fig_mechanisms

January 12, 2022

1 Figure 5 - Reaction mechanism determination

[1]:
```
import numpy as np
import pandas as pd
import scipy.stats as stats
import scipy.optimize as optimize

import ast

import pymc3 as pm
import arviz as az
import theano.tensor as tt

import networkx as nx

import matplotlib.pyplot as plt
import matplotlib.gridspec as gridspec
import seaborn as sns; sns.set_theme(style='ticks', context='paper',␣
↪font_scale=0.8);

%reload_ext watermark
%watermark -a "Mathieu Baltussen" -d -t -u -v -iv
```

```
Author: Mathieu Baltussen

Last updated: 2022-01-07 14:39:54

Python implementation: CPython
Python version       : 3.9.5
IPython version      : 7.28.0

matplotlib: 3.4.2
arviz     : 0.11.4
pandas    : 1.2.4
pymc3     : 3.11.4
networkx  : 2.6.3
numpy     : 1.20.3
scipy     : 1.6.2
```

```
seaborn    : 0.11.1
sys        : 3.9.5 | packaged by conda-forge | (default, Jun 19 2021, 00:32:32)
[GCC 9.3.0]
theano     : 1.1.2
```

1.1 Helper functions for plotting

[2]:
```
def savefig(name):
    plt.savefig(f"../figures/{name}.svg")
    plt.savefig(f"../figures/{name}.png", dpi=300)

XSIZE = 7.0 #inch
YSIZE = XSIZE/np.sqrt(2) #inch

def generate_figure(n_col, n_row):
    DX = XSIZE/n_col
    DY = YSIZE/n_col
    YLENGTH = n_row*DY

    fig = plt.figure(figsize=(XSIZE, YLENGTH), constrained_layout=True)
    gs = fig.add_gridspec(n_row, n_col)
    return fig, gs
```

1.2 Data loading

[14]:
```
experiments = pd.read_csv(f"../data/kinetic_studies.csv").query(
    f'enzyme == "G6PDH"'
)
data = []
for t in experiments.itertuples():
    df = pd.read_csv(f"../data/{t.data_path}")
    df = df.assign(
        kf=t.flowrate / (60 * t.volume),
        G6PDH=t.enzyme_concentration,
        code=t.experiment_code,
    )
    data.append(df)

data = pd.concat(data).reset_index(drop=True)

data = data.assign(
    NAD_obs=data.NAD_in - data.NADH_obs,
    G6P_obs=data.G6P_in - data.NADH_obs,
    G6PdL_obs=data.NADH_obs
)
data
```

[14]:

```
    G6P_in  NAD_in    NADH_obs     kf  G6PDH    code     NAD_obs  \
0      500    1000  324.985000  0.125   10.0  SNKS08   675.015000
1      500    1000  324.867750  0.125   10.0  SNKS08   675.132250
2      500    1000  315.605000  0.125   10.0  SNKS08   684.395000
3      500    1000  315.956750  0.125   10.0  SNKS08   684.043250
4     1000    1000  519.033750  0.125   10.0  SNKS08   480.966250
..     …       …          …      …     …       …           …
91    3000    3000  612.888491  0.125    2.0  SNKS20  2387.111509
92    3000    3000  612.610957  0.125    2.0  SNKS20  2387.389043
93    3000    3000  613.424397  0.125    2.0  SNKS20  2386.575603
94    3000    3000  612.380285  0.125    2.0  SNKS20  2387.619715
95    3000    3000  612.022450  0.125    2.0  SNKS20  2387.977550

        G6P_obs   G6PdL_obs
0    175.015000  324.985000
1    175.132250  324.867750
2    184.395000  315.605000
3    184.043250  315.956750
4    480.966250  519.033750
..          …          …
91  2387.111509  612.888491
92  2387.389043  612.610957
93  2386.575603  613.424397
94  2387.619715  612.380285
95  2387.977550  612.022450

[96 rows x 9 columns]
```

1.3 Creation of models

[15]:

```python
exp_idx, exp_coords = data.code.factorize(sort=True)
obs_idx, obs_coords = data.index.factorize(sort=True)
coords = {"exp": exp_coords, 'obs': obs_coords}

with pm.Model(coords=coords) as model_0:
    k_cat = pm.Uniform("k_cat", 0, 500)
    K_G6P = pm.Uniform("K_G6P", 1, 4000)
    K_NAD = pm.Uniform("K_NAD", 1, 2000)
    # KI_NADH = pm.Uniform("KI_NADH", 1, 5000)

    sigma = pm.Exponential("sigma", 0.5, dims='exp')

    G6PDH = data.G6PDH.values
    NADH = data.NADH_obs.values
    NAD = data.NAD_obs.values

    G6P = data.G6P_obs.values
```

```
    G6PdL = data.G6PdL_obs.values

    G6P_in = data.G6P_in.values
    NAD_in = data.NAD_in.values
    kf = data.kf.values

    NADH_obs = pm.Normal("NADH_obs",
                mu = k_cat*G6PDH*G6P*NAD/(kf*K_G6P*K_NAD*(1 + G6P/K_G6P)*(1+NAD/
↪K_NAD)),
                sigma=sigma[exp_idx],
                observed= NADH
                )

with pm.Model(coords=coords) as model_1:
    k_cat = pm.Uniform("k_cat", 0, 500)
    K_G6P = pm.Uniform("K_G6P", 1, 4000)
    K_NAD = pm.Uniform("K_NAD", 1, 2000)
    KI_NADH = pm.Uniform("KI_NADH", 1, 10000)

    sigma = pm.Exponential("sigma", 0.5, dims='exp')


    G6PDH = data.G6PDH.values
    NADH = data.NADH_obs.values
    NAD = data.NAD_obs.values

    G6P = data.G6P_obs.values
    G6PdL = data.G6PdL_obs.values

    G6P_in = data.G6P_in.values
    NAD_in = data.NAD_in.values
    kf = data.kf.values

    NADH_obs = pm.Normal("NADH_obs",
                mu = k_cat*G6PDH*G6P*NAD/(kf*K_G6P*K_NAD*(1 + G6P/K_G6P)*(1+NAD/
↪K_NAD)*(1+ NADH/KI_NADH)),
                sigma=sigma[exp_idx],
                observed= NADH
                )

with pm.Model(coords=coords) as model_2:
    k_cat = pm.Uniform("k_cat", 0, 500)
    K_G6P = pm.Uniform("K_G6P", 1, 4000)
    K_NAD = pm.Uniform("K_NAD", 1, 2000)
    KI_NADH = pm.Uniform("KI_NADH", 1, 10000)

    sigma = pm.Exponential("sigma", 0.5, dims='exp')
```

```
    G6PDH = data.G6PDH.values
    NADH = data.NADH_obs.values
    NAD = data.NAD_obs.values

    G6P = data.G6P_obs.values
    G6PdL = data.G6PdL_obs.values

    G6P_in = data.G6P_in.values
    NAD_in = data.NAD_in.values
    kf = data.kf.values

    NADH_obs = pm.Normal("NADH_obs",
                mu = k_cat*G6PDH*G6P*NAD/(kf*K_G6P*K_NAD*(1 + G6P/K_G6P)*(1+NAD/
↪K_NAD+ NADH/KI_NADH)),
                sigma=sigma[exp_idx],
                observed= NADH
                )

with pm.Model(coords=coords) as model_3:
    k_cat = pm.Uniform("k_cat", 0, 500)
    K_G6P = pm.Uniform("K_G6P", 1, 4000)
    K_NAD = pm.Uniform("K_NAD", 1, 2000)
    KI_NADH = pm.Uniform("KI_NADH", 1, 10000)

    sigma = pm.Exponential("sigma", 0.5, dims='exp')


    G6PDH = data.G6PDH.values
    NADH = data.NADH_obs.values
    NAD = data.NAD_obs.values

    G6P = data.G6P_obs.values
    G6PdL = data.G6PdL_obs.values

    G6P_in = data.G6P_in.values
    NAD_in = data.NAD_in.values
    kf = data.kf.values

    NADH_obs = pm.Normal("NADH_obs",
                mu = k_cat*G6PDH*G6P*NAD/(kf*K_G6P*K_NAD*(1 + G6P/K_G6P + NADH/
↪KI_NADH)*(1+NAD/K_NAD)),
                sigma=sigma[exp_idx],
                observed= NADH
                )
```

```
with pm.Model(coords=coords) as model_4:
    k_cat = pm.Uniform("k_cat", 0, 500)
    K_G6P = pm.Uniform("K_G6P", 1, 4000)
    K_NAD = pm.Uniform("K_NAD", 1, 2000)
    KI_NADH = pm.Uniform("KI_NADH", 1, 10000)

    sigma = pm.Exponential("sigma", 0.5, dims='exp')

    G6PDH = data.G6PDH.values
    NADH = data.NADH_obs.values
    NAD = data.NAD_obs.values

    G6P = data.G6P_obs.values
    G6PdL = data.G6PdL_obs.values

    G6P_in = data.G6P_in.values
    NAD_in = data.NAD_in.values
    kf = data.kf.values

    NADH_obs = pm.Normal("NADH_obs",
                mu = k_cat*G6PDH*G6P*NAD/(kf*K_G6P*K_NAD*(1 + G6P/K_G6P + NADH/
↪KI_NADH)*(1+NAD/K_NAD+ NADH/KI_NADH)),
                sigma=sigma[exp_idx],
                observed= NADH
                )

with pm.Model(coords=coords) as model_5:
    k_cat = pm.Uniform("k_cat", 0, 500)
    K_G6P = pm.Uniform("K_G6P", 1, 4000)
    K_NAD = pm.Uniform("K_NAD", 1, 2000)
    KI_NADH = pm.Uniform("KI_NADH", 1, 10000)

    sigma = pm.Exponential("sigma", 0.5, dims='exp')

    G6PDH = data.G6PDH.values
    NADH = data.NADH_obs.values
    NAD = data.NAD_obs.values

    G6P = data.G6P_obs.values
    G6PdL = data.G6PdL_obs.values

    G6P_in = data.G6P_in.values
    NAD_in = data.NAD_in.values
    kf = data.kf.values

    NADH_obs = pm.Normal("NADH_obs",
```

```
                mu = k_cat*G6PDH*G6P*NAD/(kf*K_G6P*K_NAD*(1 + G6P/K_G6P)*(1+NAD/
↪K_NAD)*(1+ NADH/KI_NADH)*(1+ NADH/KI_NADH)),
                sigma=sigma[exp_idx],
                observed= NADH
                )

with pm.Model(coords=coords) as model_6:
    k_cat = pm.Uniform("k_cat", 0, 500)
    K_G6P = pm.Uniform("K_G6P", 1, 4000)
    K_NAD = pm.Uniform("K_NAD", 1, 2000)
    KI_NADH = pm.Uniform("KI_NADH", 1, 10000)

    sigma = pm.Exponential("sigma", 0.5, dims='exp')

    G6PDH = data.G6PDH.values
    NADH = data.NADH_obs.values
    NAD = data.NAD_obs.values

    G6P = data.G6P_obs.values
    G6PdL = data.G6PdL_obs.values

    G6P_in = data.G6P_in.values
    NAD_in = data.NAD_in.values
    kf = data.kf.values

    NADH_obs = pm.Normal("NADH_obs",
                mu = k_cat*G6PDH*G6P*NAD/(kf*K_G6P*K_NAD*KI_NADH*(1 + G6P/
↪K_G6P)*(1+NAD/K_NAD)*(1+ NADH/KI_NADH)),
                sigma=sigma[exp_idx],
                observed= NADH
                )
```

1.4 Model sampling

[16]:
```
with model_0:
    idata_0 = pm.sample(1000, step=pm.NUTS(target_accept=0.95), tune=1000,␣
↪return_inferencedata=True)
with model_1:
    idata_1 = pm.sample(1000, step=pm.NUTS(target_accept=0.95), tune=1000,␣
↪return_inferencedata=True)
with model_2:
    idata_2 = pm.sample(1000, step=pm.NUTS(target_accept=0.95), tune=1000,␣
↪return_inferencedata=True)
with model_3:
    idata_3 = pm.sample(1000, step=pm.NUTS(target_accept=0.95), tune=1000,␣
↪return_inferencedata=True)
```

```
with model_4:
    idata_4 = pm.sample(1000, step=pm.NUTS(target_accept=0.95), tune=1000,␣
 ↪return_inferencedata=True)
with model_5:
    idata_5 = pm.sample(1000, step=pm.NUTS(target_accept=0.95), tune=1000,␣
 ↪return_inferencedata=True)
with model_6:
    idata_6 = pm.sample(1000, step=pm.NUTS(target_accept=0.95), tune=1000,␣
 ↪return_inferencedata=True)
```

```
Multiprocess sampling (4 chains in 4 jobs)
NUTS: [sigma, K_NAD, K_G6P, k_cat]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 4 chains for 1_000 tune and 1_000 draw iterations (4_000 + 4_000 draws
total) took 11 seconds.
Multiprocess sampling (4 chains in 4 jobs)
NUTS: [sigma, KI_NADH, K_NAD, K_G6P, k_cat]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 4 chains for 1_000 tune and 1_000 draw iterations (4_000 + 4_000 draws
total) took 24 seconds.
The number of effective samples is smaller than 25% for some parameters.
Multiprocess sampling (4 chains in 4 jobs)
NUTS: [sigma, KI_NADH, K_NAD, K_G6P, k_cat]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 4 chains for 1_000 tune and 1_000 draw iterations (4_000 + 4_000 draws
total) took 18 seconds.
The number of effective samples is smaller than 25% for some parameters.
Multiprocess sampling (4 chains in 4 jobs)
NUTS: [sigma, KI_NADH, K_NAD, K_G6P, k_cat]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 4 chains for 1_000 tune and 1_000 draw iterations (4_000 + 4_000 draws
total) took 16 seconds.
Multiprocess sampling (4 chains in 4 jobs)
NUTS: [sigma, KI_NADH, K_NAD, K_G6P, k_cat]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 4 chains for 1_000 tune and 1_000 draw iterations (4_000 + 4_000 draws
total) took 23 seconds.
Multiprocess sampling (4 chains in 4 jobs)
NUTS: [sigma, KI_NADH, K_NAD, K_G6P, k_cat]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 4 chains for 1_000 tune and 1_000 draw iterations (4_000 + 4_000 draws
total) took 21 seconds.
Multiprocess sampling (4 chains in 4 jobs)
NUTS: [sigma, KI_NADH, K_NAD, K_G6P, k_cat]
```

```
<IPython.core.display.HTML object>
```

```
Sampling 4 chains for 1_000 tune and 1_000 draw iterations (4_000 + 4_000 draws
total) took 7 seconds.
```

1.5 Posterior predictive sampling

[17]:
```python
with model_0:
    post_pred_0 = pm.sample_posterior_predictive(idata_0,
 ↪var_names=['NADH_obs'] )
with model_1:
    post_pred_1 = pm.sample_posterior_predictive(idata_1,
 ↪var_names=['NADH_obs'] )
with model_2:
    post_pred_2 = pm.sample_posterior_predictive(idata_2,
 ↪var_names=['NADH_obs'] )
with model_3:
    post_pred_3 = pm.sample_posterior_predictive(idata_3,
 ↪var_names=['NADH_obs'] )
with model_4:
    post_pred_4 = pm.sample_posterior_predictive(idata_4,
 ↪var_names=['NADH_obs'] )
with model_5:
    post_pred_5 = pm.sample_posterior_predictive(idata_5,
 ↪var_names=['NADH_obs'] )
```

```
<IPython.core.display.HTML object>

<IPython.core.display.HTML object>

<IPython.core.display.HTML object>

<IPython.core.display.HTML object>

<IPython.core.display.HTML object>

<IPython.core.display.HTML object>
```

1.6 Creation of figure

[18]:
```python
posterior_0 = idata_0.to_dataframe(['posterior'], include_coords=False)
posterior_1 = idata_1.to_dataframe(['posterior'], include_coords=False)
posterior_2 = idata_2.to_dataframe(['posterior'], include_coords=False)
posterior_3 = idata_3.to_dataframe(['posterior'], include_coords=False)
posterior_4 = idata_4.to_dataframe(['posterior'], include_coords=False)
posterior_5 = idata_5.to_dataframe(['posterior'], include_coords=False)
```

```
posteriors = [posterior_0,posterior_2,posterior_3, posterior_5]
```

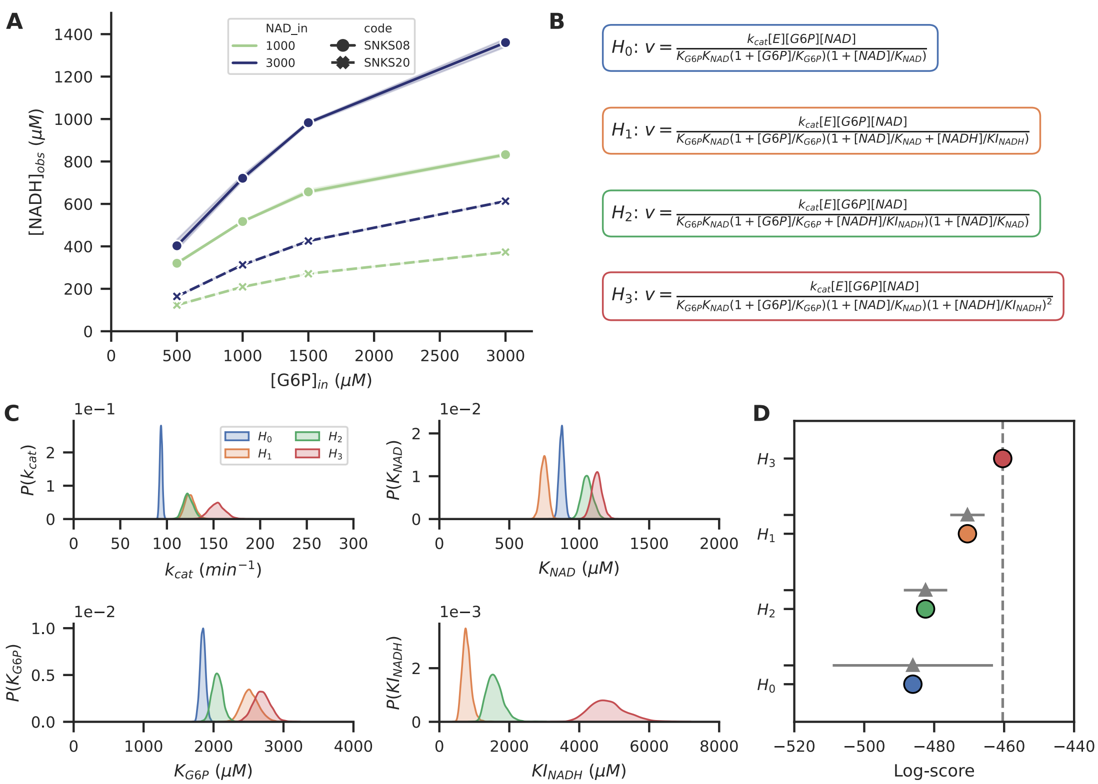
[20]:
```
fig = plt.figure(figsize=(XSIZE, YSIZE), constrained_layout=True)
gs0 = fig.add_gridspec(2, 1)

gs = gs0[0].subgridspec(1,2)

ax_1 = fig.add_subplot(gs[0])

sns.lineplot(ax=ax_1, data=data, x='G6P_in', y='NADH_obs', hue="NAD_in",␣
 ↪palette='crest', style='code', markers=True)
ax_1.set_xlim(0, 3200)
ax_1.set_ylim(0, 1500)
ax_1.set_xlabel(r"$[$G6P$]_{in}~(\mu M)$")
ax_1.set_ylabel(r"$[$NADH$]_{obs}~(\mu M)$")
ax_1.legend(loc='upper center', fontsize='x-small', ncol=2)

ax_3 = fig.add_subplot(gs[1])
ax_3.axis('off')

ax_3.text(x=-0.15, y=0.89, va='center', ha='left', fontsize=8,␣
 ↪bbox=dict(boxstyle='round', fc='white', ec='C0', pad=0.5), s=r"$H_0$: $v =␣
 ↪\frac{k_{cat}[E][G6P][NAD]}{K_{G6P}K_{NAD}(1+[G6P]/K_{G6P})(1+[NAD]/
 ↪K_{NAD})}$")
ax_3.text(x=-0.15, y=0.63, va='center', ha='left', fontsize=8,␣
 ↪bbox=dict(boxstyle='round', fc='white', ec='C1', pad=0.5), s=r"$H_1$: $v =␣
 ↪\frac{k_{cat}[E][G6P][NAD]}{K_{G6P}K_{NAD}(1+[G6P]/K_{G6P})(1+[NAD]/
 ↪K_{NAD}+[NADH]/KI_{NADH})}$")
ax_3.text(x=-0.15, y=0.37, va='center', ha='left', fontsize=8,␣
 ↪bbox=dict(boxstyle='round', fc='white', ec='C2', pad=0.5), s=r"$H_2$: $v =␣
 ↪\frac{k_{cat}[E][G6P][NAD]}{K_{G6P}K_{NAD}(1+[G6P]/K_{G6P}+[NADH]/
 ↪KI_{NADH})(1+[NAD]/K_{NAD})}$")
ax_3.text(x=-0.15, y=0.11, va='center', ha='left', fontsize=8,␣
 ↪bbox=dict(boxstyle='round', fc='white', ec='C3', pad=0.5), s=r"$H_3$: $v =␣
 ↪\frac{k_{cat}[E][G6P][NAD]}{K_{G6P}K_{NAD}(1+[G6P]/K_{G6P})(1+[NAD]/
 ↪K_{NAD})(1+ [NADH]/KI_{NADH})^2}$")

ax_1.text(-0.25, 0.95, 'A', transform=ax_1.transAxes, weight="bold", size=10)
ax_3.text(-0.3, 0.95, 'B', transform=ax_3.transAxes, weight="bold", size=10)


gs = gs0[1].subgridspec(2,3)
ax_4 = fig.add_subplot(gs[0,0])
ax_5 = fig.add_subplot(gs[1,0])
ax_6 = fig.add_subplot(gs[0,1])
ax_7 = fig.add_subplot(gs[1,1])
```

```
ax_4.ticklabel_format(style='sci', scilimits=(-1,1), axis='y')
ax_5.ticklabel_format(style='sci', scilimits=(-1,1), axis='y')
ax_6.ticklabel_format(style='sci', scilimits=(-1,1), axis='y')
ax_7.ticklabel_format(style='sci', scilimits=(-1,1), axis='y')
for i, post in enumerate(posteriors):
    sns.kdeplot(post['k_cat'], ax=ax_4, fill=True, color=f'C{i}',␣
 ↪label=r"$H_{}$".format(i))
ax_4.set_xlabel(r"$k_{cat}~(min^{-1})$")
ax_4.set_ylabel(r"$P(k_{cat})$")
ax_4.set_xlim(0, 300)
ax_4.legend(loc='upper right', ncol=2, markerscale=0.5, fontsize='x-small',␣
 ↪title_fontsize='small')

for i, post in enumerate(posteriors):
    sns.kdeplot(post['K_G6P'], ax=ax_5, fill=True, color=f'C{i}')
ax_5.set_xlabel(r"$K_{G6P}~(\mu M)$")
ax_5.set_ylabel(r"$P(K_{G6P})$")
ax_5.set_xlim(0, 4000)

for i, post in enumerate(posteriors):
    sns.kdeplot(post['K_NAD'], ax=ax_6, fill=True, color=f'C{i}')
ax_6.set_xlabel(r"$K_{NAD}~(\mu M)$")
ax_6.set_ylabel(r"$P(K_{NAD})$")
ax_6.set_xlim(0, 2000)

for i, post in enumerate(posteriors):
    try:
        sns.kdeplot(post['KI_NADH'], ax=ax_7, fill=True, color=f'C{i}')
    except KeyError as e:
        print(e)
ax_7.set_xlabel(r"$KI_{NADH}~(\mu M)$")
ax_7.set_ylabel(r"$P(KI_{NADH})$")
ax_7.set_xlim(0, 8000)

sns.despine()

ax_8 = fig.add_subplot(gs[:, 2])

model_comparison = az.compare({
    r'$H_0$': idata_0,
    r'$H_1$': idata_2,
    r'$H_2$': idata_3,
    r'$H_3$': idata_5,
}, ic='loo', method='BB-pseudo-BMA')
ax_8 = az.plot_compare(model_comparison, ax=ax_8, insample_dev=False,␣
 ↪plot_standard_error=False)
```

```
ax_8.scatter(model_comparison["loo"], ax_8.get_yticks()[::2], c=[ "C3", "C1", "C2","C0"], s=64, ec='black', zorder=10)
ax_8.set_xlabel("Log-score")
ax_8.set_xlim(-520, -440)
ax_4.text(-0.25, 1.0, 'C', transform=ax_4.transAxes, weight="bold", size=10)
ax_8.text(-0.15, 1.0, 'D', transform=ax_8.transAxes, weight="bold", size=10)

savefig('fig_mechanisms')
plt.show()
```

```
'KI_NADH'
```

```
/home/mathieu/anaconda3/envs/phd/lib/python3.9/site-packages/arviz/stats/stats.py:694: UserWarning: Estimated shape parameter of Pareto distribution is greater than 0.7 for one or more samples. You should consider using a more robust model, this is because importance sampling is less likely to work well if the marginal posterior and LOO posterior are very different. This is more likely to happen with a non-robust model and highly influential observations.
  warnings.warn(
```



1.7 Old notebook cells

[10]:
```python
def reactor_test(controls, parameters):
    def reactor(t,c, k, controls):
        G6P, NAD, NADH = c
        v = k.k_cat * controls.E * G6P * NAD / (k.K_G6P*k.K_NAD*(1+G6P/k.
↪K_G6P)*(1+NAD/k.K_NAD + NADH/k.KI_NADH))

        return [
            -v + controls.kf * (controls.G6P_in - G6P),
            -v + controls.kf * (controls.NAD_in - NAD),
            v + controls.kf * (controls.NADH_in - NADH),
        ]

    sol = integrate.solve_ivp(reactor, y0=[controls.G6P_in, controls.NAD_in,␣
↪controls.NADH_in], t_span=(0, 60), args=(parameters, controls),␣
↪vectorized=False).y
    return sol

reactor_test(control_inputs.loc[0], posterior_2.loc[0])[2]
```

```
---------------------------------------------------------------------------
NameError                                 Traceback (most recent call last)
/tmp/ipykernel_22922/134419724.py in <module>
     13     return sol
     14
---> 15 reactor_test(control_inputs.loc[0], posterior_2.loc[0])[2]

NameError: name 'control_inputs' is not defined
```

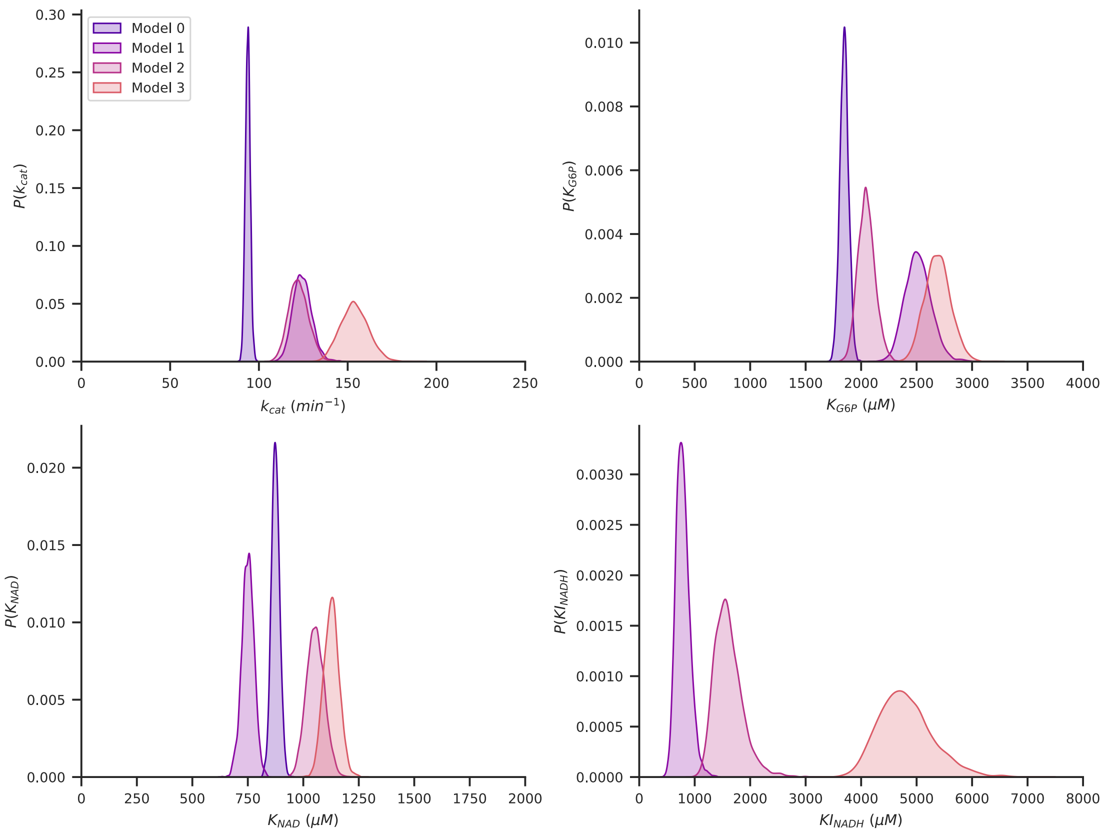
[118]:
```python
import scipy.integrate as integrate
from numba import njit

control_inputs = pd.DataFrame(
    {
        "kf": 0.125, "E": 2.0,
        # "G6P_in": [2000, 3000, 4000, 5000, 2000, 3000, 4000, 5000],
        # "NAD_in": [3000, 3000, 3000, 3000, 3000, 3000, 3000, 3000],
        "G6P_in": [3000, 3000, 3000, 3000, 3000, 3000, 3000, 3000],
        "NAD_in": [3000, 3000, 3000, 3000, 2000, 3000, 4000, 5000],
        "NADH_in": [2000, 3000, 4000, 5000, 3000, 3000, 3000, 3000]
    }
)



def reactor_2(controls, parameters):
    def reactor(t,c, k, controls):
```

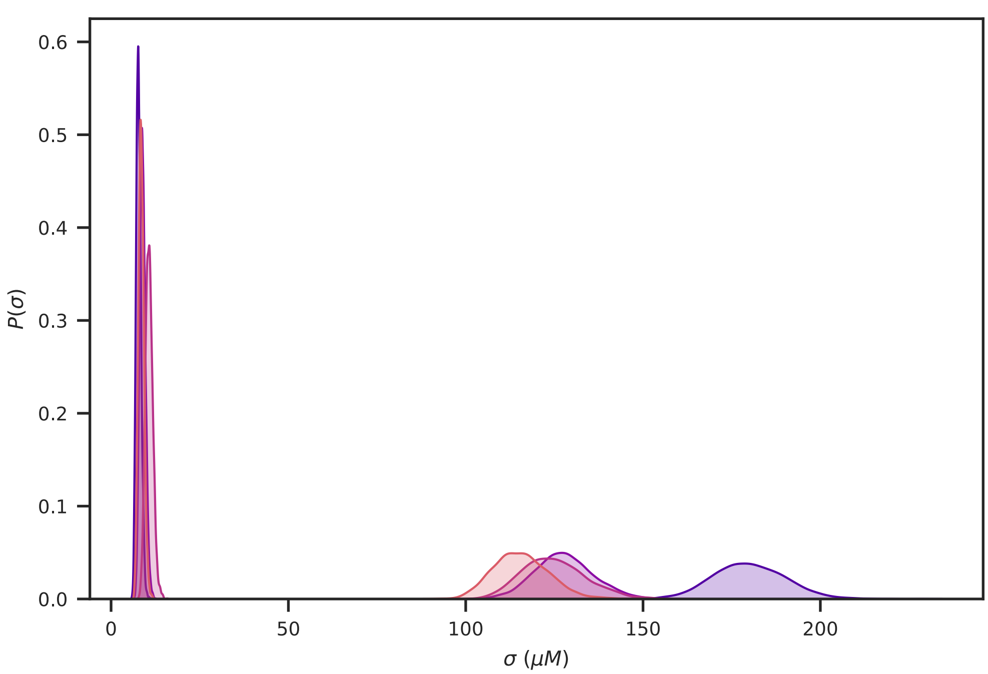
```
        G6P, NAD, NADH = c
        v = k.k_cat * controls.E * G6P * NAD / (k.K_G6P*k.K_NAD*(1+G6P/k.K_G6P)*(1+NAD/k.K_NAD + NADH/k.KI_NADH))

        return [
            -v + controls.kf * (controls.G6P_in - G6P),
            -v + controls.kf * (controls.NAD_in - NAD),
            v + controls.kf * (controls.NADH_in - NADH),
        ]

    sol = [[integrate.solve_ivp(reactor, y0=[control.G6P_in, control.NAD_in, control.NADH_in], t_span=(0, 60), args=(param, control), vectorized=False).y[2,-1] for i, control in controls.iterrows() ] for j, param in parameters.iterrows()]
    return sol

def reactor_5(controls, parameters):
    def reactor(t,c, k, controls):
        G6P, NAD, NADH = c
        v = k.k_cat * controls.E * G6P * NAD / (k.K_G6P*k.K_NAD*(1+G6P/k.K_G6P)*(1+NAD/k.K_NAD)*(1+ NADH/k.KI_NADH)**2)

        return [
            -v + controls.kf * (controls.G6P_in - G6P),
            -v + controls.kf * (controls.NAD_in - NAD),
            v + controls.kf * (controls.NADH_in - NADH),
        ]

    sol = [[integrate.solve_ivp(reactor, y0=[control.G6P_in, control.NAD_in, control.NADH_in], t_span=(0, 60), args=(param, control), vectorized=False).y[2,-1] for i, control in controls.iterrows() ]for j, param in parameters.iterrows()]
    return sol

pred_2 = reactor_2(control_inputs, posterior_2.sample(200))

pred_5 = reactor_5(control_inputs, posterior_5.sample(200))
```

[ ]:
```
with sns.color_palette('plasma', n_colors=6):

    fig, axes = plt.subplots(2,2, figsize=(8,6), constrained_layout=True)

    for i, post in enumerate(posteriors):
        sns.kdeplot(post['k_cat'], ax=axes[0][0], fill=True, color=f'C{i}', label=f"Model {i}")

    axes[0][0].set_xlabel(r"$k_{cat}~(min^{-1})$")
```

```python
    axes[0][0].set_ylabel(r"$P(k_{cat})$")
    axes[0][0].set_xlim(0, 250)
    axes[0][0].legend(loc='upper left')

    for i, post in enumerate(posteriors):
        sns.kdeplot(post['K_G6P'], ax=axes[0][1], fill=True, color=f'C{i}')
    axes[0][1].set_xlabel(r"$K_{G6P}~(\mu M)$")
    axes[0][1].set_ylabel(r"$P(K_{G6P})$")
    axes[0][1].set_xlim(0, 4000)

    for i, post in enumerate(posteriors):
        sns.kdeplot(post['K_NAD'], ax=axes[1][0], fill=True, color=f'C{i}')
    axes[1][0].set_xlabel(r"$K_{NAD}~(\mu M)$")
    axes[1][0].set_ylabel(r"$P(K_{NAD})$")
    axes[1][0].set_xlim(0, 2000)

    for i, post in enumerate(posteriors):
        try:
            sns.kdeplot(post['KI_NADH'], ax=axes[1][1], fill=True,␣
↪color=f'C{i}')
        except KeyError as e:
            print(e)
    axes[1][1].set_xlabel(r"$KI_{NADH}~(\mu M)$")
    axes[1][1].set_ylabel(r"$P(KI_{NADH})$")
    axes[1][1].set_xlim(0, 8000)

    sns.despine()
    plt.show()

    fig, ax = plt.subplots(figsize=(6,4))
    for i, post in enumerate(posteriors):
        sns.kdeplot(post['sigma[0]'], ax=ax, fill=True, color=f'C{i}')
        sns.kdeplot(post['sigma[1]'], ax=ax, fill=True, color=f'C{i}')
        # sns.kdeplot(post['sigma[0]'], ax=ax, fill=True, color=f'C{i}')

    ax.set_xlabel(r"$\sigma~(\mu M)$")
    ax.set_ylabel(r"$P(\sigma)$")
# ax.set_xlim(0, 2000)
```

```
'KI_NADH'
```


Model 0
Model 1
Model 2
Model 3
$P(k_{cat})$
k_{cat} (min^{-1})
$P(K_{G6P})$
K_{G6P} (μM)
$P(K_{NAD})$
K_{NAD} (μM)
$P(KI_{NADH})$
KI_{NADH} (μM)

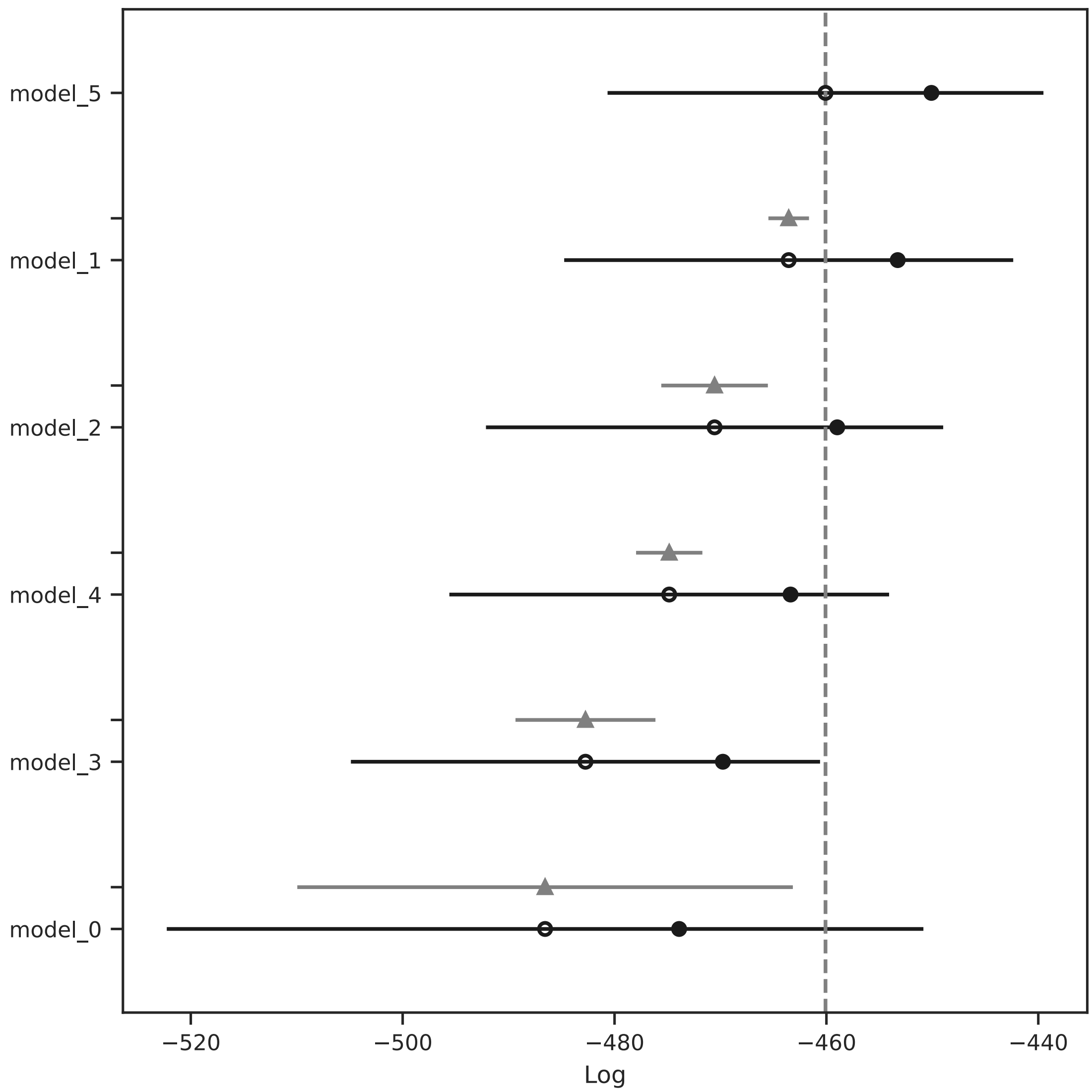

$P(\sigma)$
σ (μM)

[ ]:
```python
model_comparison = az.compare({
    'model_0': idata_0,
    'model_1': idata_1,
    'model_2': idata_2,
    'model_3': idata_3,
    'model_4': idata_4,
    'model_5': idata_5,
}, ic='loo')
print(model_comparison)
az.plot_compare(model_comparison)
```

```
/home/mathieu/anaconda3/envs/phd/lib/python3.9/site-
packages/arviz/stats/stats.py:145: UserWarning: The default method used to
estimate the weights for each model,has changed from BB-pseudo-BMA to stacking
  warnings.warn(
/home/mathieu/anaconda3/envs/phd/lib/python3.9/site-
packages/arviz/stats/stats.py:655: UserWarning: Estimated shape parameter of
Pareto distribution is greater than 0.7 for one or more samples. You should
consider using a more robust model, this is because importance sampling is less
likely to work well if the marginal posterior and LOO posterior are very
different. This is more likely to happen with a non-robust model and highly
influential observations.
  warnings.warn(
```

```
         rank         loo      p_loo      d_loo        weight         se  \
model_5     0 -460.086011   9.995511   0.000000  4.308970e-01  20.572814
model_1     1 -463.559869  10.288714   3.473858  0.000000e+00  21.193274
model_2     2 -470.557057  11.579056  10.471046  0.000000e+00  21.580386
model_4     3 -474.838169  11.453683  14.752158  2.548756e-13  20.754832
model_3     4 -482.743593  12.970784  22.657582  4.585695e-13  22.142735
model_0     5 -486.556216  12.652510  26.470204  5.691030e-01  35.711813

               dse  warning loo_scale
model_5   0.000000    False       log
model_1   1.915862    False       log
model_2   5.030913    False       log
model_4   3.128812    False       log
model_3   6.605258    False       log
model_0  23.389344     True       log
```

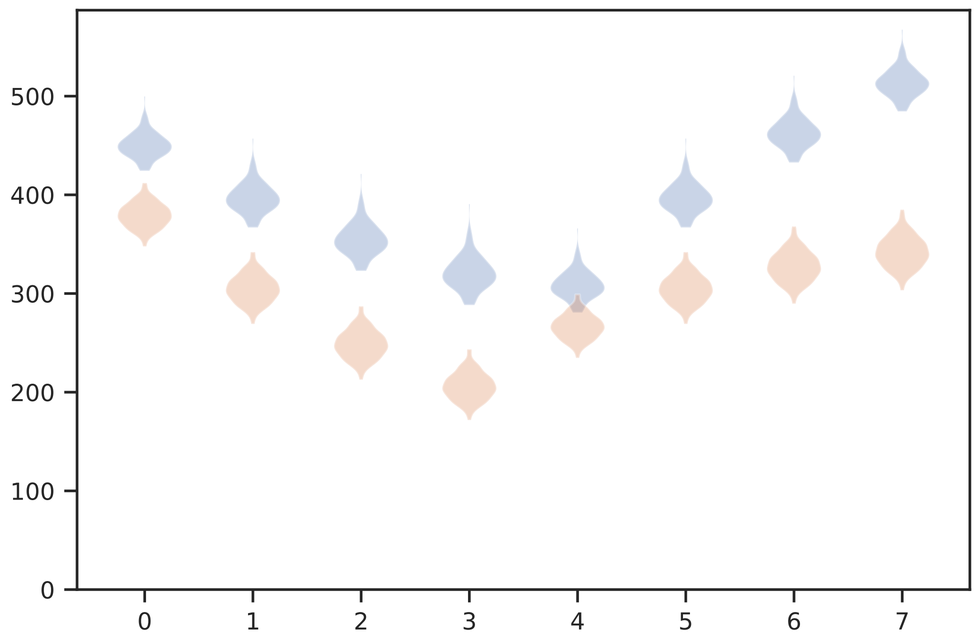
```
<AxesSubplot:xlabel='Log'>
```



[119]:
```
pred_2_arr = np.array(pred_2) - control_inputs.NADH_in.values
pred_5_arr = np.array(pred_5) - control_inputs.NADH_in.values
```

[120]:
```
plt.violinplot(pred_2_arr, positions=np.arange(0, len(control_inputs)),␣
 ↪showextrema=False)
plt.violinplot(pred_5_arr, positions=np.arange(0, len(control_inputs)),␣
 ↪showextrema=False)
plt.ylim(0)
```

[120]: (0.0, 587.1013063884353)


500
400
300
200
100
0
0
1
2
3
4
5
6
7

```
[ ]:
```