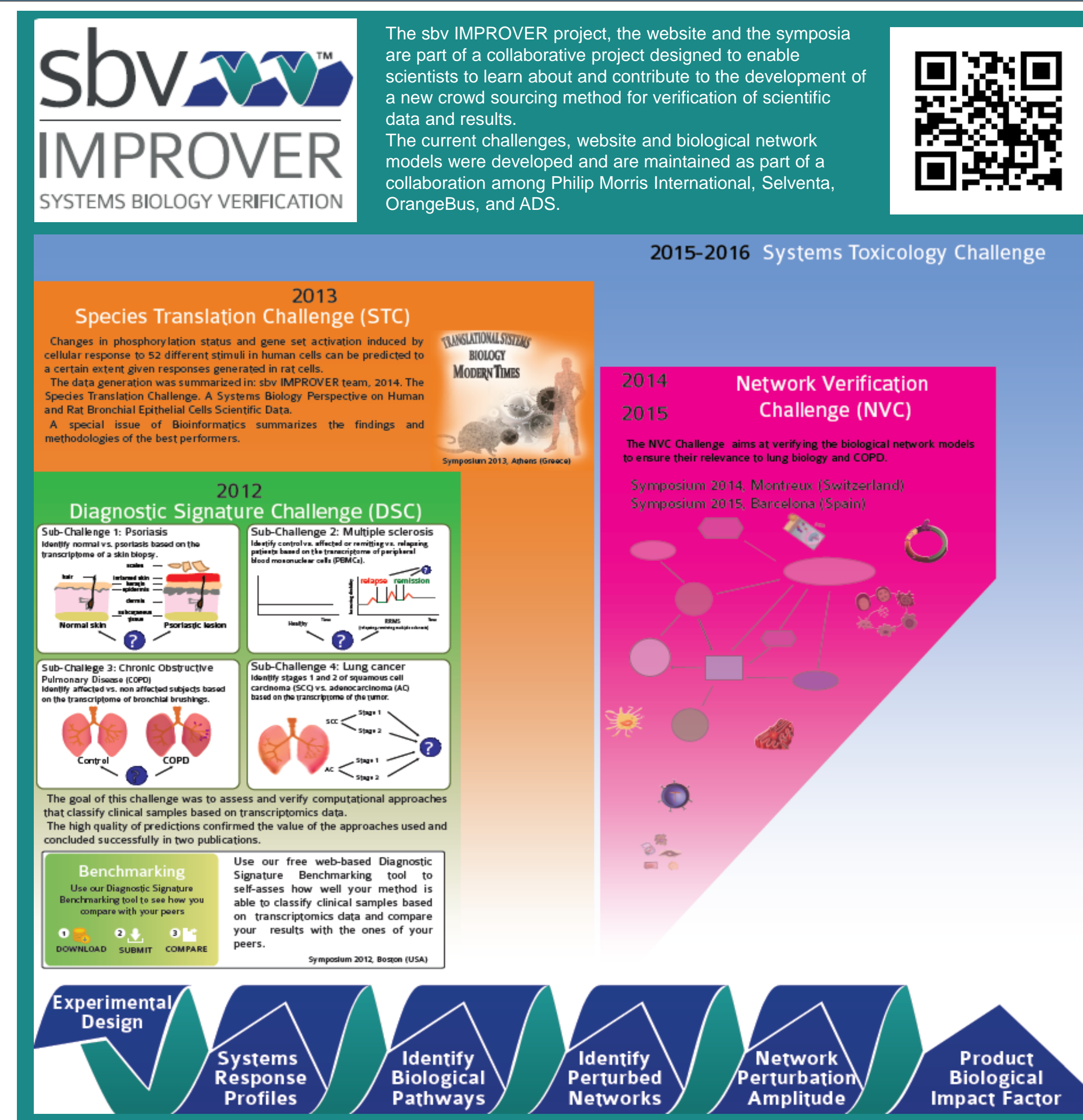
Summary

The high performance computing (HPC) infrastructure enables research and development of new products that may have the potential to reduce the risks of smoking-related diseases. HPC is helping PMI to understand underlying disease mechanisms, perform biomarker discovery, bioinformatics, text mining, genome sequencing, computational fluid dynamics and molecular dynamics simulations.

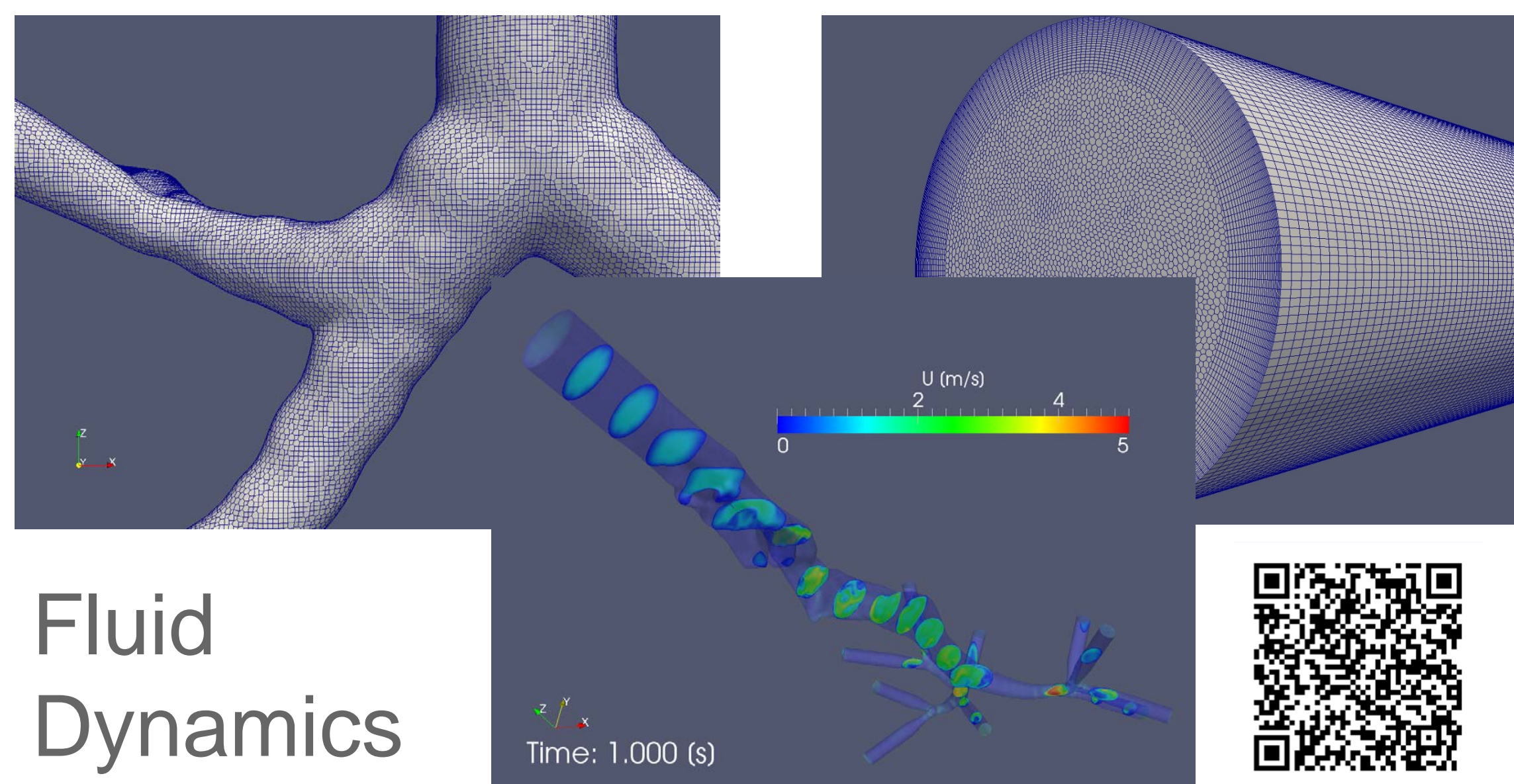
Infrastructure



sbv IMPROVER



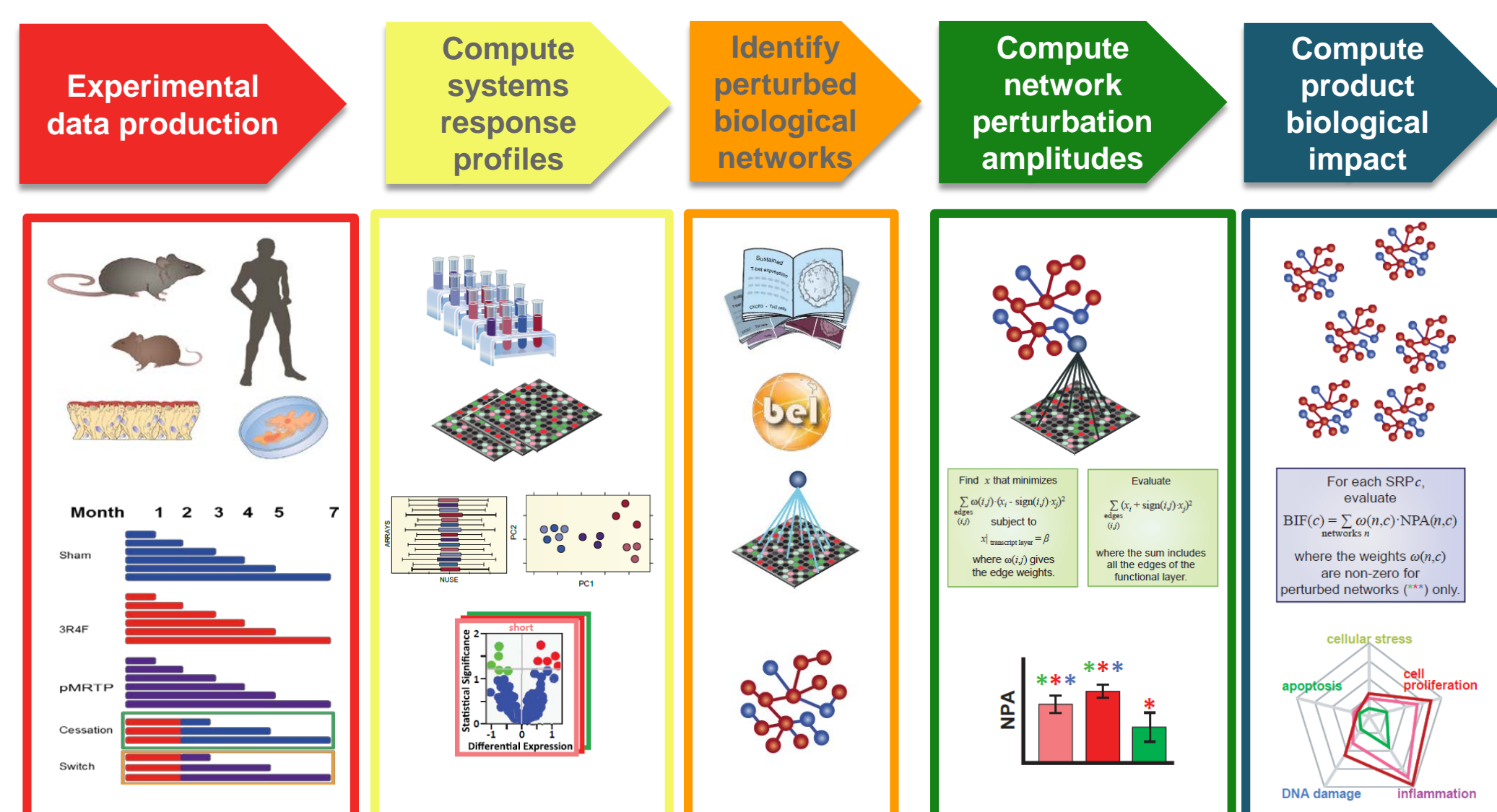
Computational Applications



Fluid Dynamics

Computational Fluid Dynamics (CFD) simulations, based on the established laws of physics integrated with smoke / aerosol transport, evolution, and deposition mechanisms helps understand where and how much of the smoke / aerosol is deposited in the respiratory system. <https://www.pmiscience.com/toxicological-assessment/2-systems-toxicology/systems-toxicology-infrastructure/high-performance/cloud>.

Quantitative Mechanism-Based Systems Impact Assessment



Our method consists in (1) measuring multiple perturbations across multiple experimental systems, (2) computing differential response profiles from large number of measured biological variables, (3) identifying the biological mechanisms perturbed by a product, (4) quantifying the perturbations of individual networks (NPA) and finally (5) quantifying the overall perturbation induced by products.

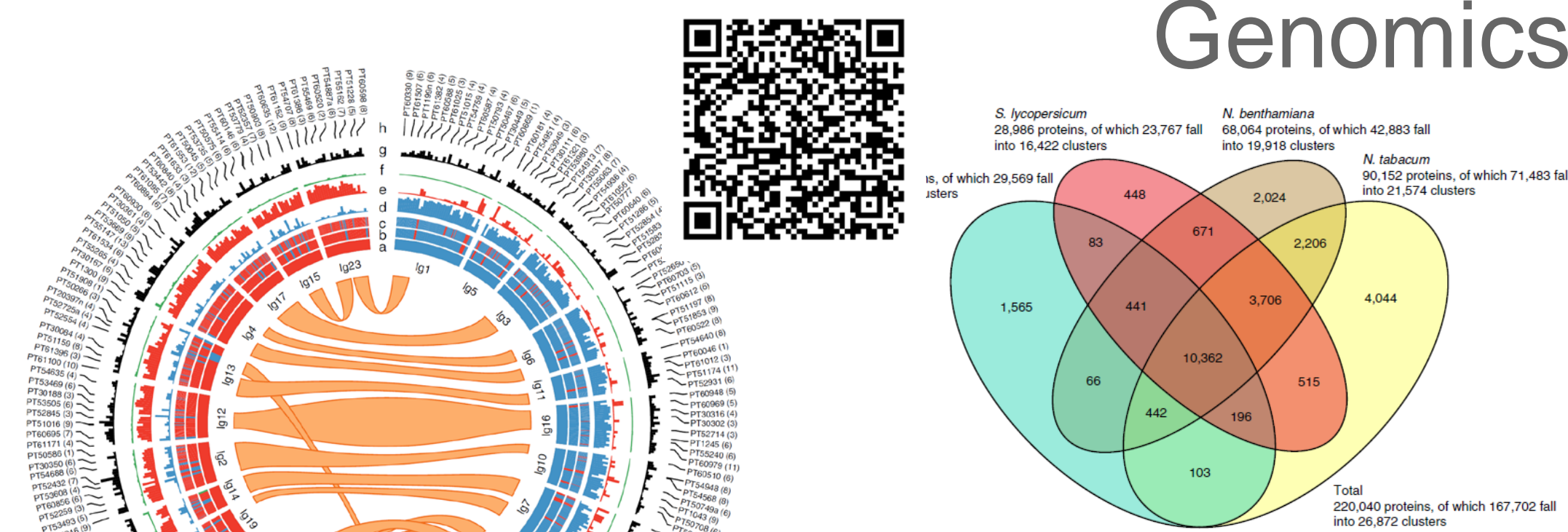
This "Biological Impact Factor" (BIF) represents the system-wide and pan-mechanistic biological impact of a given substance in a mixture.

On the right, several perturbations (colored diamonds) have different quantitative impact on the organism for each network.

Hoeng J, Deehan R, Pratt D, Martin F, Sewer A, Thomson TM, Drubin DA, Waters CA, de Graaf D, Peitsch MC (2012) A network-based approach to quantifying the impact of biologically active substances. *Drug discovery today* 17: 413-418



Genomics



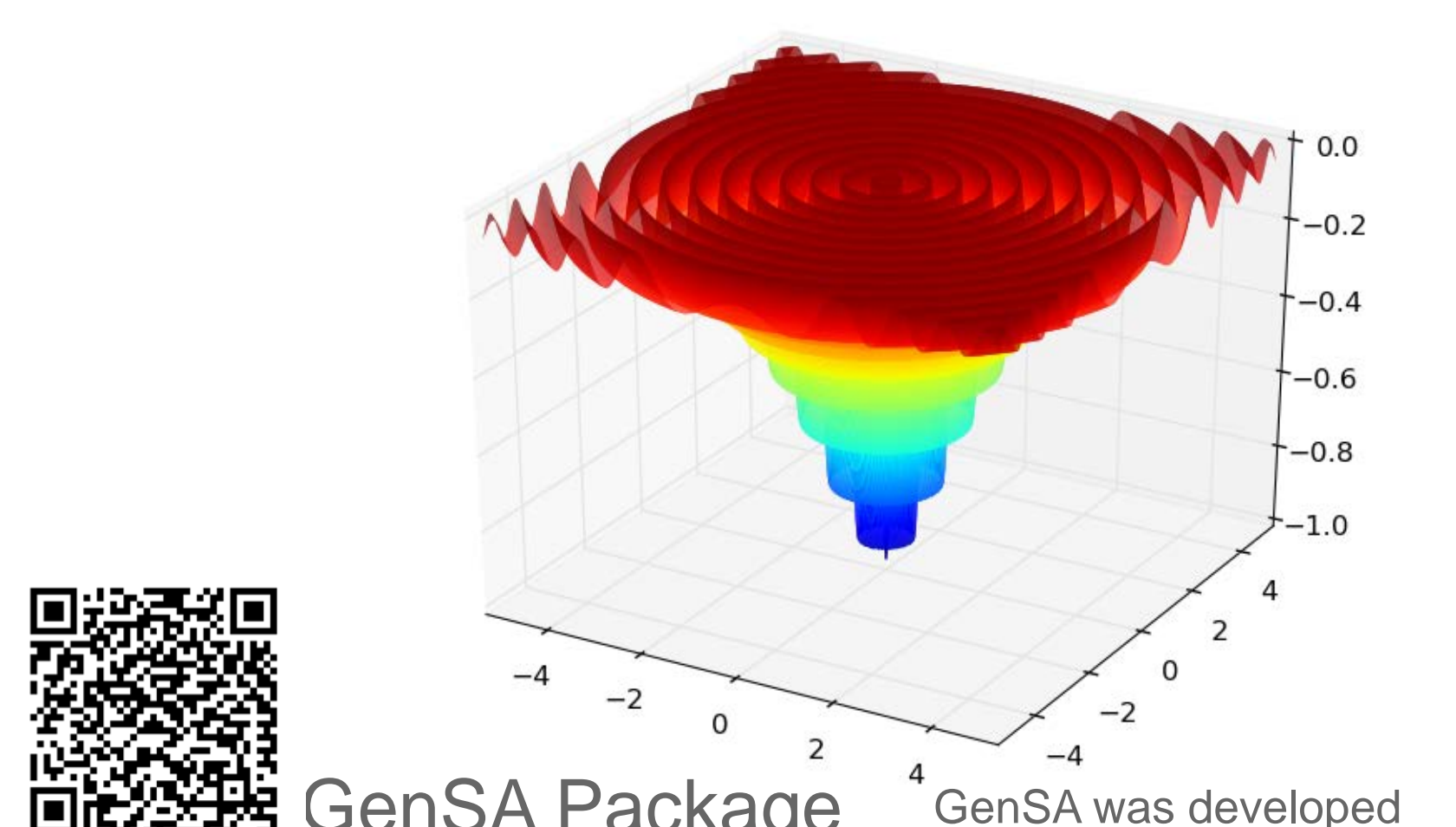
Nicolas Sierro, James N.D. Battey, Sonia Ouadi, Nicolas Bakaher, Lucien Bovet, Adrian Willig, Simon Goepfert, Manuel C. Peitsch, Nikolai V. Ivanov: **The tobacco genome sequence and its comparison with those of tomato and potato.** *Nature Communications* 2014. 5: p. 3833

Our Genomics capabilities, including Next Generation Sequencing, microarray and gene quantification technologies, enable us to gain important insights into the potential of Reduced-Risk Products (RRPs).

<https://www.pmiscience.com/toxicological-assessment/systems-toxicology/systems-toxicology-technology-infrastructure/genomics>

Reduced Risk Products ("RRPs") is the term Philip Morris International use to refer to products with the potential to reduce individual risk and population harm in comparison to smoking cigarettes. PMI's RRPs are in various stages of development and commercialization, and we are conducting extensive and rigorous scientific studies to determine whether we can support claims for such products of reduced exposure to harmful and potentially harmful constituents in smoke, and ultimately claims of reduced disease risk, when compared to smoking cigarettes. Before making any such claims, we will rigorously evaluate the full set of data from the relevant scientific studies to determine whether they substantiate reduced exposure or risk. Any such claims may also be subject to government review and approval authorization, as is the case in the USA today.

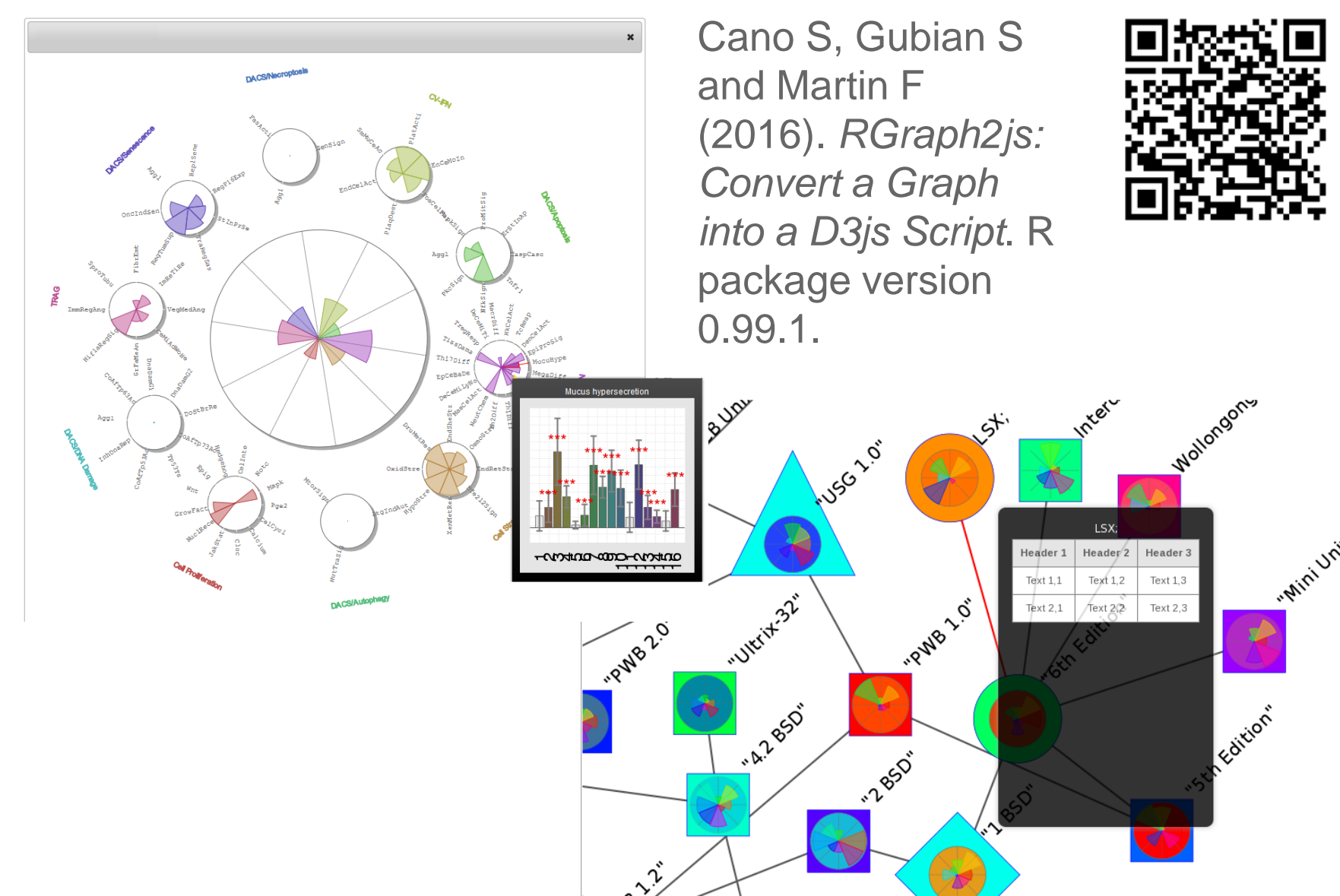
Targeted Development



GenSA Package

GenSA was developed For generalized simulated annealing to process complicated non-linear objective functions with a large number of local minima, especially for functions in many dimensions. Y Xiang, S Gubian, B Suomela, J Hoeng: **Generalized Simulated Annealing for Global Optimization: The GenSA Package.**

Data Visualization



Data visualization tools such as the hierarchical star plot (on the left) and the network display (on the right) help scientists interpret their data, thanks to enriched contents such as contextual popup information and hyperlinks.

All authors are employees of Philip Morris International. Philip Morris International is the sole source of funding and sponsor of this project.



PMI RESEARCH & DEVELOPMENT

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