

### **Appendix 3 - Exploring the Parameter Space**

To gain insight into the behavior of the model, we carried out large numbers of model simulations using randomly generated parameter sets. A small set of parameter values, (Supplementary Table 2) were obtained from (White et al. 2007), which contains a model of the RA signaling gradient without binding proteins or RA receptors. Most parameter values in our model can be estimated to within some order of magnitude. In order to obtain the general properties of a model, we sampled these parameter values within a large but realistic range. This method is useful given that some parameters are unknown and reliable estimates are not available. Because we considered most parameters in the range of within 2 to 3 orders of magnitude, we found it necessary to generate random samples in the logarithmic scale. For example, if parameter P ranges from  $10^{-1}$  to  $10^2$ . This parameter was generated using  $10^{2-3X}$  where x is a random variable uniformly distributed between 0 and 1. The parameters and their ranges are summarized in Supplementary Table 3.