Supplementary Material

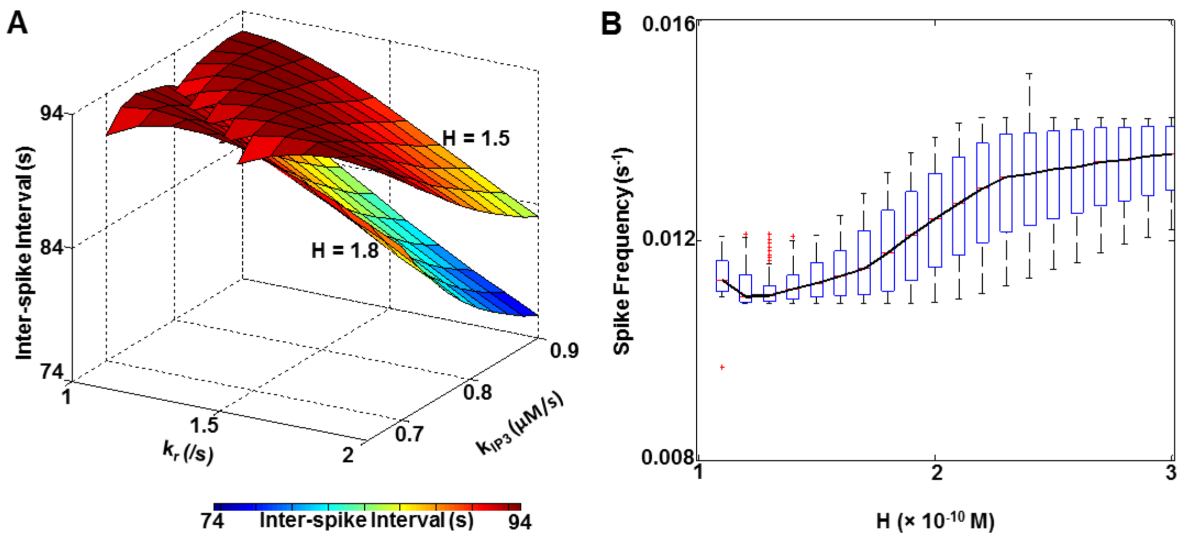

Figure S1: (A) Variation in inter-spike interval of a single hepatocyte with model parameters. Increase in H from 1.5×10^{-10} M to 1.8×10^{-10} results in a decrease in inter-spike interval illustrating frequency encoding as observed experimentally. Increase in k_r or k_{IP3} causes a decrease in inter-spike interval. All parameter values except k_r, k_{IP3}, and H were fixed at the nominal values reported in Table S1. k_r was varied between 1 and 2/s, k_{IP3} was varied between 0.7 and 0.9 μM/s while H took two values (1.5 and 1.8 × 10^{-10}M); (B) Spike frequency ranges for hepatocytes with varying vasopressin concentrations. For each vasopressin concentration value, 100 hepatocytes were initialized with uniformly sampled k_r values (ϵ [1, 2]/s) and k_{IP3} values (ϵ [0.7, 0.9] μM/s), the remaining parameters fixed at their respective nominal values.

Table S1: Nominal parameter values

Parameter ID	Value
k_r	1.5 /s
k_d	0.34 /s
k_{Hr}	$1/10^{-10}$ M-s
H	1.8×10^{-10} M
k_{IP3}	0.8 μM/s
k_{cat}	0.45
k_3	1 μM
D	1.6 /s
G	NA
A	0.2 μM/s
k_1	0.5 μM
L	0.00015 μM/s
B	0.082 μM/s
k_2	0.15 μM
E	$1/(\mu M)^4$-s
F	0.01 /s

Table S2: Initial intracellular species concentrations in model simulations. In every simulation, initial concentration of intracellular signaling species acquired the following values

Species ID	Value
r_i	0.5
$IP3_i$	0.1 μM
CaI_i	0.2 μM
CaT_i	500 μM
g_i	0.25

Table S3: Parameter values used in **Figure 2**; **2A**: All hepatocytes were initialized with parameter and initial values reported in Tables S1 and S2 respectively. G_{ij} = {0, 0.9} for all i,j pairs represent uncoupled and gap junction coupled hepatocytes; **2B**: Nominal values were used for all parameters *except* k_r *and* k_{IP3}. Values used for these parameters were:

	k_r	k_{IP3}
Hepatocyte 1	1	0.785714
Hepatocyte 2	1.5	0.885714
Hepatocyte 3	1.928571	0.757143
Hepatocyte 4	1.357143	0.857143
Hepatocyte 5	1.857143	0.842857
Hepatocyte 6	1.785714	0.814286
Hepatocyte 7	1.571429	0.742857
Hepatocyte 8	1.714286	0.828571
Hepatocyte 9	1.142857	0.771429
Hepatocyte 10	1.642857	0.728571
Hepatocyte 11	1.428571	0.714286
Hepatocyte 12	2	0.871429
Hepatocyte 13	1.214286	0.9
Hepatocyte 14	1.071429	0.7
Hepatocyte 15	1.285714	0.8

G_{ij} = {0, 0.9} for all i,j pairs.

Table S4: Parameters used to generate **Figure 3**. Only k_r (Figure 5A) or k_{IP3} (Figure 5B) values for each hepatocyte were varied, the other parameter fixed at its nominal value:

	Fig. 3A	**Fig. 3B**
Variable parameter ID	k_r	k_{IP3}
Hepatocyte 1	2	0.9
Hepatocyte 2	1.928571	0.885714
Hepatocyte 3	1.857143	0.871429
Hepatocyte 4	1.785714	0.857143
Hepatocyte 5	1.714286	0.842857
Hepatocyte 6	1.642857	0.828571
Hepatocyte 7	1.571429	0.814286
Hepatocyte 8	1.5	0.8
Hepatocyte 9	1.428571	0.785714
Hepatocyte 10	1.357143	0.771429
Hepatocyte 11	1.285714	0.757143
Hepatocyte 12	1.214286	0.742857
Hepatocyte 13	1.142857	0.728571
Hepatocyte 14	1.071429	0.714286
Hepatocyte 15	1	0.7

Table S5: k_{IP3} values used in **Figure 4** with other hepatocyte parameters at nominal values. k_r gradient was the same as that used in Figure 3A.

	Figure 4A	**Figure 4B**	**Figure 4C**	**Figure 4D**
	k_{IP3}	k_{IP3}	k_{IP3}	k_{IP3}
Hepatocyte 1	0.9	0.8	0.7	0.728571
Hepatocyte 2	0.885714	0.8	0.714286	0.714286
Hepatocyte 3	0.871429	0.8	0.728571	0.828571
Hepatocyte 4	0.857143	0.8	0.742857	0.857143
Hepatocyte 5	0.842857	0.8	0.757143	0.771429
Hepatocyte 6	0.828571	0.8	0.771429	0.7
Hepatocyte 7	0.814286	0.8	0.785714	0.785714
Hepatocyte 8	0.8	0.8	0.8	0.742857
Hepatocyte 9	0.785714	0.8	0.814286	0.9
Hepatocyte 10	0.771429	0.8	0.828571	0.757143
Hepatocyte 11	0.757143	0.8	0.842857	0.871429
Hepatocyte 12	0.742857	0.8	0.857143	0.8
Hepatocyte 13	0.728571	0.8	0.871429	0.814286
Hepatocyte 14	0.714286	0.8	0.885714	0.842857
Hepatocyte 15	0.7	0.8	0.9	0.885714

Table S6: k_r and G_{ij} values were systematically varied across the sinusoid to obtain **Figure 5**. Variations in k_r in **Figure 5-A**, **B**, and **C** were as follows:

	Figure 5A	**Figure 5B**	**Figure 5C**
	k_r	k_r	k_r
Hepatocyte 1	0.5	2	2
Hepatocyte 2	0.5	1.928571	1.888889
Hepatocyte 3	0.5	1.857143	1.777778
Hepatocyte 4	0.5	1.785714	1.666667
Hepatocyte 5	0.5	1.714286	1.555556
Hepatocyte 6	2	0.5	1.444444
Hepatocyte 7	1.888889	0.5	1.333333
Hepatocyte 8	1.777778	0.5	1.222222
Hepatocyte 9	1.666667	0.5	1.111111
Hepatocyte 10	1.555556	0.5	1
Hepatocyte 11	1.444444	1.285714	0.5
Hepatocyte 12	1.333333	1.214286	0.5
Hepatocyte 13	1.222222	1.142857	0.5
Hepatocyte 14	1.111111	1.071429	0.5
Hepatocyte 15	1	1	0.5

While all G_{ij} values were equal to 0.9 for all hepatocytes pairs in case of Ca^{2+} signal propagation shown in Figure 5-A, B and C, column I, they were variable for columns II and III. For columns II and III, G_{ij} values were:

Figure 5A: G_{ij} = 2 (column II) or 5 (column III) for {i,j} = {1,2}, {2,1}, {2,3}, {3,2}, {3,4}, {4,3}, {4,5}, {5,4}, {5,6}; G_{ij} = 0.9 otherwise

Figure 5B: G_{ij} = 2 (column II) or 5 (column III) for {i,j} = {5,6}, {6,5}, {6,7}, {7,6}, {7,8}, {8,7}, {8,9}, {9,10}, {10,9}, {10,11}, {11,10}; G_{ij} = 0.9 otherwise

Figure 5C: G_{ij} = 2 (column II) or 5 (column III) for {i,j} = {10,11}, {11,10}, {11,12}, {12,11}, {12,13}, {13,12}, {13,14}, {14,13}, {14,15}; G_{ij} = 0.9 otherwise

Supplement S7: MATLAB Code

Supplement S8: SBML Model

The SBML model was created using VCell[1] 5.3 (build 12).

References:

[1]: Moraru, Ion I., et al. "Virtual Cell modelling and simulation software environment." IET systems biology 2.5 (2008): 352-362.