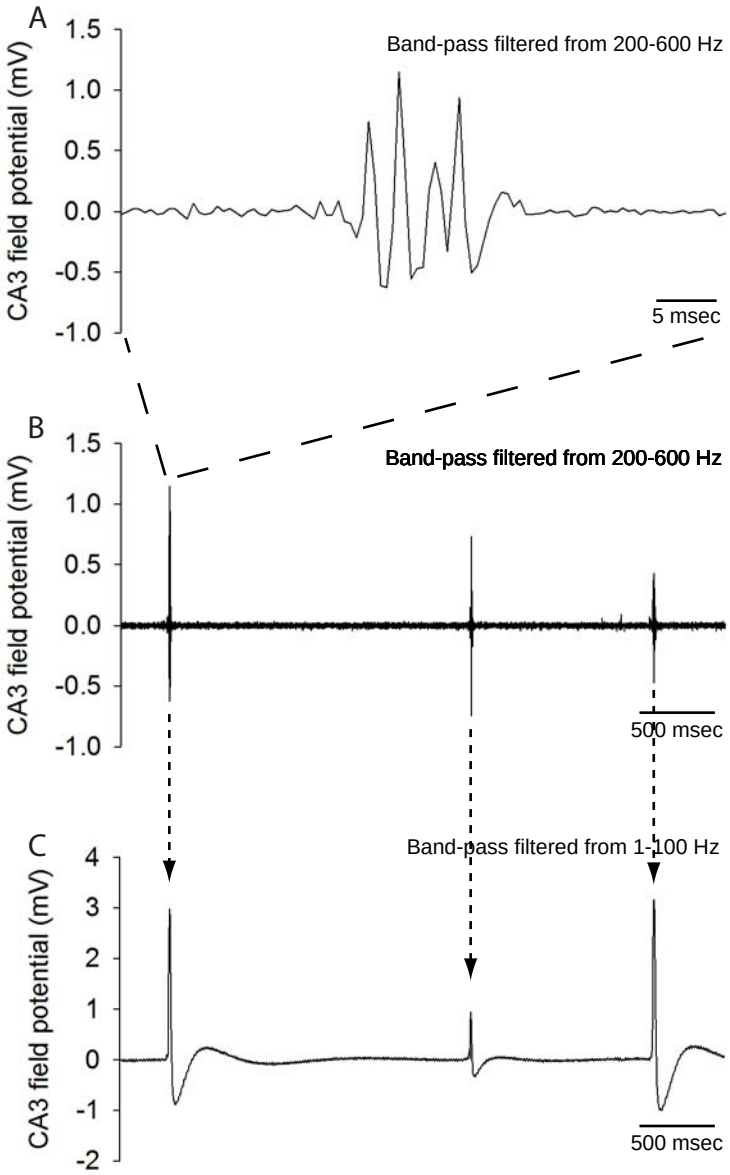
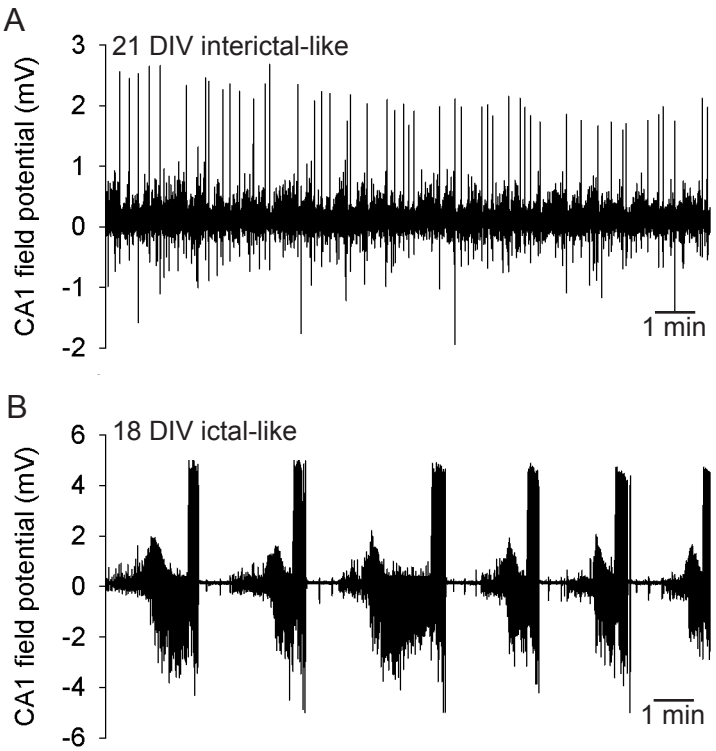
Supplementary Figure 1




**Supplementary Figure 1: Fast ripple-like activity during epileptogenesis is associated with Inter-ictal spikes. A.** Band-pass filtered (8-pole Bessel filter at 200 Hz, Gaussian filter at 600 Hz) field potential recording from area CA3 of a 14 DIV organotypic slice culture reveals fast ripple-like complexes. **B.** These fast ripple-like complexes occured at intervals larger than 1 sec. **C.** Fast ripple-like complexes were associated with interictal-like spikes (trace filtered w. 8 pole Bessel filter at 1 Hz, Gaussian filter at 100 Hz).

Supplementary Figure 2



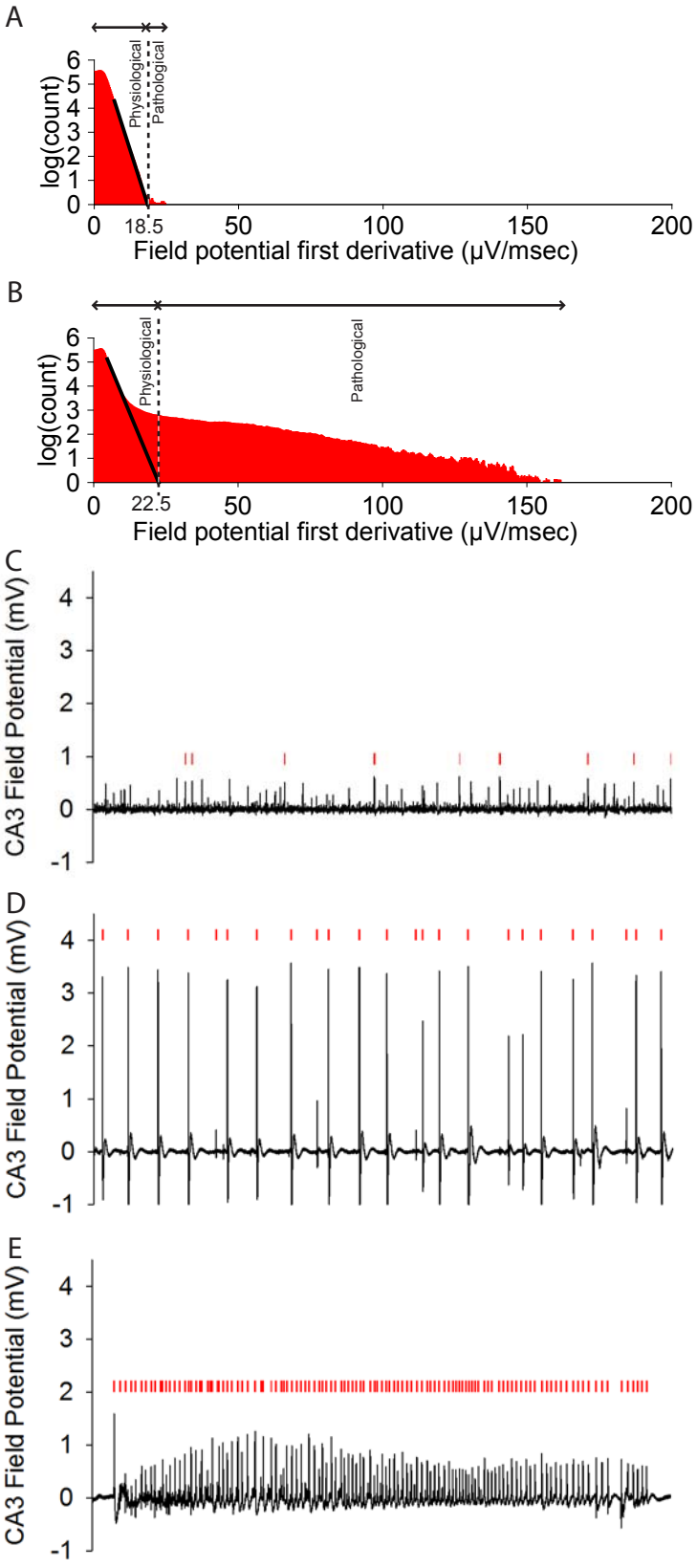

**Supplementary Figure 2: Spontaneous epileptiform activity in interface-type cultures.**
**A.** Interictal-like acticity recorded from area CA1 in an interface-type culture after 21 DIV.
**B.** Ictal-like activity recorded from area CA1 in an interface-type culture after 18 DIV.

**Organotypic hippocampal slice cultures – modified interface method.**
Modified interface-type cultures were prepared as described earlier[1]. Briefly, hippocampal slices of 350 µm thickness were dissected from postnatal day 3-4 Sprague Dawley rat pups (Harlan Laboratories, USA, and Charles River Laboratories, Wilmington, MA) and placed into polydimethylsiloxane (Sylgard 184, Dow Corning, Midland, MI) wells on poly-D-lysine (Sigma-Aldrich, St. Louis, MO) coated 35 mm tissue-culture dishes (Becton Dickinson, Franklin Lakes, NJ). The dishes were then filled with just enough serum-containing medium composed of 25% horse serum (Sigma-Aldrich, St. Louis, MO), 25% Hanks' Balanced Salt Solution, and 50% Basal Medium Eagle, supplemented with 1 mM GlutaMAX and 30 µg/ml gentamicin, all from Invitrogen, Carlsbad, CA) to cover the bottom of the dish and incubated in a humidified 5% $CO_2$ incubator at 37° C. Serum-free medium (Neurobasal A/B27, with 0.5 mM GlutaMAX and 30 µg/ml gentamicin, all from Invitrogen) was substituted in on the second day of organotypic culture, and was used in all subsequent medium changes (every 3 days).

**Field Potential Recordings**
Petri dishes with organotypic cultures were removed from tissue culture incubator, and transferred to an interface recording chamber with a humidified 95% air / 5% $CO_2$ atmosphere at 37° C. Cultures were recorded in their original medium. Field potential recordings were carried out with a tungsten recording electrode placed in area CA1, visualized with a stereo microscope. Signals were amplified and low-pass filtered at 30 kHz with a multiple channel amplifer (Dagan Corporation, Minneapolis, MN), digitized, and recorded with custom-designed software dClamp written in Microsoft Visual C++.

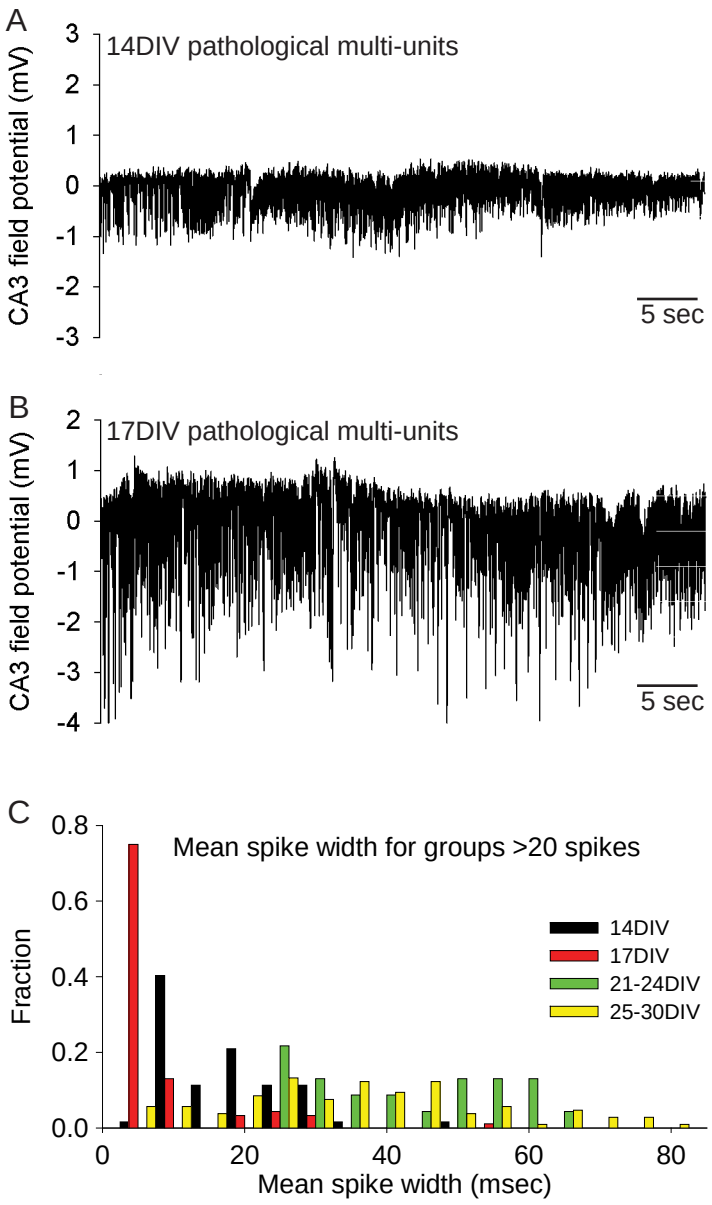
[1]Berdichevsky, Y., Sabolek, H., Levine, J.B., Staley, K.J. & Yarmush, M.L. Microfluidics and multielectrode array-compatible organotypic slice culture method. J Neurosci Methods (2008).

Supplementary Figure 3




**Supplementary Figure 3: Automated detection of pathological spike activity. A,B.** Pathological spikes were detected in CA3 field potential traces using a previously published method (White et al., 2006). Briefly, a powerlaw (black line) is fitted to the steepest slope of the initial part of the first-derivative distribution of the signal (in red, **A.** a 7 DIV slice culture with some pathological multi-unit activity, **B.** a 14 DIV slice culture with interictal-like discharges), yielding the cutoff between physiological and pathological activity as the intercept with the x-axis. This method reliably detected individual spikes (marked in red) from **C.** pathological multi-unit activity, **D.** interictal-like activity and **E.** ictal-like discharges.

Supplementary Figure 4




**Supplementary Figure 4: Long lasting ≥ 2 Hz activity at 14-17 DIV. A.** High frequency pathological multi-unit activity at 14 DIV. **B.** High frequency pathological multi-unit activity at 14 DIV. **C.** Mean spike width distributions for groups of consecutive high frequency spikes at 14-30 DIV. Note that mean spike widths at 14-17 DIV predominantly fall below 20 msec, consistent with multi-unit discharges.