scipy-fed-batch

May 21, 2024

[151]:
```
# %pip install openpyxl
import pandas as pd
import numpy as np
from matplotlib import pyplot as plt
import scipy
import numpy as np
from scipy.integrate import solve_ivp
from scipy.optimize import minimize
from sklearn.metrics import r2_score
from scipy.optimize import differential_evolution, minimize
```

[152]:
```
df = pd.read_excel("ANN_amox/Semibat_convertido_clean.xlsx")
df.columns =␣
 ↪['Ester_t','Ester_gl','Ester_mM','Amox_t','Amox_gl','Amox_mM','APA_t','APA_gl','APA_mM','PO
df
```

[152]:

	Ester_t	Ester_gl	Ester_mM	Amox_t	Amox_gl	Amox_mM	\
0	9.859813	6.133333	34.040034	14.719626	0.883436	2.417722	
1	20.017523	5.866667	32.560033	29.906542	1.262440	3.454954	
2	29.827687	5.733333	31.820032	39.953271	1.546012	4.231013	
3	39.986371	5.511111	30.586697	59.929907	2.110429	5.775669	
4	50.145055	5.288889	29.353363	85.864486	2.797546	7.656119	
5	59.973715	6.000000	33.300033	103.037383	3.067485	8.394868	
6	70.132399	5.777778	32.066699	112.149533	3.042945	8.327709	
7	80.292056	5.600000	31.080031	141.939252	3.558282	9.738047	
8	90.103193	5.511111	30.586697	155.257009	3.975460	10.879749	
9	100.261877	5.288889	29.353363	181.191589	4.073620	11.148384	
10	110.091511	6.044444	33.546700	191.004673	4.368098	11.954292	
11	120.251168	5.866667	32.560033	213.084112	4.736196	12.961676	
12	130.061332	5.733333	31.820032	223.247664	5.030675	13.767583	
13	140.221963	5.600000	31.080031	266.004673	5.496933	15.043603	
14	150.031153	5.422222	30.093363	276.168224	5.914110	16.185305	
15	160.210280	6.133333	34.040034	NaN	NaN	NaN	
16	170.019470	5.955556	33.053366	NaN	NaN	NaN	
17	180.180101	5.822222	32.313366	NaN	NaN	NaN	
18	189.989291	5.644444	31.326698	NaN	NaN	NaN	
19	200.149922	5.511111	30.586697	NaN	NaN	NaN	

20	210.309579	5.333333	29.600030	NaN	NaN	NaN
21	220.140187	6.133333	34.040034	NaN	NaN	NaN
22	230.299844	5.955556	33.053366	NaN	NaN	NaN
23	240.109034	5.777778	32.066699	NaN	NaN	NaN
24	250.269665	5.644444	31.326698	NaN	NaN	NaN
25	260.079829	5.511111	30.586697	NaN	NaN	NaN
26	270.240460	5.377778	29.846697	NaN	NaN	NaN

	APA_t	APA_gl	APA_mM	POHPG_t	POHPG_gl	POHPG_mM
0	10.163551	15.409471	71.254373	15.070093	-0.024540	-0.146805
1	19.976636	15.186630	70.223941	29.789720	0.368098	2.202071
2	30.140187	15.008357	69.399596	39.953271	0.417178	2.495680
3	39.953271	15.498607	71.666546	59.929907	0.736196	4.404142
4	49.766355	15.320334	70.842200	86.214953	0.073620	0.440414
5	59.929907	15.186630	70.223941	103.037383	1.079755	6.459408
6	69.742991	15.008357	69.399596	111.799065	0.858896	5.138165
7	79.906542	15.498607	71.666546	142.289720	0.809816	4.844556
8	90.070093	15.364903	71.048287	155.257009	1.055215	6.312603
9	100.233645	15.186630	70.223941	181.542056	1.128834	6.753017
10	110.046729	15.097493	69.811768	191.355140	1.398773	8.367869
11	120.210280	15.543175	71.872632	213.084112	1.472393	8.808283
12	130.023364	15.454039	71.460460	223.247664	1.742331	10.423135
13	139.836449	15.275766	70.636114	266.004673	2.159509	12.918816
14	150.000000	15.186630	70.223941	276.518692	2.233129	13.359230
15	160.163551	15.008357	69.399596	NaN	NaN	NaN
16	169.976636	15.498607	71.666546	NaN	NaN	NaN
17	180.140187	15.364903	71.048287	NaN	NaN	NaN
18	189.953271	15.275766	70.636114	NaN	NaN	NaN
19	199.766355	15.142061	70.017855	NaN	NaN	NaN
20	209.929907	15.052925	69.605682	NaN	NaN	NaN
21	219.742991	15.632312	72.284805	NaN	NaN	NaN
22	230.257009	15.454039	71.460460	NaN	NaN	NaN
23	240.420561	15.320334	70.842200	NaN	NaN	NaN
24	249.883178	15.275766	70.636114	NaN	NaN	NaN
25	260.046729	15.097493	69.811768	NaN	NaN	NaN
26	269.859813	15.052925	69.605682	NaN	NaN	NaN

[153]:
```
CAB_medida  = df.loc[:,'Ester_mM'].dropna().to_numpy()
CAN_medida = df.loc[:,'Amox_mM'].dropna().to_numpy()
CNH_medida = df.loc[:,'APA_mM'].dropna().to_numpy()
CAOH_medida = df.loc[:,'POHPG_mM'].dropna().to_numpy()
t_cab = df.loc[:,'Ester_t'].dropna().to_numpy().round(0)
t_can = df.loc[:,'Amox_t'].dropna().to_numpy().round(0)
t_cnh = df.loc[:,'APA_t'].dropna().to_numpy().round(0)
t_caoh = df.loc[:,'POHPG_t'].dropna().to_numpy().round(0)
tempo_substratos = t_cab
tempo_produtos = t_can
```

```
CAB_medida_t = np.hstack([CAB_medida.reshape(-1,1),t_cab.reshape(-1,1)])
CAN_medida_t = np.hstack([CAN_medida.reshape(-1,1),t_can.reshape(-1,1)])
CNH_medida_t = np.hstack([CNH_medida.reshape(-1,1),t_cab.reshape(-1,1)])
CAOH_medida_t = np.hstack([CAOH_medida.reshape(-1,1),t_can.reshape(-1,1)])
medidas_exp_list = [CAB_medida_t,CAN_medida_t,CNH_medida_t,CAOH_medida_t]
t_total = np.unique(np.sort(np.hstack([t_can,t_cab])))
```

[154]:
```
fed_ab = np.array([5,10,15,21])

fed_ab_t = np.array([t_cab[fed_ab[0]],
                     t_cab[fed_ab[1]],
                     t_cab[fed_ab[2]],
                     t_cab[fed_ab[3]]])

fed_ab_c = np.array([CAB_medida[fed_ab[0]],
                     CAB_medida[fed_ab[1]],
                     CAB_medida[fed_ab[2]],
                     CAB_medida[fed_ab[3]]])
fed_ab = np.vstack([fed_ab_t,fed_ab_c])

fed_nh = np.array([3,7,11,16,21])

fed_nh_t = np.array([t_cnh[fed_nh[0]],
                     t_cnh[fed_nh[1]],
                     t_cnh[fed_nh[2]],
                     t_cnh[fed_nh[3]],
                     t_cnh[fed_nh[4]],
                     ])
fed_nh_c = np.array([CNH_medida[fed_nh[0]],
                     CNH_medida[fed_nh[1]],
                     CNH_medida[fed_nh[2]],
                     CNH_medida[fed_nh[3]],
                     CNH_medida[fed_nh[4]]])
fed_nh = np.vstack([fed_nh_t,fed_nh_c])

print(fed_nh)
```

```
[[ 40.          80.         120.         170.         220.        ]
 [ 71.66654602  71.66654602  71.87263242  71.66654602  72.28480522]]
```

[155]:
```
def enzymic_amox(t, y, kcat1, kcat2, Km1, Km2, Tmax, Ken, kAB, kAN, kAOH, kNH):
    FAB = 0
    FNH = 0

    CAB = y[0]
    CAN = y[1]
    CNH = y[2]
```

```
    CAOH = y[3]

    Cez = 1  # Assuming a constant value for Cez if not provided

    # Consumo de ester
    VAB = (kcat1 * CAB * Cez) / ((Km1 * (1 + (CAN/kAN) + (CAOH/kAOH))) + CAB)

    # Hidrolise de amoxicilina
    VAN = (kcat2 * CAN * Cez) / ((Km2 * (1 + (CAB/kAB) + (CNH/kNH) + (CAOH/
↪kAOH))) + CAN)

    # Enzima saturada com 6-apa
    X = CNH / (Ken + CNH)

    # Sintese enzimatica
    VS = VAB * Tmax * X

    # Hidrolise de ester
    Vh1 = (VAB - VS)

    dy = np.zeros(4)

    # C. ester
    dy[0] = (-(VS - VAN) - (Vh1 + VAN)) + FAB

    # C. amox
    dy[1] = VS - VAN

    # C. 6-apa
    dy[2] = -(VS - VAN) + FNH

    # C. POHPG
    dy[3] = Vh1 + VAN

    return dy
```

[156]:
```
fed_ab = np.array([5,10,15,21])

fed_ab_t = np.array([t_cab[fed_ab[0]],
                     t_cab[fed_ab[1]],
                     t_cab[fed_ab[2]],
                     t_cab[fed_ab[3]]])

fed_ab_c = np.array([CAB_medida[fed_ab[0]],
                     CAB_medida[fed_ab[1]],
                     CAB_medida[fed_ab[2]],
                     CAB_medida[fed_ab[3]]])
```

```
fed_ab = np.vstack([fed_ab_t,fed_ab_c])

fed_nh = np.array([3,7,11,16,21])

fed_nh_t = np.array([t_cnh[fed_nh[0]],
                     t_cnh[fed_nh[1]],
                     t_cnh[fed_nh[2]],
                     t_cnh[fed_nh[3]],
                     t_cnh[fed_nh[4]],
                     ])
fed_nh_c = np.array([CNH_medida[fed_nh[0]],
                     CNH_medida[fed_nh[1]],
                     CNH_medida[fed_nh[2]],
                     CNH_medida[fed_nh[3]],
                     CNH_medida[fed_nh[4]]])
fed_nh = np.vstack([fed_nh_t,fed_nh_c])

print(fed_nh)
```

```
[[ 40.          80.         120.         170.         220.        ]
 [ 71.66654602  71.66654602  71.87263242  71.66654602  72.28480522]]
```

[157]:
```
kcat1        = 0.181
kcat2        = 0.395
Km1          = 5.449
Km2          = 1.694
Tmax         = 0.824
Ken          = 7.947
kAB          = 0.682
kAN          = 1.989
kAOH         = 9.856
kNH          = 9.763

P = np.zeros(10)
P[0]   = kcat1
P[1]   = kcat2
P[2]   = Km1
P[3]   = Km2
P[4]   = Tmax
P[5]   = Ken
P[6]   = kAB
P[7]   = kAN
P[8]   = kAOH
P[9]  = kNH
Np = len(P)
```

[158]:
```
def ode15s_amox_fed(P,t):
    fed_t = np.unique(np.sort(np.hstack([fed_ab[0],fed_nh[0]])))
    CI_ode = np.
 ↪array([CAB_medida[0],CAN_medida[0],CNH_medida[0],CAOH_medida[0]])
    all_t = []
    for i,fed in enumerate(fed_t):
        all_t.insert(i,[])
        count = 0
        for p in t:
            all_t[i].append(p)
            count += 1
            if p == fed:
                break
        t = t[count-1:]
    all_t.append(t)

    final_Y = np.zeros([4,1])
    for t in all_t:
        Y = scipy.integrate.
 ↪solve_ivp(enzymic_amox,t_span=(t[0],t[-1]),t_eval=t,y0=CI_ode,method='BDF',args=P)
        Y = Y.y
        CI_ode = Y[:,-1]
        if t[-1] in fed_ab[0]:
            CI_ode[0] = fed_ab[1][list(fed_ab[0]).index(t[-1])]
        if t[-1] in fed_nh[0]:
            CI_ode[2] = fed_nh[1][list(fed_nh[0]).index(t[-1])]
        final_Y = np.hstack([final_Y,Y[:,:-1]])
    final_Y = np.hstack([final_Y,Y[:,-1].reshape(-1,1)])
    final_Y = np.delete(final_Y,0,1)
    return final_Y
```

[159]:
```
def calculate_error(model_matrix, experimental_data_list):
    # Extract model time points
    model_time = model_matrix[:, -1]
    total_error = 0
    for var_index, experimental_data in enumerate(experimental_data_list):
        # Extract variable model data
        model_variable_data = model_matrix[:, var_index]
        # Match time points between model and experimental data
        exp_time = experimental_data[:, -1]
        exp_values = experimental_data[:, 0]

        for t, exp_value in zip(exp_time, exp_values):
            if not np.isnan(exp_value):  # Skip NaN values in experimental data
                # Find corresponding model value at time t
                model_value = model_variable_data[model_time == t]
                if model_value.size > 0:  # If there's a matching time point
```

```
                    total_error += (exp_value - model_value[0]) ** 2
    print(total_error,end="\r")
    return total_error
```

[173]:
```
def objective_function(params):
    kcat1, kcat2, Km1, Km2, Tmax, Ken, kAB, kAN, kAOH, kNH = params
    record.append(params)
    sol = ode15s_amox_fed(params,t_total)
    model_output = sol.T

    model_output = np.hstack([model_output,t_total.reshape(-1,1)])
    return calculate_error(model_output,medidas_exp_list)
```

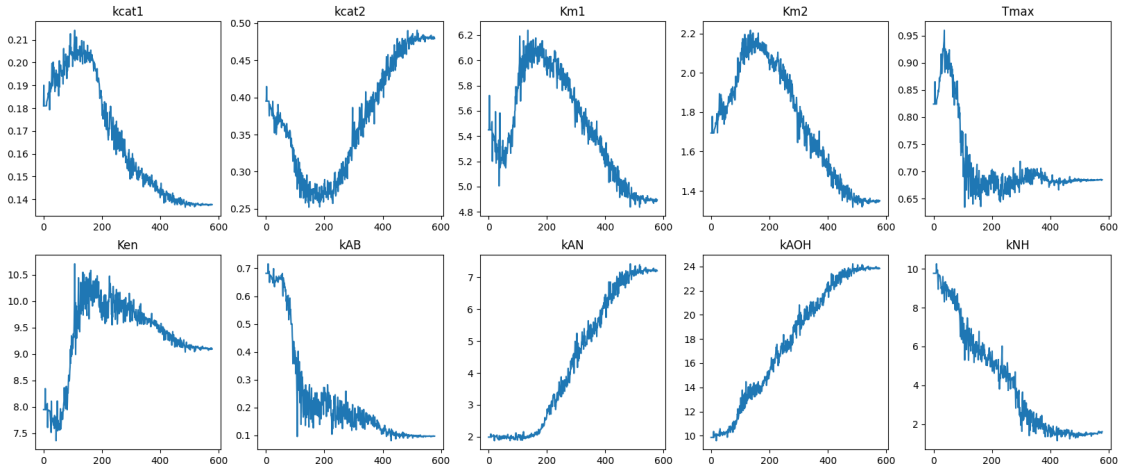
[249]:
```
options = {'maxiter':400}
record = []
bounds = [(0.001, None) for _ in range(len(P))]

result = minimize(objective_function, P,␣
 ↪method='Nelder-Mead',bounds=bounds,options=options)
record = np.array(record)
# Optimized parameters
optimized_parameters = result.x
print("Optimized Parameters:", optimized_parameters)
P_new = optimized_parameters
```

```
Optimized Parameters: [ 0.13774187  0.47860872  4.89771429  1.35408369
0.68420837  9.10175497
  0.09727782  7.18711047 23.81970143  1.62049931]
```

[250]:
```
fig,ax = plt.subplots(2,5,figsize=[20,8])
ax = ax.flatten()
labels = ['kcat1',
'kcat2',
'Km1',
'Km2',
'Tmax',
'Ken',
'kAB',
'kAN',
'kAOH',
'kNH']
print(record.shape)
for idx,g in enumerate(ax):
    g.plot(record[:,idx])
    g.set_title(labels[idx])
fig.savefig('scipy_methods/NelderMead.png',dpi=400)
```

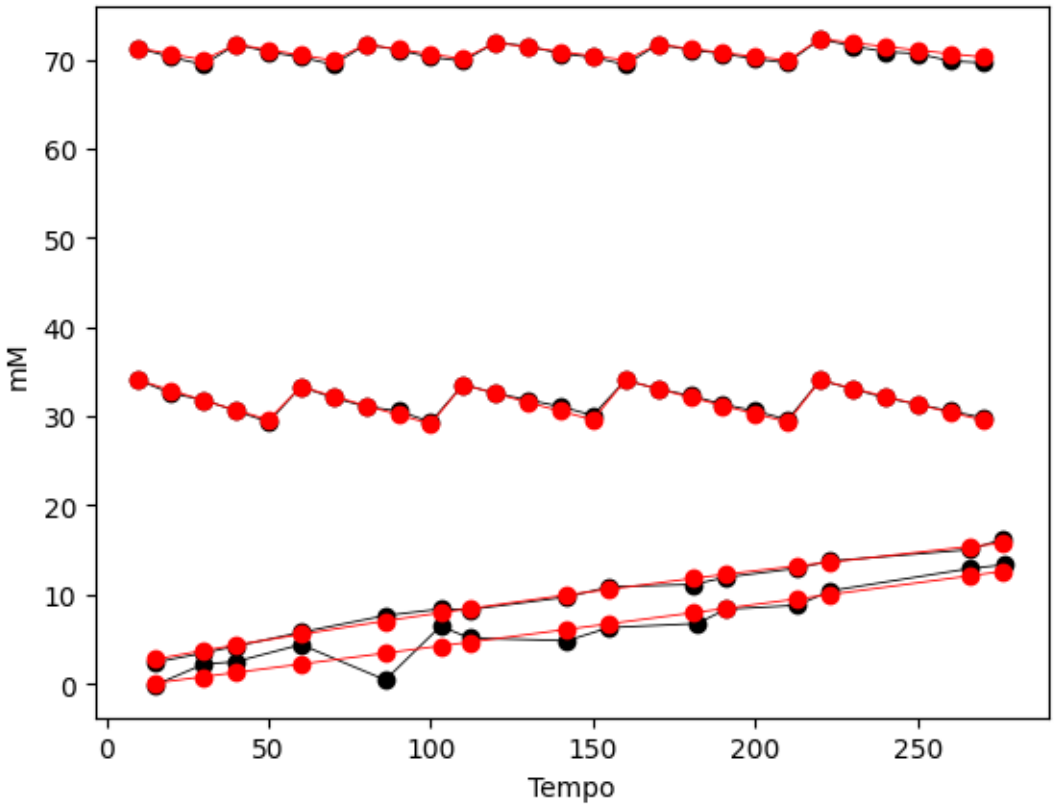
```
(579, 10)
```



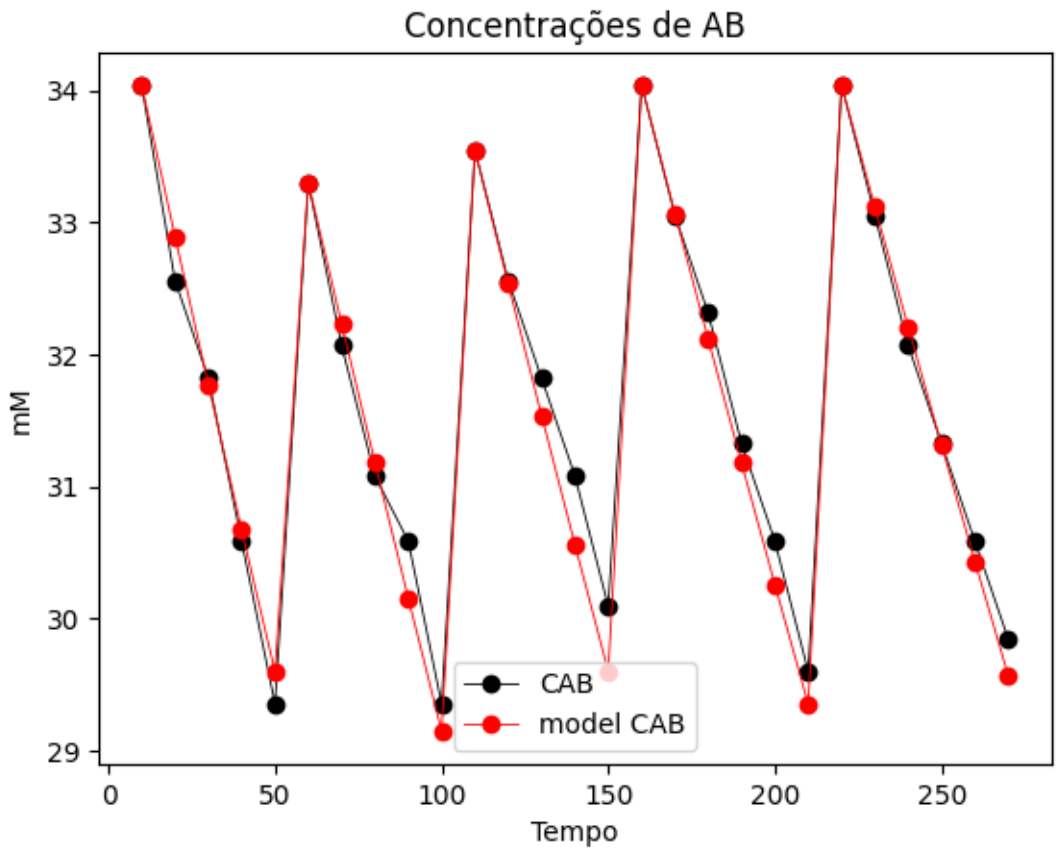
[252]:
```
sol = ode15s_amox_fed(P_new,t_total)
pidx = np.isin(t_total, tempo_produtos)
sidx = np.isin(t_total, tempo_substratos)
CAB  = sol[0][sidx]
CAN  = sol[1][pidx]
CNH  = sol[2][sidx]
CAOH = sol[3][pidx]
t_p = t_total[pidx]
t_s = t_total[sidx]
```

[253]:
```
fig = plt.figure()
plt.plot(t_cab, CAB_medida,'-ok',linewidth=0.6)
plt.plot(t_can, CAN_medida,'-ok',linewidth=0.6)
plt.plot(t_cnh, CNH_medida,'-ok',linewidth=0.6)
plt.plot(t_caoh,CAOH_medida,'-ok',linewidth=0.6)
plt.plot(t_s, CAB,'-or',linewidth=0.6)
plt.plot(t_p, CAN,'-or',linewidth=0.6)
plt.plot(t_s, CNH,'-or',linewidth=0.6)
plt.plot(t_p, CAOH,'-or',linewidth=0.6)
plt.xlabel('Tempo')
plt.ylabel('mM')
```

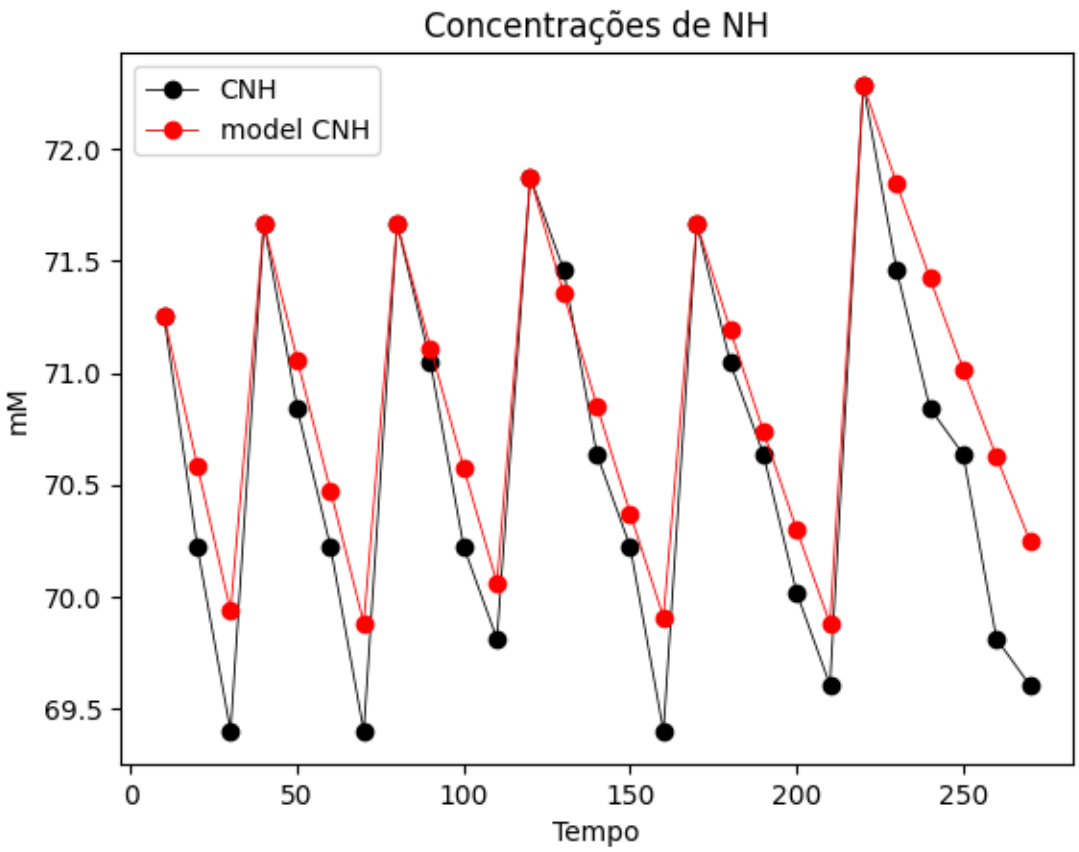
[253]:
```
Text(0, 0.5, 'mM')
```



[254]:
```
fig = plt.figure()
plt.plot(t_cab, CAB_medida,'-ok',linewidth=0.6)
plt.plot(t_s, CAB,'-or',linewidth=0.6)
plt.title(f'Concentrações de AB')
plt.legend(['CAB','model CAB'])
plt.xlabel('Tempo')
plt.ylabel('mM');
```

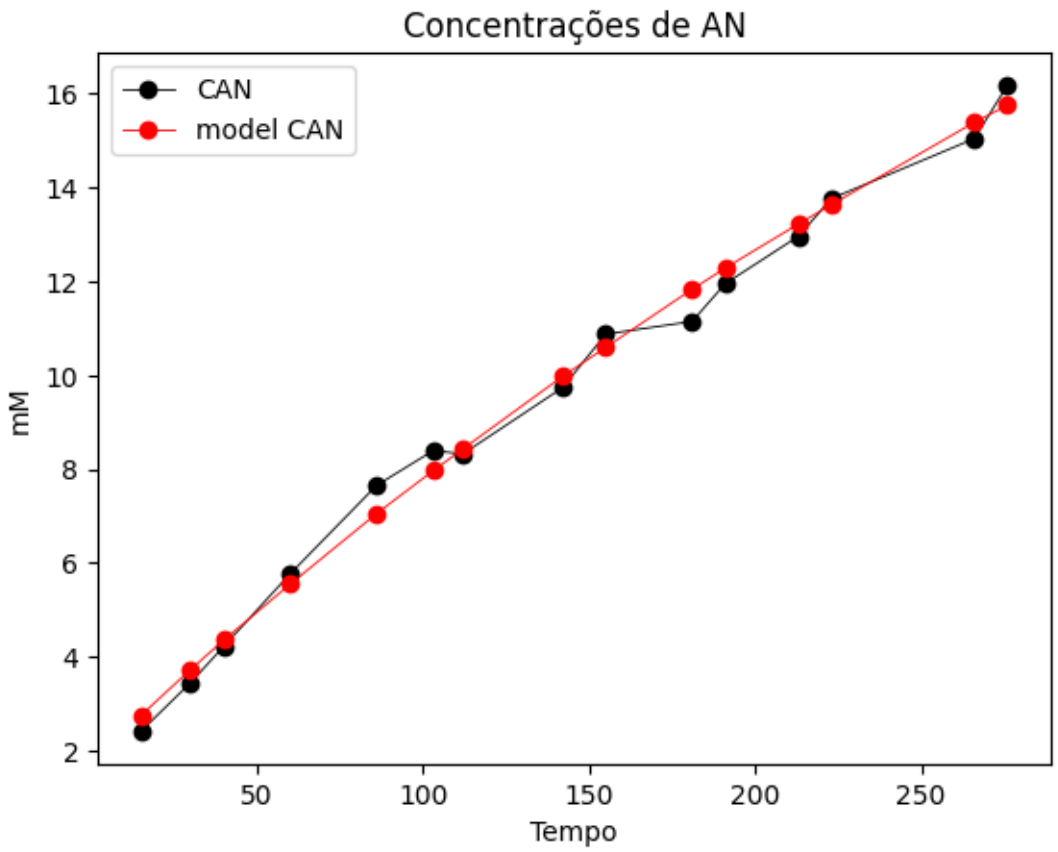


[255]:
```
fig = plt.figure()
plt.plot(t_cnh, CNH_medida,'-ok',linewidth=0.6)
plt.plot(t_s, CNH,'-or',linewidth=0.6)
plt.title(f'Concentrações de NH')
plt.legend(['CNH','model CNH']);
plt.xlabel('Tempo')
plt.ylabel('mM');
```



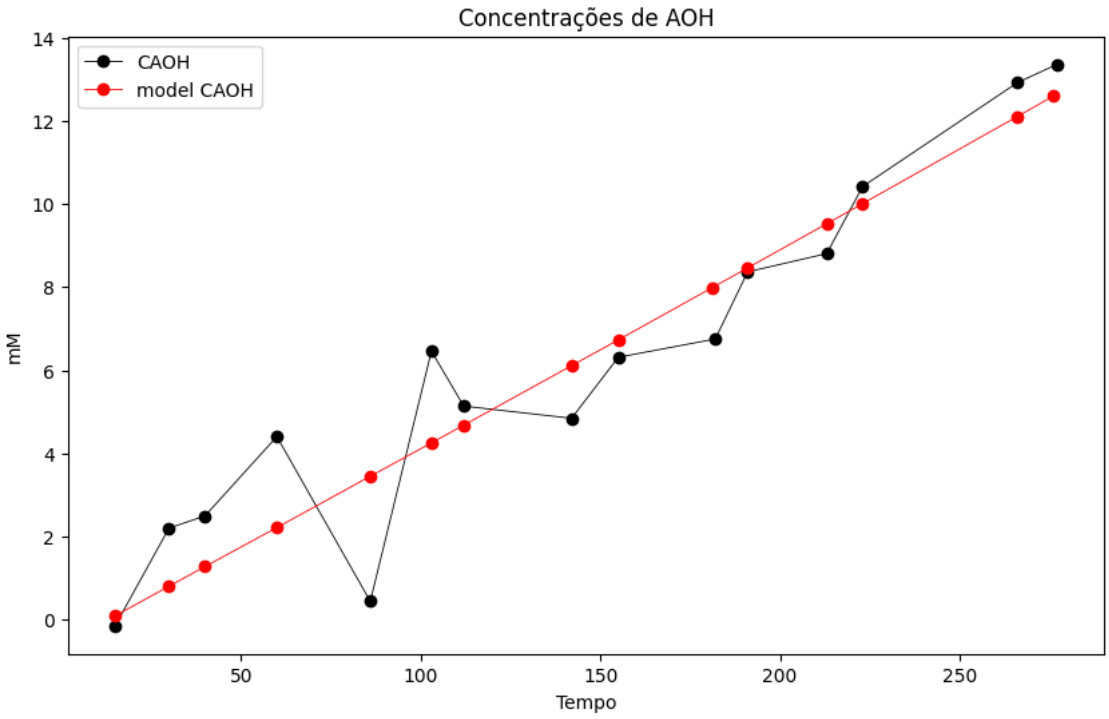
[256]:
```
fig = plt.figure()

plt.plot(t_can, CAN_medida,'-ok',linewidth=0.6)
plt.plot(t_p, CAN,'-or',linewidth=0.6)
plt.title(f'Concentrações de AN')
plt.legend(['CAN','model CAN']);
plt.xlabel('Tempo')
plt.ylabel('mM');
```



[257]:
```
fig = plt.figure(figsize=(10,6))

plt.plot(t_caoh,CAOH_medida,'-ok',linewidth=0.6)
plt.plot(t_p, CAOH,'-or',linewidth=0.6)
plt.title(f'Concentrações de AOH')
plt.legend(['CAOH','model CAOH'])
plt.xlabel('Tempo')
plt.ylabel('mM');
```


Concentrações de AOH
CAOH
model CAOH
mM
Tempo
0
2
4
6
8
10
12
14
50
100
150
200
250