Computer simulations shed light on how immune cells identify foreign antigens

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How do immune cells manage to sort through vast numbers of similar-looking proteins within the body to detect foreign invaders and fight infections? McGill researchers used computational tools to examine what kind of solutions immune systems may use to detect small concentrations of foreign antigens (characteristic of potentially harmful infections) in a sea of "self-antigens" normally present at the surface of cells.

"For immune cells, singling out foreign proteins is like looking for a needle in a haystack – where the needle may look very much like a straw, and where some straws may also look very much like a needle," notes McGill University physics professor Paul François.

Understanding how immune cells tackle this formidable challenge is important, because it could provide crucial insights into the understanding of immune diseases, from AIDS to auto-immune disorders.

In a study published May 21 in the journal *Physical Review Letters*, François and McGill graduate student Jean-Benoît Lalanne used computational tools to examine what kind of solutions immune systems may use to detect small concentrations of foreign antigens (characteristic of potentially harmful infections) in a sea of "self-antigens" normally present at the surface of cells.

The researchers' computer simulations yielded a surprisingly simple

solution related to the well-known phenomenon of biochemical adaptation – a general biochemical mechanism that enable organisms to cope with varying environmental conditions.

To find solutions, the computer uses an algorithm inspired by Darwinian evolution. This algorithm, designed previously within the François research group, randomly generates mathematical models of biochemical networks. It then scores them by comparing properties of these networks to predefined properties of the immune system. Networks with best scores are duplicated in the next generation and mutated, and the process is iterated over many simulated "generations" until networks reach a perfect score.

In this case, almost all solutions found were very similar, sharing a common core structure or motif.

"Our approach provides a simpler theoretical framework and understanding of what happens" as immune cells sort through the "haystack" to detect foreign antigens and trigger the immune response, François says. "Our model shares many similarities with real immune networks. Strikingly, the simplest evolved solution we found has both similar characteristics and some of the blind spots of real immune cells we studied in a previous collaborative study with the groups of Grégoire Altan-Bonnet (Memorial Sloane Kettering, New York), Eric Siggia (Rockefeller University, New York) and Massimo Vergassola (Pasteur Institute, Paris)."

More information: prl.aps.org/abstract/PRL/v110/i21/e218102

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