Supplementary figure 1: Initiation of dendritic sodium spikes is not dependent on the frequency of activation.

A, Voltage responses to paired pulse stimulations with different inter stimulus intervals (ISI 20-1000ms) in a neuron that initiated a dendritic sodium spike. The stimulation intensities is presented in pseudocolor scale (see insert).

B and C, Somatic responses vs. stimulation intensity for single pulse (grey) and for paired pulse stimulation with ISI of 20ms ***B*** and 100ms ***C*** for the cell shown in ***A***. There was no statistically significant difference between paired and single pulse stimulations in somatic EPSP amplitude or in stimulation intensity required to initiate a local sodium spike.

D, PPR for subthreshold (open circles) and sodium spike (filled circles) responses for 2 cells. The high standard deviation values for spike responses stem from the fact that local sodium spikes were initiated almost equally at the first and the second inputs, leading to very high or very low PPR.

Supplementary figure 2: In vitro stimulation by in vivo recorded signals.

A, *In-vivo* somatic voltage recordings from layer 5 pyramidal neurons. Four-second-long random areas of interest were selected from the raw data.

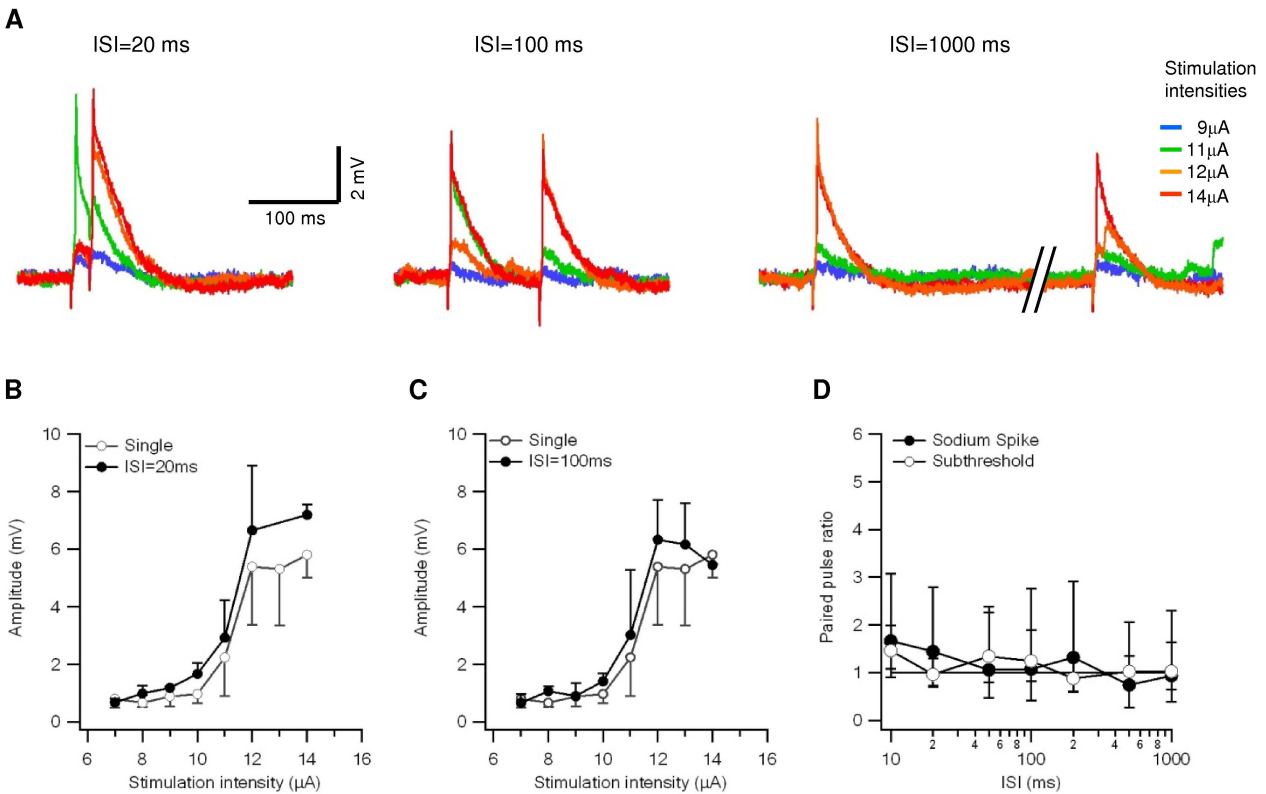
B, Left – action potentials were truncated from the raw recording and the underlying subthreshold potentials were converted to current signals which were injected in current clamp mode to in vitro neurons.

Right - Action potential timing from different *in-vivo* traces was used to create the temporal stimulation pattern. This temporal pattern was used to drive the stimulation electrode located next to one of the basal branches in vitro.

Supplementary figure 3: Simulation of the dendritic and somatic voltage transients during NMDA-spike.

A, Simulation of the dendritic (red) and somatic (black) potentials during paired pulse (ISI=20ms, solid line) and single pulse activation (dotted line). Stimulation intensity was 12nS and 6nS per pulse for NMDA and AMPA conductances respectively. Model parameters and synapse location as in Figure 7.

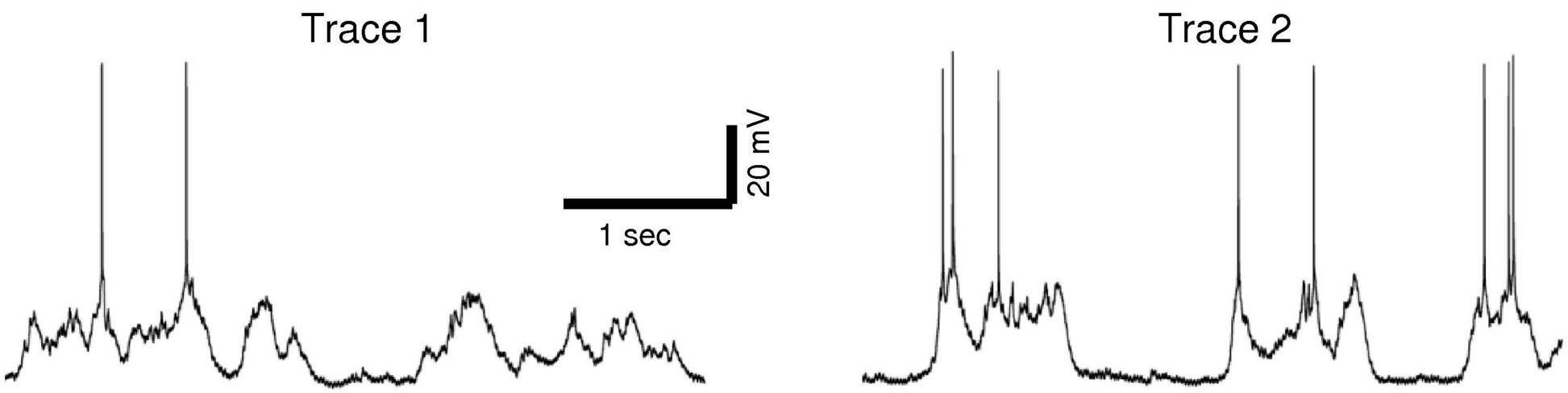
B, Simulation of the dendritic and somatic voltages when only NMDA conductance is present. Colour coding and NMDA conductance as in ***A***.
C, Zoom on the somatic traces of ***A*** and ***B***.
D, Simulation of the forward and backward dendritic attenuation. The peak local voltage is plotted as a function of the distances from the soma for synaptic stimulations depicted in ***A-C*** (solid red – paired pulse, dotted red – single pulse stimulation). The voltage attenuation profile for somatic current injection (black trace, 100pA) is also shown. Unlike the significant attenuation of the dendritic potentials, somatic current injection propagates effectively to the synaptic location (5% attenuation). The arrows indicate the direction of propagation.
E, Simulation of a typical synapse at the dendrite containing AMPA-R and NMDA-R components. Upper and middle plots: activation of a single synapse containing NMDA (black, 1.5nS) and AMPA (grey, 0.75nS) currents at the dendritic location marked by a red circle at the cell shown in Figure 8 (distance of 256μm from soma). Membrane potentials were +40mV for the top and -60mV for the middle plots. Bottom plot shows the corresponding local dendritic (red) and somatic (black) EPSP at -60mV.


A
ISI=20 ms
ISI=100 ms
ISI=1000 ms
Stimulation intensities
9μA
11μA
12μA
14μA
2 mV
100 ms
B
Single
ISI=20ms
Amplitude (mV)
Stimulation intensity (μA)
C
Single
ISI=100ms
Amplitude (mV)
Stimulation intensity (μA)
D
Sodium Spike
Subthreshold
Paired pulse ratio
ISI (ms)

Polsky-supp 2

A

In vivo somatic voltage recordings



Extraction of subthreshold and suprathreshold signals

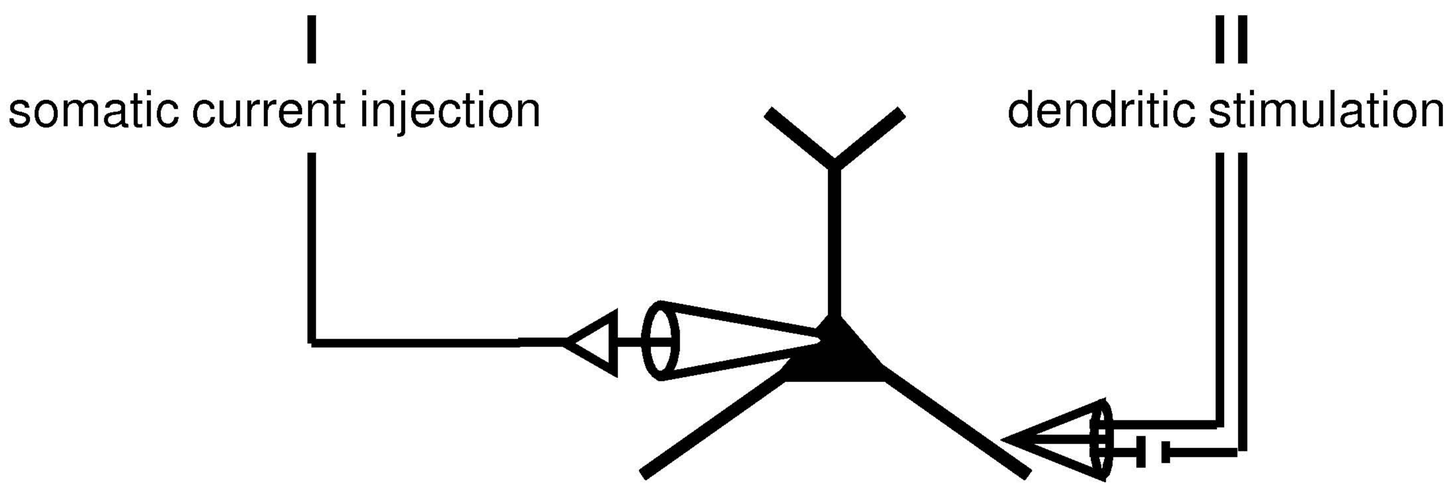
B

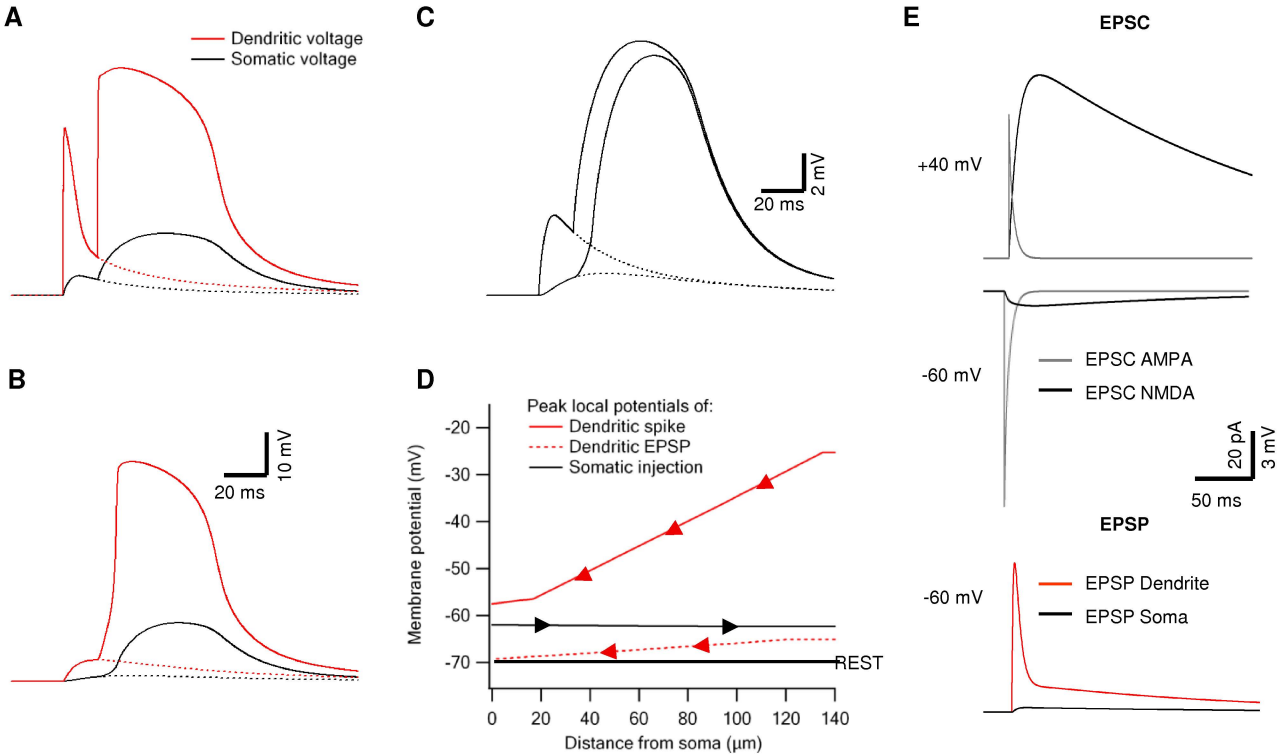
Subthreshold somatic currents

Action potential occurrences

Subthreshold somatic potentials

In vitro somatic current injection and dendritic stimulation




A
Dendritic voltage
Somatic voltage
B
10 mV
20 ms
C
2 mV
20 ms
D
Peak local potentials of:
Dendritic spike
Dendritic EPSP
Somatic injection
Membrane potential (mV)
-20
-30
-40
-50
-60
-70
REST
0
20
40
60
80
100
120
140
Distance from soma (µm)
E
EPSC
+40 mV
-60 mV
EPSC AMPA
EPSC NMDA
20 pA
3 mV
50 ms
EPSP
-60 mV
EPSP Dendrite
EPSP Soma