

8. Appendix: Mathematical Analysis

The analysis of Eqs. 1–5 is as follows. By examining the system when all of the derivatives are equal to zero, each of the five equations can be solved for the respective populations in steady state. We remark that the model is reasonable in that no population will go negative (i.e., it can be shown that the non-negative orthant $R_+^5 = \{x \in R^5 \mid x \geq 0\}$ is positively invariant). By solving this quintic system, and using the parameter values in Table 2, five steady states arise, of which three contain negative-valued population sizes that will not be obtained with our (non-negative) initial conditions (based on the positive invariance and positive parameter values). In the fourth steady state, the *non-colonized steady state*, $\bar{A} = \bar{M} = \bar{E} = 0$ and the values of \bar{I} and \bar{N} are free (i.e., they can assume any non-negative values). This implies that in the absence of bacteria, the host response has an infinite number of states, each defined by values of \bar{I} and \bar{N} . This steady state is a stable, degenerate node (i.e., 4 eigenvalues with negative real-part and 1 zero eigenvalue) for biologically appropriate parameter values. This state could represent the conditions in which the host clears the bacteria. The final steady state, the *colonized steady state*, is the only positive, non-trivial steady state. Using the parameter values in Table 2, the steady state $\bar{M} = 7640$, $\bar{A} = 2107$, $\bar{N} = .037$, $\bar{E} = 80134$, and $\bar{I} = 80$. This steady state is locally, asymptotically stable, as it has five corresponding eigenvalues with a negative real-part. To show a portion of the

analytical derivation of this state, we note that the steady-state population value for E is calculated in terms of three of the other populations in Eq. 4; hence, once values for those are known, the steady-state value for \bar{E} can be directly calculated. This also is true for the host-response equation, Eq. 5, which has steady-state value $\bar{I} = I_0$ if \bar{M} and \bar{A} are zero and has value $\bar{I} = k_2$ if \bar{M} and \bar{A} are positive. To simplify the notation, let $\epsilon = c\tau$, and $\hat{\beta} = b/(b + k_2)$. Substituting the expression for \bar{E} obtained by setting Eq. 4 equal to zero leaves three equations and three unknowns:

$$\bar{M} = \frac{-\delta\bar{A}}{g_M - \mu_M - a(K - \bar{A})}, \quad [6]$$

$$\bar{A} = \frac{aK\bar{M}}{\delta - g_A\bar{N} + \mu_A + a\bar{M}}, \quad [7]$$

$$\bar{N} = \frac{\hat{\beta}\epsilon(\bar{M} + \bar{A})}{(\tau + \bar{N})\eta(g_M\bar{M} + g_A\bar{A})}. \quad [8]$$

Solving this now algebraic system is intractable analytically as a quintic arises for N when Eqs. 6 and 7 are substituted into Eq. 8. Thus, depending on choices for parameters, some of these states may yield positive steady states. As mentioned above, for the parameter values in Table 2, there is only one non-trivial, positive steady state.