The Selector Switch: A Mixed Offense-Defense Network Module in *Staphylococcus aureus*

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***Staphylococcus aureus* is a pathogenic bacterium causing a wide-range of human diseases, due to the expression of numerous virulence factors. We identify the selector switch, a mixed network module which regulates the activity of the bacteria to either an offensive or a defensive mode, according to quorum sensing signal. We suggest two non-exclusive explanations that would benefit the bacteria employing the selector switch module. We analyze the dynamics of the regulation mechanism using a mathematical model and show that the selector switch offers a tight and effective target regulation and carries vital advantages for *S. aureus* upon change in external conditions.**

***Keywords* — Selector switch, network module, noncoding small RNA.**

Staphylococcus aureus is an opportunist gram-positive pathogenic bacterium causing a wide-range of human diseases, from mild skin infections to severe diseases such as pneumonia and septic shock [1-3]. The high diversity of disease manifestations caused by *S. aureus* stems from the expression of numerous virulence factors and stress response pathways, exhibiting distinct spatial and temporal expression patterns, thus requiring precise regulation [3, 4]. Within *S. aureus* virulence pathways lies a network module termed here "selector switch" which regulates the activity of the bacteria to one of two possible modes according to quorum sensing signal [5]. The first is a defensive mode which allows the bacteria to use camouflage techniques, protecting it from phagocytosis. The second is an offensive mode, allowing the bacteria to produce and excrete toxins which penetrate and damage its target cells [6, 7]. The selector switch involves both transcriptional and post-transcriptional layers of regulation, via the transcription factor ROT and the RNA regulator RNAIII, respectively. Altogether, the selector switch forms an integrated double feed forward loop structure, each independently coherent [6-9].

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We hypothesize that temporal activation of the defense and offense functions in a switch - like fashion is of great significance for the virulence competence of *S. aureus*, and we suggest two possible non-exclusive explanations that would benefit bacteria carrying this mechanism, both in the context of growing bacterial population and static population size.

We use deterministic formulation to set a mathematical model that allows us to analyze the dynamics of this intriguing mechanism. We demonstrate the selector switch bi-directional and double-layered regulation properties, leading to a tighter and a more effective control over its targets. We also compare the selector switch to network modules that are structurally identical but have different distribution of regulators and show that the specific configuration of *S. aureus* selector switch carries crucial advantages for the bacteria upon change in external conditions [10].

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