Celegans_nonlinear_control

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1 *C. elegans* low dimensional activity modeled by a nonlinear dynamical system with control

C. elegans neural activity and its relation to behavior is difficult to characterize as both the dynamics and control are nonlinear. We propose a minimally parameterized nonlinear control model that can be fit to have the same features as those observed in the neural activity data. Nonlinear interpretable models such as this may give us insight into *C. elegans* dynamics in ways that linear models are unable to due to the intrinsic nonlinearities in the system.

This notebook reproduces select results from the paper "Neuro-sensory integration in the nematode *C. elegans* as a nonlinear dynamical system with control". More specifically, we implement PCA on the neural activity of a single *C. elegans* and generate a nonlinear control model with tunable parameters that emulates the *C. elegans* low dimensional activity. We compare the state distributions of the data and model and quanitify goodness of fit of the model to the data by calculating the Kullback–Leibler divergence between the probability distribution functions.

1.1 Table of contents


```
In [956]: import matplotlib.pyplot as plt
          import seaborn as sns
          import matplotlib
          import numpy as np
          import os
          import scipy.io as spio
          import sdeint  # SDE integrator
          from scipy.stats.kde import gaussian_kde
          from scipy.signal import find_peaks

          #directory = os.getcwd()
          #print("Current working directory:", directory)
```

1.2 *C. elegans* dimensionality reduction

1.2.1 Function to load data in matlab files

```
In [148]: def loadmat(filename):
              '''
              this function should be called instead of direct spio.loadmat
              as it cures the problem of not properly recovering python dictionaries
              from mat files. It calls the function check keys to cure all entries
              which are still mat-objects
              '''
              data = spio.loadmat(filename, struct_as_record=False, squeeze_me=True)  #False,
              return _check_keys(data)

          def _check_keys(dict):
              '''
              checks if entries in dictionary are mat-objects. If yes
              todict is called to change them to nested dictionaries
              '''
              for key in dict:
                  if isinstance(dict[key], spio.matlab.mio5_params.mat_struct):
                      dict[key] = _todict(dict[key])
              return dict

          def _todict(matobj):
              '''
              A recursive function which constructs from matobjects nested dictionaries
              '''
              dict = {}
              for strg in matobj._fieldnames:
                  elem = matobj.__dict__[strg]
                  if isinstance(elem, spio.matlab.mio5_params.mat_struct):
                      dict[strg] = _todict(elem)
                  else:
                      dict[strg] = elem
              return dict
```

1.2.2 Load *C. elegans* data

```
In [181]: file = 'celegan_data'
          celegan_data = loadmat('celegan_data.mat')
          sevenStateColoring = loadmat('sevenStateColoring.mat')
          sevenStateColoring_dataset = scipy.io.loadmat('sevenStateColoring_dataset.mat')

          sevenStateColor = sevenStateColoring['sevenStateColoring']
          colors = sevenStateColor['colorMap']
          state_timeseries = sevenStateColoring_dataset['dataset2'][0][0][0][0]
```

1.2.3 Retrieve calcium imaging timeseries

```
In [211]: wbData = celegan_data['wbData']
          mat = np.transpose(wbData['deltaFOverF'])

          # 129 neurons, and 3021 timepoints
          mat.shape
```

```
Out[211]: (129, 3021)
```

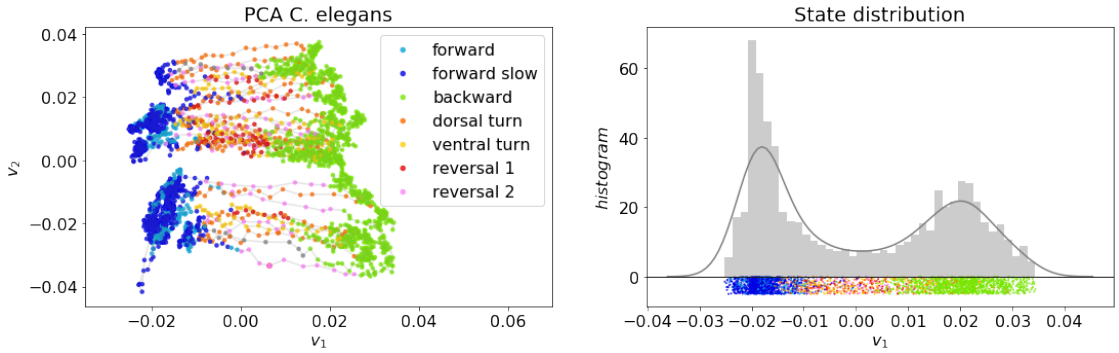
1.2.4 PCA on neuron activity timeseries

```
In [46]: # Center data
         avg = np.mean(mat, axis=1)
         mat = mat-avg.reshape((-1,1))

         # PCA
         u, s, vh = np.linalg.svd(mat, full_matrices=False)
```

1.2.5 Plot the *C. elegans* trajectories in PCA space

```
In [964]: # Create plot

          font = {'family' : 'normal',
                  'size'   : 16}
          matplotlib.rc('font', **font)

          fig, ax = plt.subplots(1, 2, sharey=False,figsize=(18,5))

          c = colors[state_timeseries-1,:]
          ax[0].scatter(vh[0,90], vh[1,90], alpha=0.8, c=c[90,:].reshape((1,-1)), s=30, label =
          ax[0].scatter(vh[0,0], vh[1,0], alpha=0.8, c=c[0,:].reshape((1,-1)), s=30, label = '
          ax[0].scatter(vh[0,400], vh[1,400], alpha=0.8, c=c[400,:].reshape((1,-1)), s=30,label
          ax[0].scatter(vh[0,70], vh[1,70], alpha=0.8, c=c[70,:].reshape((1,-1)), s=30, label =
          ax[0].scatter(vh[0,170], vh[1,170], alpha=0.8, c=c[260,:].reshape((1,-1)), s=30, labe
          ax[0].scatter(vh[0,170], vh[1,170], alpha=0.8, c=c[280,:].reshape((1,-1)), s=30, labe
          ax[0].scatter(vh[0,170], vh[1,170], alpha=0.8, c=c[170,:].reshape((1,-1)), s=30, labe

          ax[0].plot(vh[0,:], vh[1,:], alpha = 0.2, c=[0.5, 0.5, 0.5])
          ax[0].scatter(vh[0,:], vh[1,:], alpha=0.8, c=c, s=20, edgecolors='none')
          ax[0].set_xlabel('$v_1$')
          ax[0].set_ylabel('$v_2$')
          ax[0].set_title('PCA C. elegans')
          ax[0].set_xlim([-0.035, 0.07])

          ax[0].legend()

          ax[1].scatter(vh[0,:], -5*np.random.rand(len(vh[0,:])), alpha=0.8, c=c, s=4, edgecolo
          sns.distplot(vh[0,:],bins=40,color="grey");
```

```
ax[1].set_xlabel('$v_1$')
ax[1].set_ylabel('$histogram$');
ax[1].set_title('State distribution');
xwidth = ax[1].get_xlim()
ax[1].plot(xwidth,[0,0],color=[0.1,0.1,0.1], linewidth=1)
ax[1].set_xlim(xwidth);

fig.savefig("figures/PCA_Celegans", bbox_inches='tight')
```



1.3 Nonlinear control model

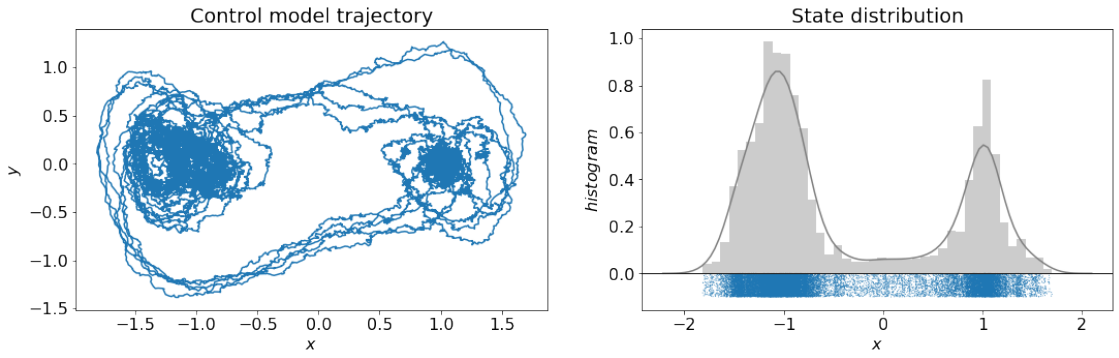
In [937]:
```
###################################
##### set parameters #############
###################################
beta = 0.05     # fixed point stability, # beta = 0.1
gamma = -0.8   # damping term, # gamma = -1
sigma = 0.1  # stochasticity, # sigma = 0.2
omega = 0.1  # average control signal frequency, # omega = 0.1
dur = 2      # average control signal duration, # dur = 2

#########################################################################
##### define dynamical system with and without control signals #######
#########################################################################
def f_default(x, t):
    return np.array([x[1], -1*(x[0]+1)*(x[0]-beta)*(x[0]-1) + gamma*x[1]])

def f_control_forward(x, t):
    return np.array([x[1], -1*(x[0]+1)*(x[0]-beta)*(x[0]-1) + gamma*x[1] +1])

def f_control_backward(x, t):
    return np.array([x[1], -1*(x[0]+1)*(x[0]-beta)*(x[0]-1) + gamma*x[1] -1])

def G(x, t):
    return np.diag([sigma, sigma]) # diagonal, so independent driving Wiener process
```

In [950]:
```
##########################################################
### randomly generate control signals ##################
##########################################################
num_switches = 20 #20
fp_times = (1/omega+(0.25/omega)*np.random.randn(num_switches,1));
switch_times = np.cumsum(fp_times);

vals = np.zeros(num_switches)
for i in range(num_switches):
    vals[i] = 2*np.random.randint(0,2)-1
```

In [951]:
```
##########################################
#### simulate dynamics ###################
##########################################
x0 = np.random.randn(2)
dt = 0.01

result_all = np.empty((0,2))

for i in range(num_switches-1):

    ######################################################
    ### generate trajectory under the control signal ###
    ######################################################

    control_sig_duration = dur + 0.5*dur*np.random.rand(1)
    tspan_control = np.arange(switch_times[i],switch_times[i]+control_sig_duration,dt

    if vals[i]>0:
        result_control = sdeint.itoint(f_control_forward, G, x0, tspan_control)
    else:
        result_control = sdeint.itoint(f_control_backward, G, x0, tspan)

    result_all = np.append(result_all, result_control, axis = 0)
    x0 = result_control[-1,:]

    ######################################################################
    ### generate trajectory under default system (no control signal) ###
    ######################################################################

    tspan = np.arange(switch_times[i]+control_sig_duration,switch_times[i+1],dt)

    result = sdeint.itoint(f_default, G, x0, tspan)

    result_all = np.append(result_all, result, axis = 0)

    x0 = result[-1,:]
```

1.3.1 Plot control model trajectory and histogram

In [962]:
```
# Create plot
font = {'family' : 'normal',
        'size'   : 16}
matplotlib.rc('font', **font)

fig, ax = plt.subplots(1, 2, sharey=False,figsize=(18,5))

ax[0].plot(result_all[:,0],result_all[:,1])
ax[0].set_xlabel('$x$')
ax[0].set_ylabel('$y$')
ax[0].set_title('Control model trajectory')

ax[1]
sns.distplot(result_all[:,0],bins=40,color="grey");

ax[1].scatter(result_all[:,0],-0.1*np.random.rand(len(result_all)), alpha = 0.8, s=1
#ax[1].hist(result_all[:,0],bins=40);
ax[1].set_xlabel('$x$')
ax[1].set_ylabel('$histogram$');
ax[1].set_title('State distribution');
xwidth = ax[1].get_xlim()
ax[1].plot(xwidth,[0,0],color=[0.1,0.1,0.1], linewidth=1)
ax[1].set_xlim(xwidth);

#fig.savefig("figures/nonlin_control_model", bbox_inches='tight')
```



1.4 Compare distributions

In [953]:
```
##########################################################################################
### rescale C. elegans distribution to match the scale of the model's distribution #
##########################################################################################
x = result_all[:,0]
v1 = vh[0,:]
```

```
        ## find dist between model guassians
        KDEpdf_model = gaussian_kde(x)
        x_plot = x_plot = np.linspace(-3,3,10000)
        x_pdf = KDEpdf_model(x_plot)
        peaks_x, _ =find_peaks(x_pdf, height=0)

        dist_x = x_plot[peaks_x[-1]]-x_plot[peaks_x[0]]

        ## rescale the PCA C. elegans distribution - align the guassians to the model guassi
        KDEpdf_data = gaussian_kde(v1)
        v1_plot = np.linspace(-0.1,0.1,1000)
        v1_pdf_tmp = KDEpdf_data(v1_plot)
        peaks, _ = find_peaks(v1_pdf_tmp, height=0)
        stretch = v1_plot[peaks[-1]]-v1_plot[peaks[0]]
        v1 = (dist_x/stretch)*v1
        KDEpdf_data = gaussian_kde(v1)

        v1_pdf = KDEpdf_data(x_plot)
        peaks, _ = find_peaks(v1_pdf, height=0)

        diff = x_plot[peaks_x[0]] - x_plot[peaks[0]]

        v1 = v1+diff
        KDEpdf_data = gaussian_kde(v1)
        v1_pdf = KDEpdf_data(x_plot)
        peaks, _ = find_peaks(v1_pdf, height=0)
```

In [954]:
```
        ##############################################################################
        ## compute KL divergence between the pdfs of the model data and C. elegans data ####
        ##############################################################################

        KL = 0;
        for i in range(len(x_plot)):
            Px = v1_pdf[i]
            Qx = x_pdf[i]
            KL += Px*np.log(Px/Qx)

        print('KL = ', KL)
```

```
KL =  264.60650142393604
```

1.4.1 Overlay distributions

In [963]:
```
        fig, ax = plt.subplots(sharey=False,figsize=(10,5))

        ax.plot(x_plot,v1_pdf,'r',label="C. elegans data",color="red")
```

```
ax.plot(x_plot,x_pdf,'r',label="Control model",color="blue")

ax.fill_between(x_plot,v1_pdf, color="red", alpha=0.15)
ax.fill_between(x_plot,x_pdf, color="blue", alpha=0.15)
ax.set_title('KL = ' + str(round(KL,3)))
ax.set_xlabel('$x$')
ax.set_ylabel('$pdf$')

ax.legend();

fig.savefig("figures/PCA_Celegans", bbox_inches='tight')

fig.savefig("figures/KL_distributions", bbox_inches='tight')
```