Appendix 2 - Numerical Methods

A dimensionless form of the model is obtained by applying the following scales,
$\tau = x_{\max}^2 / D, X = x_{\max} x, T = \tau t$,
$\{a,b,c,d,e,f\} = \{[RA]_{out},[RA]_{in},[R],[RA-R],[BP],[RA-BP]\}/c_0$.

We use the following set of lumped parameters for clarity,
$\{V_{bp},V_r,V_{ra}\} = \tau / c_0 \{V_{BP},V_R,V_{RA}\}$,
$k_1 = \tau k_p, \{k_2,k_6\} = \tau c_0 \{ra_{\deg}, rabp_{\deg}\}$,
$\{k_{41},k_{42},k_{51},k_{52}\} = \tau\{r_{\deg 1}, r_{\deg 2}, dp_{\deg 1}, dp_{\deg 2}\}$,
$\{r_1,r_2,m_1,m_2,j_1,j_2\} = \tau\{c_0 r_{on}, r_{off}, c_0 m_{on}, m_{off}, c_0 j_{on}, j_{off}\}$.

The model reduces to

$$\begin{aligned}
\frac{\partial a}{\partial t} &= \frac{\partial^2 a}{\partial x^2} + v(x) - (1+\beta)k_1 a + k_1 b, \\
\frac{\partial b}{\partial t} &= k_1 a - (k_2[cyp] + k_1)b - r_1 bc + r_2 d - m_1 be + m_2 f + k_{42} d + k_{52} f, \\
\frac{\partial c}{\partial t} &= V_r - k_{41} c - r_1 bc + r_2 d - j_1 fc + j_2 ed, \\
\frac{\partial d}{\partial t} &= r_1 bc - r_2 d + j_1 fc - j_2 ed - k_{42} d, \\
\frac{\partial e}{\partial t} &= V_{bp} - k_{51} e + k_6[cyp]f - m_1 be + m_2 f + j_1 fc - j_2 ed, \\
\frac{\partial f}{\partial t} &= -j_1 fc + j_2 ed + m_1 be - m_2 f - k_6[cyp]f - k_{52} f.
\end{aligned} \tag{0.1}$$

Because we are concerned with RA signal gradient formation at the gastrula stage, the system can be assumed to be at a steady state. Therefore, we solve the model at the steady state. The model reduces to a boundary value problem with respect to a,

$$0 = D\frac{d^2 a}{dx^2} + v(x) - (1+\beta)k_1 a + k_1 b, \tag{0.2}$$

and five algebraic equations at the steady state.

The boundary value problem is solved using a fourth order Runge-Kutta method together with the shooting method. The values *b, d* and *f* are obtained by finding the roots of the equations,

$$0 = r_1 bc - r_2 d + j_1 fc - j_2 ed - k_{42} d, \tag{0.3}$$

$$0 = -j_1 fc + j_2 ed + m_1 be - m_2 f - k_6[cyp]f - k_{52} f, \tag{0.4}$$

$$0 = k_1 a - [cyp](k_2 b + k_6 f) - k_1 b. \tag{0.5}$$

These values then give $e = \frac{V_{bp} - k_{52}f}{k_{51}}$, and $c = \frac{V_r - k_{42}d}{k_{41}}$.

The Gauss-Newton method is used to solve the algebraic equations for *b, d* and *f*. For simulations that do not converge (successfully find the roots of the system) using Gauss-Newton alone, we iteratively use the bisection method on (0.5) to find *b* and the Levenberg-Marquardt method to solve (0.3) and (0.4) for *d* and *f*. We check the validity of the steady state numerical solver by feeding its output (steady state solutions) as the inputs into a numerical solver for the entire partial differential equation model (0.1) to make sure that the solutions are indeed steady states. The full partial differential equation model was solved by a fourth order Runge-Kutta method in time and finite differences in space. All numerical methods were implemented in the C programming language.