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1 Transition to Oscillations in Two Coupled Variables

1.1 Mathematical Model

Single Variable, first-order differential equation

The equation:

$$\begin{split} \frac{dEx}{dt} &= h_{ex} - Ex + c_1 * tanh(Ex) - c_2 * tanh(In) \\ \frac{dIn}{dt} &= h_{in} - In + c_3 * tanh(Ex) - c_4 * tanh(In) \end{split}$$

where Ex and In are variables that changes with time t, h_{ex} and c_i are model parameters, tanh is the tangens hyperbolicus.

For $c_2 = c_3 = 0$, the two variables are uncoupled and independent.

The model dynamics can be characterised by scans of parameter h_ex. Here, we use a slow continuous change of this parameter to simulate spontaneous qualitative transitions of dynamics in the human EEG.

1.2 Import Functions

```
[3]: from scipy.integrate import odeint from scipy.signal import find_peaks, butter, sosfilt

from numpy import zeros, tanh, linspace, sqrt, fill_diagonal, ndarray from numpy import asarray, array, around, arange, flip, var from numpy.random import default_rng

from matplotlib.pyplot import subplots
```

1.3 Model and Functions

```
[6]: def sigmoid(u): return tanh(u)
```

```
def single_oscillator(y, t, h_ex, h_in, pars):
   tau_ex, tau_in, c_1, c_2, c_3, c_4 = pars
   dydt = (
        (h_ex - y[0] + c_1*sigmoid(y[0]) - c_2*sigmoid(y[1]))*tau_ex,
        (h_{in} - y[1] + c_3*sigmoid(y[0]) - c_4*sigmoid(y[1]))*tau_in,
   return dydt
def single_oscillator_plus_driving(y, t, h_ex, h_in, pars, sr, time_stop, __
 →driving, driving_strength):
   tau_ex, tau_in, c1, c2, c3, c4 = pars
   index = int(t*sr)
   if index >= time_stop*sr:
       dydt = zeros(2)
       return dydt
   h_ex_driven = h_ex + driving_strength*driving[index]
   dydt = (
        (h_ex_driven - y[0] + c1*sigmoid(y[0]) - c2*sigmoid(y[1]))*tau_ex,
                    - y[1] + c3*sigmoid(y[0]) - c4*sigmoid(y[1]))*tau_in,
  )
   return dydt
def single_oscillator_plus_driving_plus_noise(y, t, h_ex, h_in, pars, sr,_
 stime_stop, driving, driving_strength, random_data, random_strength):
   tau_ex, tau_in, c1_ex, c2_ex, c3_in, c4_in = pars
   index = int(t*sr)
   if index >= time_stop*sr:
       dydt = zeros(2)
       return dydt
```

```
[8]: def plot_series(time, data, time_begin, time_end, sr):
         N = data.shape[1]//2
         name_vars = ('Ex', 'In')
        no_vars = 2*N
         fig, ax = subplots(ncols=2*N, figsize=(6, 4))
         for ind in arange(no_vars):
             ax[ind].plot(time[time_begin*sr:time_end*sr], data[time_begin*sr:

→time_end*sr, ind], linewidth=2, c='b')
             ax[ind].set_xticks(linspace(0, time_end-time_begin, 5));
             ax[ind].set_xticklabels(linspace(0, time_end-time_begin, 5));
             ax[ind].set_xlabel('Time', fontsize=12);
             ax[ind].set_ylabel(name_vars[ind], fontsize=12)
             y_min, y_max = ax[ind].get_ylim()
             ax[ind].set_yticks(linspace(y_min, y_max, 3));
             ax[ind].set_yticklabels(around(linspace(y_min, y_max, 3),1),__

¬fontsize=14);
         fig.tight_layout()
         return fig, ax
     def plot_series_statespace(time, data, time_begin, time_end, sr):
         N = data.shape[1]//2
         name_vars = ('Ex', 'In')
```

```
no_vars = 2*N
  fig, ax = subplots(ncols=2*N, figsize=(6, 4))
  ax[0].plot(time[time_begin*sr:time_end*sr], data[time_begin*sr:time_end*sr,_u
→0], linewidth=2, c='b')
  ax[0].set_xticks(linspace(0, time_end-time_begin, 5));
  ax[0].set_xticklabels(linspace(0, time_end-time_begin, 5));
  ax[0].set_xlabel('Time', fontsize=12);
  y_min, y_max = ax[0].get_ylim()
  ax[0].set_yticks(linspace(y_min, y_max, 3));
  ax[0].set_yticklabels(around(linspace(y_min, y_max, 3),1), fontsize=14);
  ax[0].set_ylabel(name_vars[0], fontsize=12);
  ax[1].plot(data[time_begin*sr:time_end*sr, 1], data[time_begin*sr:
→time_end*sr, 0], linewidth=2, c='b')
  x_min, x_max = ax[1].get_xlim()
  ax[1].set_xticks(linspace(x_min, x_max, 3));
  ax[1].set_xticklabels(around(linspace(x_min, x_max, 3),1));
  ax[1].set_xlabel(name_vars[1], fontsize=12);
  ax[1].set_ylabel(name_vars[0], fontsize=12)
  y_min, y_max = ax[1].get_ylim()
  ax[1].set_yticks(linspace(y_min, y_max, 3));
  ax[1].set_yticklabels(around(linspace(y_min, y_max, 3),1), fontsize=14);
  ax[1].set_ylabel(name_vars[0], fontsize=12);
  fig.tight layout()
  return fig, ax
```

```
if not isinstance(ye, ndarray):
        ax.scatter(xe, ye, c='r', s=5)
    else:
        ax.scatter([xe] * len(ye), ye, c='m', s=50, marker='x')
for xe, ye in zip(flip(par_set), results_max_b[0]):
    if not isinstance(ye, ndarray):
        ax.scatter(xe, ye, c='r', s=5)
    else:
        ax.scatter([xe] * len(ye), ye, c='b', s=20, marker='P')
for xe, ye in zip(flip(par_set), results_min_b[0]):
    if not isinstance(ye, ndarray):
        ax.scatter(xe, ye, c='r', s=5)
    else:
        ax.scatter([xe] * len(ye), ye, c='b', s=20, marker='P')
ax.set_xticks(linspace(par_min, par_max, 5));
ax.set_xticklabels(around(linspace(par_min, par_max, 5), 2), fontsize=16);
ax.set_xlabel('Parameter', fontsize=16)
ax.set_ylabel('Ex', fontsize=14)
y_min, y_max = ax.get_ylim()
ax.set_yticks(linspace(y_min, y_max, 3));
ax.set_yticklabels(around(linspace(y_min, y_max, 3),2), fontsize=14);
fig.tight_layout()
return fig, ax
```

1.4 Time Series

```
[13]: # Excitatory input parameter
h_ex_0 = -4.5
h_in_0 = -4

# Supercritical Hopf parameters
pars = (1, 1, 4, 6, 6, 0)
# Bistability parameters
# pars = (1, 1, 4, 1, 6, 0)

# Initial conditions
```

```
SEED = 123
rng = default_rng()
y_ini = rng.uniform(size=2)
\# y_i = y[-1, :]
# Time array
time\_stop = 30
         = 1000
          = linspace(start=0, stop=time_stop, num=time_stop*sr)
time
# Simulation
y = odeint(func=single_oscillator, y0=y_ini, t=time,
          args=(h_ex_0, h_in_0, pars),
          hmax=0.1)
# Show final values of all variables
print('End of run:', list(around(y[-1,:],3)))
print('')
```

End of run: [np.float64(-2.44), np.float64(-9.909)]

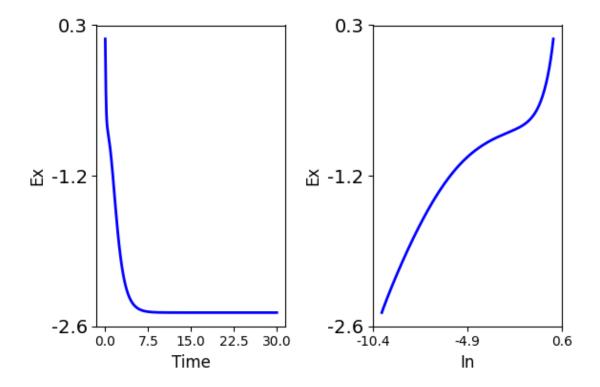
```
[15]: time_begin, time_end = 0, time_stop

fig, ax = plot_series_statespace(time, y, time_begin, time_end, sr)

title_chars = 'Figs/SNIC_Timeseries_h_ex' + str(h_ex_0) + '.png'

# fig.savefig(title_chars, format='png')
print(title_chars)
```

Figs/SNIC_Timeseries_h_ex-4.5.png



1.5 Bifurcation Diagram

```
[18]: # Initial conditions
      y_{ini} = y[-1, :]
      # Bifurcation parameter range
      steps = 50
      par_min, par_max = -5, 2
      par_set = linspace(par_min, par_max, steps)
      # Stop time
      time_stop = 500
      time = linspace(start=0, stop=time_stop, num=time_stop*sr)
                      = dict()
      results_max_f
      results_max_inds_f = dict()
      results_min_f
                     = dict()
      results_min_inds_f = dict()
      rows = time.size
```

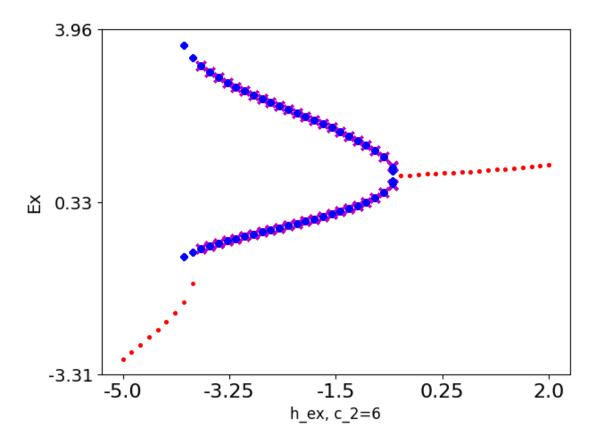
```
# Simulation "forward"
for par in par_set:
   h_ex = par
   y_f = odeint(func=single_oscillator, y0=y_ini, t=time,
             args=(h_ex, h_in_0, pars),
            hmax=0.1)
   for num, series in enumerate(y_f[rows//2:,:-1:2].T):
        if var(series) < 0.00005:</pre>
            if num not in results_max_f:
                results_max_f[num]
                                     = [series[-1]]
                results_max_inds_f[num] = [0]
                                     = [series[-1]]
                results_min_f[num]
                results_min_inds_f[num] = [0]
            else:
                results_max_f[num].append(series[-1])
                results_max_inds_f[num].append(0)
                results_min_f[num].append(series[-1])
                results_min_inds_f[num].append(0)
        else:
            y_f_max_inds = find_peaks(series, distance=100)
                      = series[y_f_max_inds[0]]
           y_f_maxs
           y_f_min_inds = find_peaks(-series, distance=100)
           y_f_mins = series[y_f_min_inds[0]]
            if num not in results_max_f:
                results max f[num]
                                     = [y_f_maxs]
                results_max_inds_f[num] = [y_f_max_inds]
                results min f[num]
                                   = [y f mins]
                results_min_inds_f[num] = [y_f_min_inds]
            else:
                results_max_f[num].append(y_f_maxs)
                results_max_inds_f[num].append(y_f_max_inds)
```

```
results_min_f[num].append(y_f_mins)
                results_min_inds_f[num].append(y_f_min_inds)
   if par != par_set[-1]:
       y_{ini} = y_{f}[-1, :]
results_max_b = dict()
results_max_inds_b = dict()
results_min_b = dict()
results_min_inds_b = dict()
# Simulation "backward"
for par in flip(par_set):
   h_ex = par
   y_b = odeint(func=single_oscillator, y0=y_ini, t=time,
             args=(h_ex, h_in_0, pars),
            hmax=0.1)
   for num, series in enumerate(y_b[rows//2:,:-1:2].T):
        if var(series) < 0.00005:</pre>
            if num not in results_max_b:
                results_max_b[num] = [series[-1]]
                results_max_inds_b[num] = [0]
                results_min_b[num]
                                     = [series[-1]]
                results_min_inds_b[num] = [0]
            else:
                results_max_b[num].append(series[-1])
                results_max_inds_b[num].append(0)
                results_min_b[num].append(series[-1])
                results_min_inds_b[num].append(0)
        else:
            y_b_max_inds = find_peaks(series, distance=100)
            y_b_maxs
                      = series[y_b_max_inds[0]]
            y_b_min_inds = find_peaks(-series, distance=100)
                     = series[y_b_min_inds[0]]
            y_b_mins
```

```
if num not in results_max_b:
                results_max_b[num]
                                     = [y_b_{maxs}]
                results_max_inds_b[num] = [y_b_max_inds]
                results_min_b[num]
                                        = [y_b_mins]
                results_min_inds_b[num] = [y_b_min_inds]
            else:
                results_max_b[num].append(y_b_maxs)
                results_max_inds_b[num].append(y_b_max_inds)
                results_min_b[num].append(y_b_mins)
                results_min_inds_b[num].append(y_b_min_inds)
    y_{ini} = y_{b}[-1, :]
print('')
print('Scan complete!')
print('')
```

Scan complete!

[20]: 'losc_Bifs_h_ex, c_2=6.png'



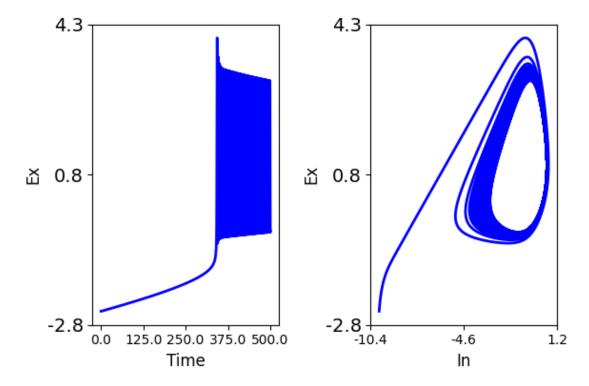
1.6 Transition to oscillation

```
print('End of run:', y.shape)
print('')
```

End of run: (500000, 2)

```
[25]: time_begin, time_end = 0, time_stop
fig, ax = plot_series_statespace(time, y, time_begin, time_end, sr)
if pars[1] == 1:
    title_chars = 'Figs/N=1/Onset_SNIC_h_ex.png'
elif pars[1] == 2:
    title_chars = 'Figs/N=1/Onset_Homoclinic_h_ex.png'
# fig.savefig(title_chars, dpi=300, format='png', bbox_inches='tight')
print(title_chars)
```

Figs/N=1/Onset_SNIC_h_ex.png



1.7 With added noise

```
[28]: # Set Initial conditions:
      \# y_i = y[-1, :]
      # Time array
      time_stop = 50
      time
               = linspace(start=0, stop=time_stop, num=time_stop*sr)
      # Initial parameter value
      h_ex_0
             = -4.2
      # Driving
      driving = linspace(0, 1, time.size)
      driving_strength = 1.0
      # Noise
      SEED = 123
      rng = default_rng(SEED)
      random_data = rng.normal(size=(time.size, y.shape[1]))
      order, band_low, band_high = 5, 1, 10
      sos = butter(order, (band_low, band_high), btype='bandpass', fs=sr,_

output='sos')
      random_data_filtered = zeros((time.size, y.shape[1]))
      for index, column in enumerate(random_data.transpose()):
          forward = sosfilt(sos, column)
          backwards = sosfilt(sos, forward[-1::-1])
          random_data_filtered[:, index] = backwards[-1::-1]
      random_strength = 10
      # Simulation /Add noise arrays to params
      y = odeint(func=single_oscillator_plus_driving_plus_noise, y0=y_ini, t=time,
                args=(h_ex_0, h_in_0, pars, sr, time_stop, driving, driving_strength,
                 random_data_filtered, random_strength), hmax=0.1)
      print('End of run:')
      print('')
```

End of run:

```
[29]: time_begin, time_end = 0, time_stop

fig, ax = plot_series_statespace(time, y, time_begin, time_end, sr)

if pars[1] == 1:

    title_chars = 'Figs/N=1/Onset_SNIC_h_ex.png'

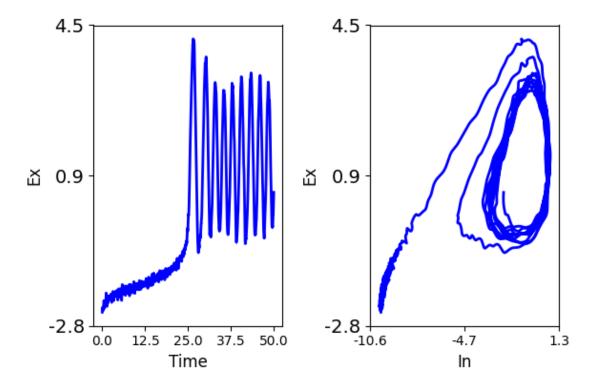
elif pars[1] == 2:

    title_chars = 'Figs/N=1/Onset_Homoclinic_h_ex.png'

# fig.savefig(title_chars, dpi=300, format='png', bbox_inches='tight')

print(title_chars)
```

Figs/N=1/Onset_SNIC_h_ex.png



[]:

2 Try it Yourself

Re-run the above code with these parameter settings:

```
pars = (1.2, 0.1, 4, 6, 6, 0)
h_ex_0 = 0.2
driving_strength = -2
```

to simulate an onset with small fast oscillations that grow in amplitude. This is another common type of seizure onset in humans.

3 Notes on the Reading

3.1 A taxonomy of seizure dynamotypes, Maria Luisa Saggio et al

In this paper, transitions to epileptic seizures as recorded in invasive EEG are classified according to a small number of bifurcations in two-variable dynamical systems. Seizure onset is considered as a transition from fixed point to oscillations and there are four types of such transitions as a function of changes in a single parameter. Saddle-node in invariant cycle (SNIC) lead to sudden onset of large amplitude slow frequency oscillations. Supercritical Hopf bifurcations results in small amplitude fast oscillations with increasing amplitude. Figure 1 is a schematic of all possible types of this low-dimensional approach. Appendix 1, page 29, gives clinical examples of seizure onsets and their interpretation according to dynmical systems theory.