# FINDING THE KEY TO A SYNAPSE


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## 1 Introduction

Experimental data have shown that synapses are heterogeneous: different synapses respond with different sequences of amplitudes of postsynaptic responses to the same spike train.

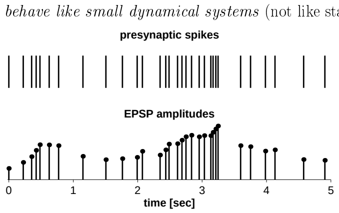
Neither the role of synaptic dynamics itself nor the role of the heterogeneity of synaptic dynamics for computations in neural circuits is well understood.

We present in this article two computational methods that make it feasible to compute for a given synapse with known synaptic parameters the spike train that is optimally fitted to the synapse in a certain sense.

Our methods provide a new approach for computational analysis of dynamic synapses.

## Dynamic synapses

*Biological synapses behave like small dynamical systems* (not like static weights).



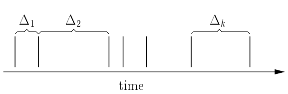

The dynamics of a synapse is usually described by a few *characteristic parameters*, e.g. in the model of [Markram, Wang, and Tsodyks, *PNAS*, 1998]:

$U \approx$ initial release probability

$F =$ time constant for recovery from facilitation

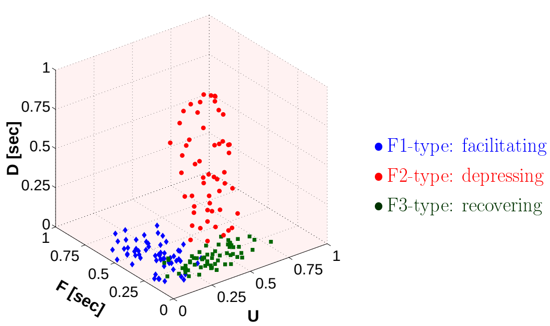
$D =$ time constant for recovery from depression

On the basis of these parameters *one can compute the amplitude $A_k$ of the postsynaptic response* for the $k$th spike in a spike train.

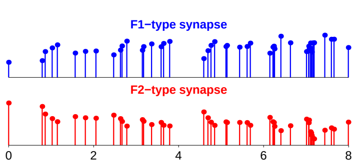



$$\begin{aligned} A_k &= A \cdot u_k \cdot R_k \\ u_k &= U + u_{k-1}(1-U)e^{-\Delta_k/F} \\ R_k &= 1 + (R_{k-1} - u_{k-1}R_{k-1} - 1)e^{-\Delta_k/D} \end{aligned}$$

Experimental results show that for biological synapses the *characteristic parameters $U$, $D$, $F$ are quite heterogeneous* (data according to [Gupta, Wang, and Markram, *Science*, 2000]).



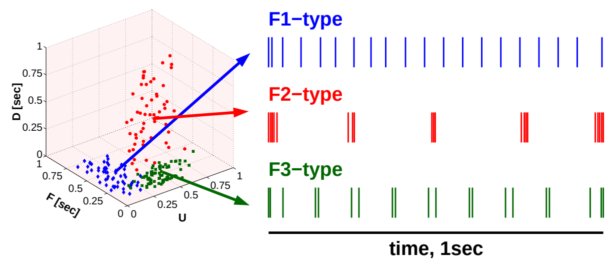

The *same input spike train* can yield *markedly different outputs* for different values of the characteristic parameters.




## 2 Our work

We have found a *computational technique* that allows us *to compute for a synapse* with given characteristic parameters the *temporal pattern which is "optimal"* for this synapse.

For example, compute the *temporal pattern of $N = 20$ spikes in $T = 1$ sec that produces the largest integral of postsynaptic current* for (biological) synapses whose parameters have been determined.




Our *computational techniques can also be applied* to compute the temporal pattern of a spike train that *maximizes*

- the *amplitude of a specific (e.g. the last) postsynaptic response*
- the *maximal amplitude of the largest postsynaptic response*
- the *maximal peak of postsynaptic membrane potential*
- ...

## The computational techniques

We present two methods

- A computational intensive method that is guaranteed to to find the optimal spike train (up to discretization error).
- A quick method that provides a heuristic solution ("locally" optimal spike trains)

### The constraint optimization problem

Fix a time *interval* $T$, a *minimum value* $\Delta_{\min}$ *for ISIs*, the *number of spikes* $N$ and synaptic parameters $U$, $D$, and $F$.
*Find a sequence of ISIs* $\Delta_1, \ldots, \Delta_{N-1}$ *("actions")* such that the

$$\text{"total reward"} \quad J(\Delta_1, \ldots, \Delta_{N-1}) = \sum_{k=1}^{N} A \cdot u_k \cdot R_k$$

is maximized under the constraints

$$\sum_{k=1}^{N-1} \Delta_k \leq T \text{, and } \Delta_{\min} \leq \Delta_k.$$

### The Dynamic Programming Approach

- *Is guaranteed to find the optimal solution!*
- Similar techniques are used in reinforcement learning
  - state: $\langle u_k, R_k, t_k \rangle$
  - action: ISI $\Delta_k$
  - total reward: $\sum_{k=1}^{N} A \cdot u_k \cdot R_k$

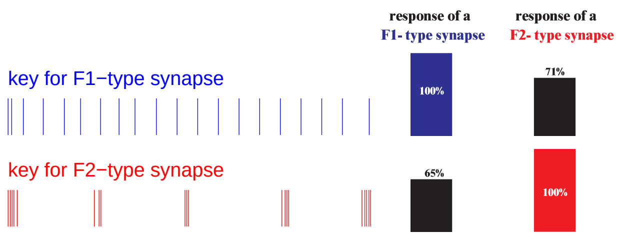
### Sequential Quadratic Programming

- Heuristics based *state of the art approach* for solving constrained optimization problems
- *Not guaranteed* to find the optimal solution, *but usually does.*
- One needs to supply gradient information
- Takes *much less computation time* than the Dynamic Programming approach

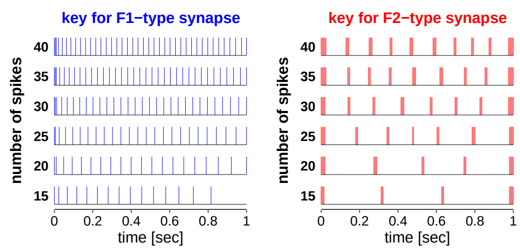
# 3 Results

## The "key" to a synapse

Let us refer informally to *the temporal pattern that produces the largest response for a given synapse as the "key" to this synapse.* Unfortunately this notation of a "key" is somewhat misleading:

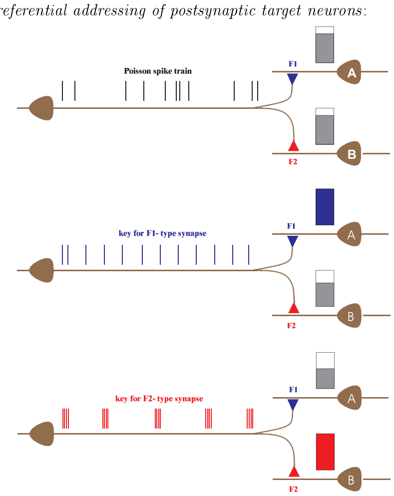



The *qualitative structure of the temporal patterns of these "keys" are quite robust* with respect to changes of the number $N$ of spikes and the length of the time interval $T$.



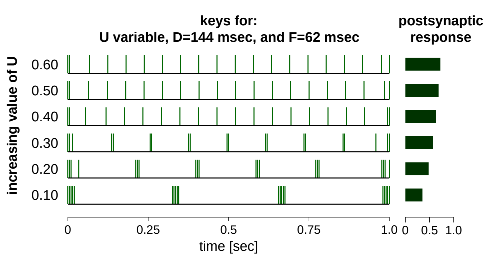

## Addressing of postsynaptic targets

One *possible functional role of temporal patterns* as "keys" to specific synapses is the possibility of *preferential addressing of postsynaptic target neurons*:




## "Inverse analysis"

The *"inverse analysis"* that our computational techniques provide also *give us a better intuition about the role of individual synaptic parameters*:




⇒ If $U$ *changes from 0.1 to 0.6* the pattern changes from bursting to regular.

⇒ The *integral of postsynaptic current generated by the optimal spike pattern is not proportional to* $U$ (remember: $U \approx$ initial release probability).

## Food for thought

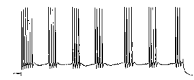
### Relation to discharge patterns

*All these "keys" to specific synapses occur as characteristic discharge pattern of biological neurons* (found in vitro and in vivo) under constant current injection.

*non accommodating (NAC), in vitro*
[Gupta, et.al., *Science*, 2000]

*accommodating (AC), in vitro*
[Gupta, et.al., *Science*, 2000]

*stuttering (STUT), in vitro*
[Gupta, et.al., *Science*, 2000]

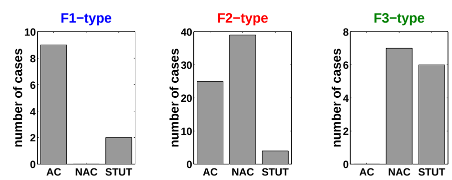


*bursting, in vivo*
[Steriade, et.al, *J. Neurophys.*, 1998]

### Synaptic organization

⇒ For F1-type and F3-type synapses the optimal spike train *agrees with the most often found firing pattern* of presynaptic neurons reported in [Gupta, et.al., *Science*, 2000].

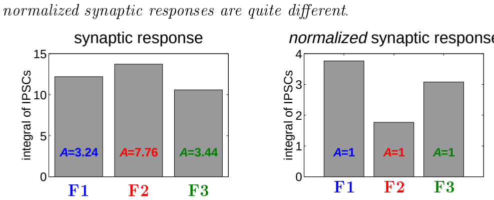
⇒ For F2-type synapses we find *no such agreement.*




Discharge patterns of presynaptic neurons found in [Gupta, et.al., *Science*, 2000]

### What is the role of the absolute synaptic strength $A$?

- The values of $A$ vary strongly among synapses of the F1-, F2-, and F3-type [Gupta, et.al., *Science*, 2000].
- The *response* of a synapse to its "key" *is almost the same for each synapse.*
- The *normalized synaptic responses are quite different.*




⇒ Question: *Is the system designed in such a way that each synapse should have an equal influence on the postsynaptic neuron when it receives its optimal spike train?*

# 4 Summary

- ***We found two computational techniques for computing the "key" to a given dynamic synapse.***
  - Dynamic Programming
  - Sequential Quadratic Programming
- ***These methods can also be applied for other criteria (see e.g. Section 2), and work for any common synaptic model.***
- ***New types of questions can be addressed:***
  - relationship between specific discharge patterns and synaptic parameters
  - What is the role of $U$, $D$, $F$?
  - Why are the parameters $U$, $D$, $F$ heterogeneous?

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