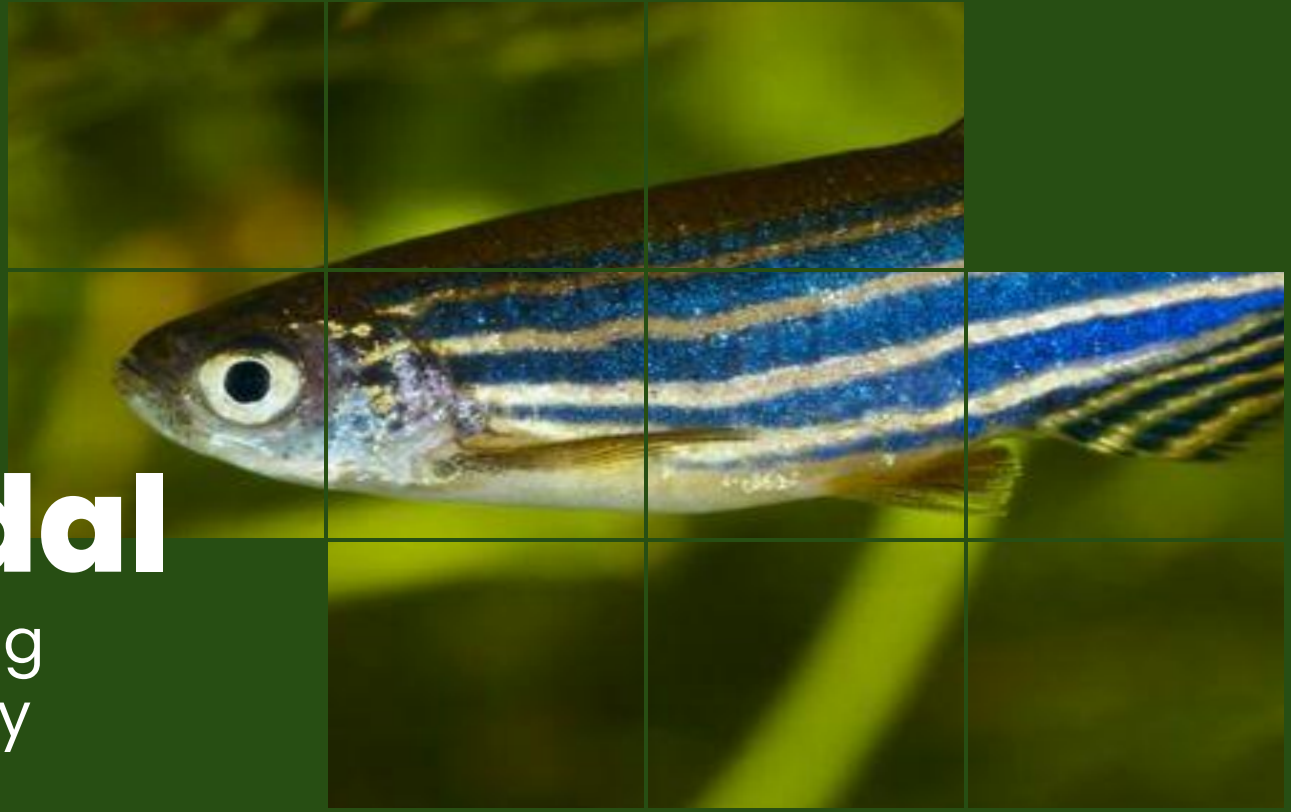


Nodal

Signaling pathway

Presented by
Bairavi, Divyashree
and Anuran

WHAT

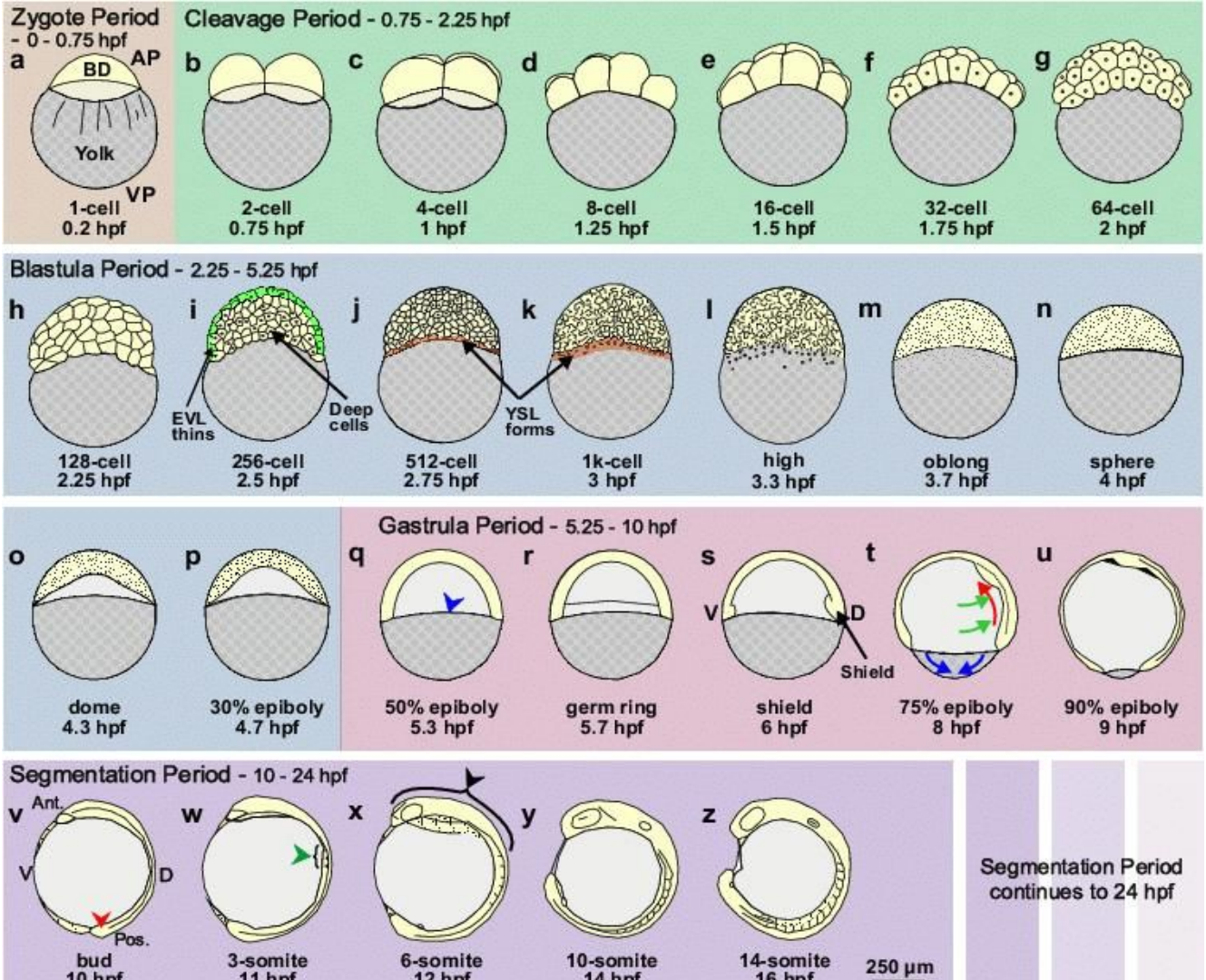
Nodal is a morphogen that provides positional information to cells and influence their fate and behavior during embryonic development.

WHY

We chose this topic to understand the embryogenesis of zebrafish which is well known model organism for human genetic studies.

HOW

We tried to understand the nodal signaling pathway, then we built equations which was then simulated.



Source: Au.p.s et al 2007

Nodal Ligand

The pathway of the signaling starts with the Nodal.

Nodal is already present in epiblast through the maternal contribution

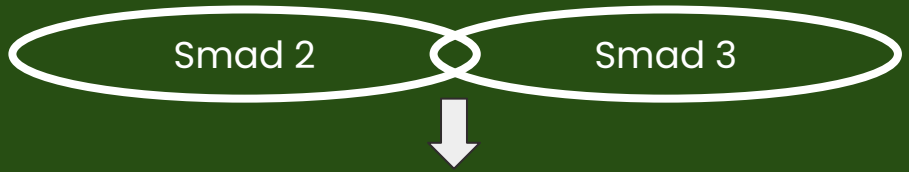
Cell membrane

Receptors

Receptors are of type 1 and type 2 activin like receptors

Phosphorylation of

Smad Complex



Phosphorylated
smad complex

Gene Expression

Of the genes squint and cyclop

- Pattern formation in the mesendoderm
- Formation of left to right axis
- Formation of endoderm

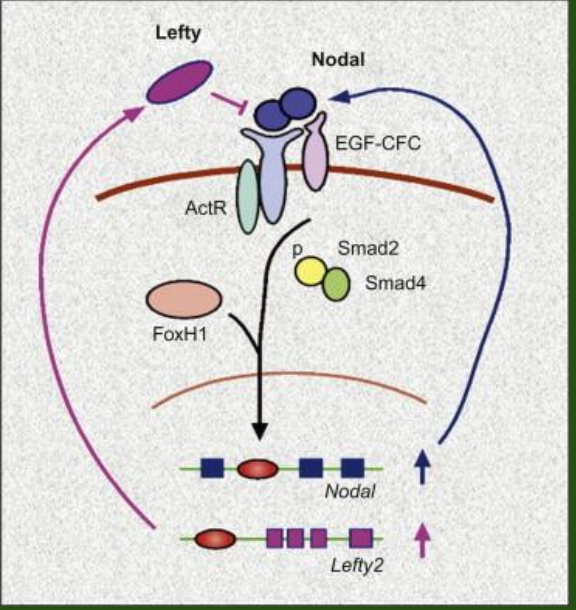
But, once all the functions are over, does this signaling process then continue?

PHOSPHORYLATED

Smad Complex

Lefty

Nodal



N

S

Initially

G

Later

L

$$\frac{\partial N}{\partial t} = -N\left(\frac{L^h}{L^h + k_N}\right)\beta_N$$

$$\frac{\partial \mathrm{S}}{\partial t} = \left(\frac{N^h}{N^h + k_S}\right)\alpha_S - S\lambda_S$$

$$\frac{\partial \mathrm{L}}{\partial t} = \left(\frac{S^h}{S^h + k_L}\right)\alpha_L - L\lambda_L$$

These were the **initial equations** where

N = Nodal

S = phosphorylated Smad

L = Lefty

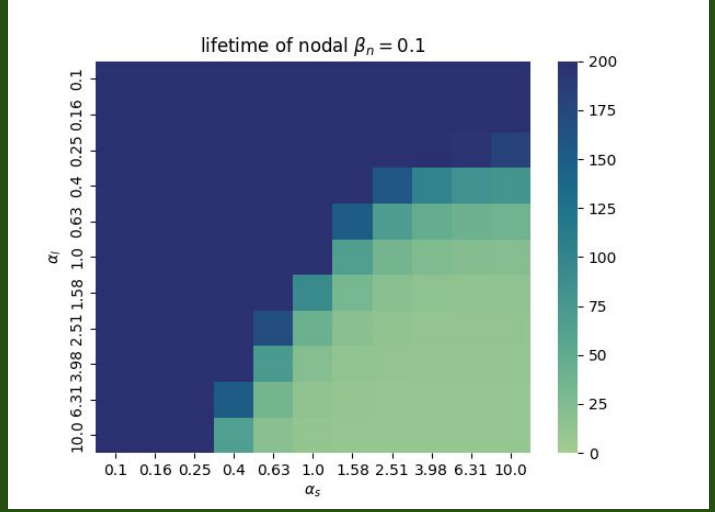
Since there were more parameters, the equations were **non-dimensionalized.**

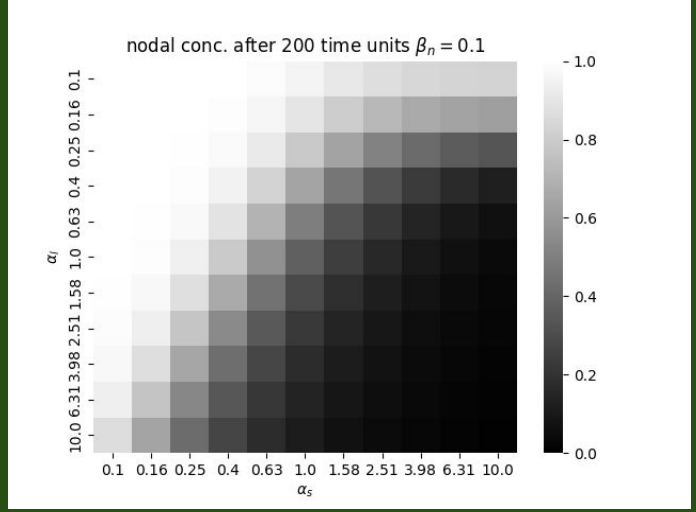
Using the quasi-steady-state approximation, **ds/dT** was assumed to be **zero.**

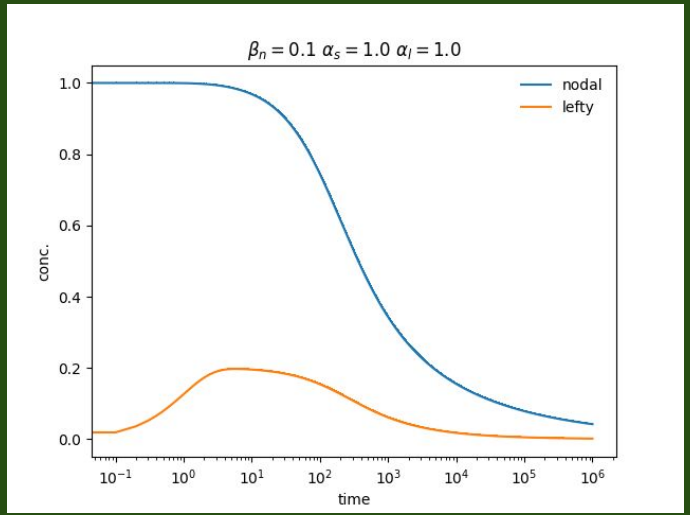
$$\frac{\partial n}{\partial \tau} = -n\left(\frac{l^h}{l^h+1}\right)\beta_n$$

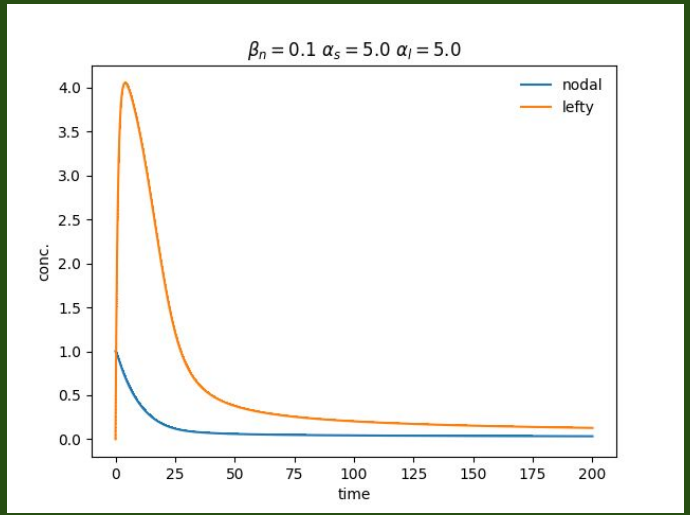
$$\frac{\partial \mathrm{s}}{\partial \tau} = \left(\frac{n^h}{n^h+1}\right)\alpha_s - s$$

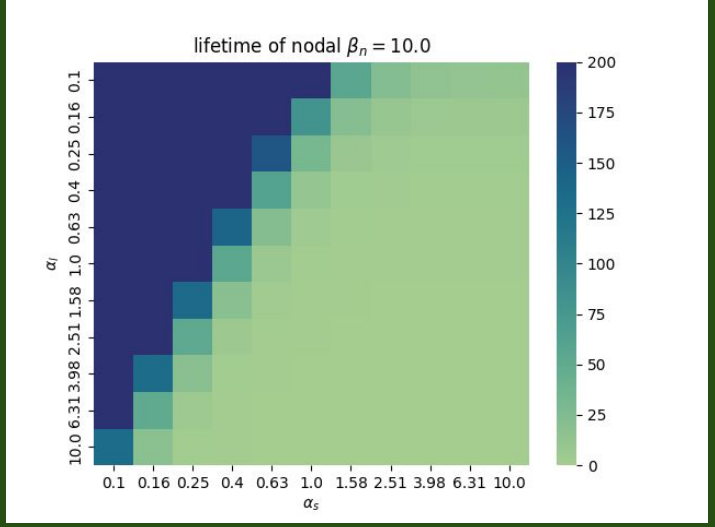
$$\frac{\partial \mathrm{l}}{\partial \tau} = \left(\frac{s^h}{s^h+1}\right)\alpha_l - l$$

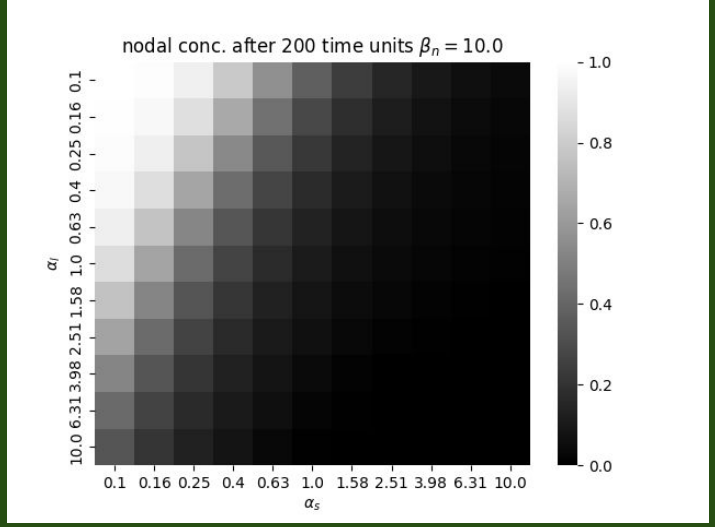

lifetime of nodal $\beta_n = 0.1$
α_l
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
α_s
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
200 175 150 125 100 75 50 25 0

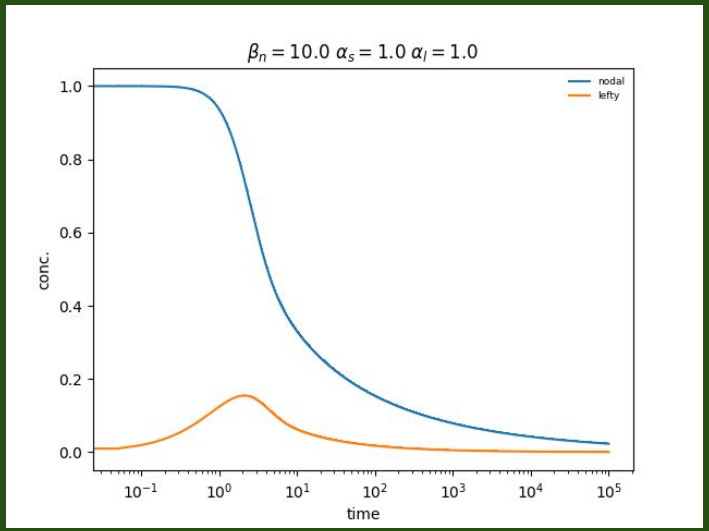

nodal conc. after 200 time units $\beta_n = 0.1$
α_l
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
α_s
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
1.0 0.8 0.6 0.4 0.2 0.0

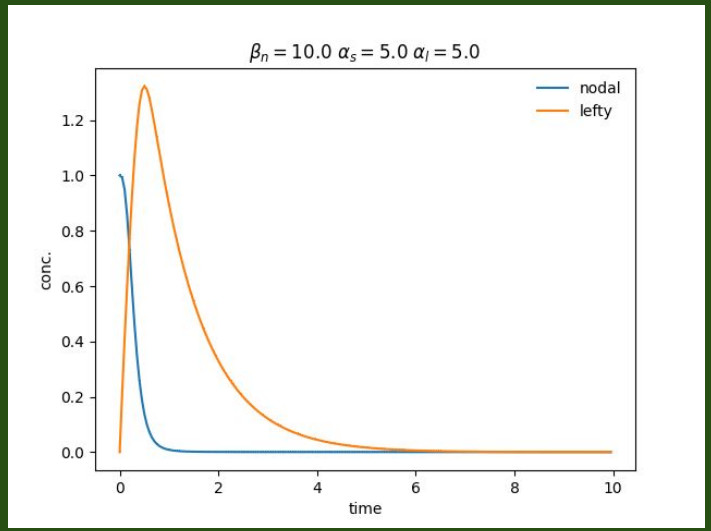

$\beta_n = 0.1$ $\alpha_s = 1.0$ $\alpha_l = 1.0$
nodal
lefty
conc.
1.0 0.8 0.6 0.4 0.2 0.0
10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5} 10^{6}
time


$\beta_n = 0.1$ $\alpha_s = 5.0$ $\alpha_l = 5.0$
nodal
lefty
conc.
4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
0 25 50 75 100 125 150 175 200
time


lifetime of nodal $\beta_n = 10.0$
α_l
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
α_s
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
200 175 150 125 100 75 50 25 0


nodal conc. after 200 time units $\beta_n = 10.0$
α_l
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
α_s
0.1 0.16 0.25 0.4 0.63 1.0 1.58 2.51 3.98 6.31 10.0
1.0 0.8 0.6 0.4 0.2 0.0


$\beta_n = 10.0$ $\alpha_s = 1.0$ $\alpha_l = 1.0$
nodal
lefty
conc.
1.0 0.8 0.6 0.4 0.2 0.0
10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5}
time


$\beta_n = 10.0$ $\alpha_s = 5.0$ $\alpha_l = 5.0$
nodal
lefty
conc.
1.2 1.0 0.8 0.6 0.4 0.2 0.0
0 2 4 6 8 10
time

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GROUP MENTORS

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HAREESH SIR

Thank You