

Vasopressin: Why bother bursting?

#### Gareth Leng

Vasopressin secretion is proportional to plasma osmotic pressure over a wide dynamic range, and secretion is sustained at a stable level in response to a maintained stimulus







Neurons send information to each other by EPSPs and IPSPs exponentially decaying pulses that affect the membrane potential of the neuron

When the membrane potential crosses a "spike threshold" a spike is generated.



#### Problem

 The more that cells are depolarised, the more excitable they become – non-linear increase in response





## Vasopressin cells



Fire phasically and asynchronously

2 Minutes



## Phasic firing is *efficient* for vasopressin secretion .... maybe

### The spike-response model

- EPSPs and IPSPs are random exponentially decaying pulses
- When the membrane potential crosses a "spike threshold" a spike is generated.



 After each spike, the cell is transiently hyperpolarised (HAP) /depolarised (DAP)



Spiking is governed 0.02 by a random (Poisson) process subject to a post-spike refractoriness followed by a depolarisation -



- Easy to model





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## Activitydependent dynorphin release

HAP, DAP and AHP: (amplitudes, half-lives: 6 parameters)





4 parameters, 2 can be fixed





 Slow inhibition, amplitude and half life (~dynorphin; 2 parameters)

• Membrane bistability (2 parameters)

• Slow depolarising drift (half-life)



- Model has 15 parameters: 13 free, 2 fixed
- Pick random values for all parameters
- Generate a simulated recording
- How well does the simulation fit the data?



- Target recording (20 min)
- 4,000 models with different parameters
- Run each model to simulate 20 min of activity
- Select those with best fits to the data
- "Breed" from these varying and recombining parameters

Continue for 20 generations; 80,000 models

### Fixing individual parameters









# In a heterogeneous population of vasopressin cells, firing rate increases very linearly with input rate

## Extending the model: vasopressin secretion



Properties of nerve terminals added to model to match the characteristics of stimulus-secretion coupling in vitro



#### single neuron : non-linear spike driven secretion





100 neurons, homogeneous population



#### Mike Ludwig Nancy Sabatier Duncan Macgregor Alan Murray Tom Clayton

Macgregor DJ, Leng G (2012) Phasic firing in vasopressin cells: Understanding Its functional significance through computational models *PLoS Comput Biol.* 

Clayton TF, Murray AF, Leng G(2010) Modelling the in vivo spike activity of phasically-firing vasopressin cells. *J Neuroendocrinol.* 22:1290-300



"Hang on, Betty. ... Someone's bound to see us eventually."