# SNF

**Task:** Optimize all 5 parameters: {At, Ka, alpha, Km, beta\_max}

**Criteria:**

1. Relative amp of Ptot > 0.25

2. max(Ptot) is minimized s.t Kd is maximized

**Method**: simulated annealing with fmincon for the final step; Options: {'TemperatureFcn','temperatureboltz', 'AnnealingFcn','annealingboltz'}

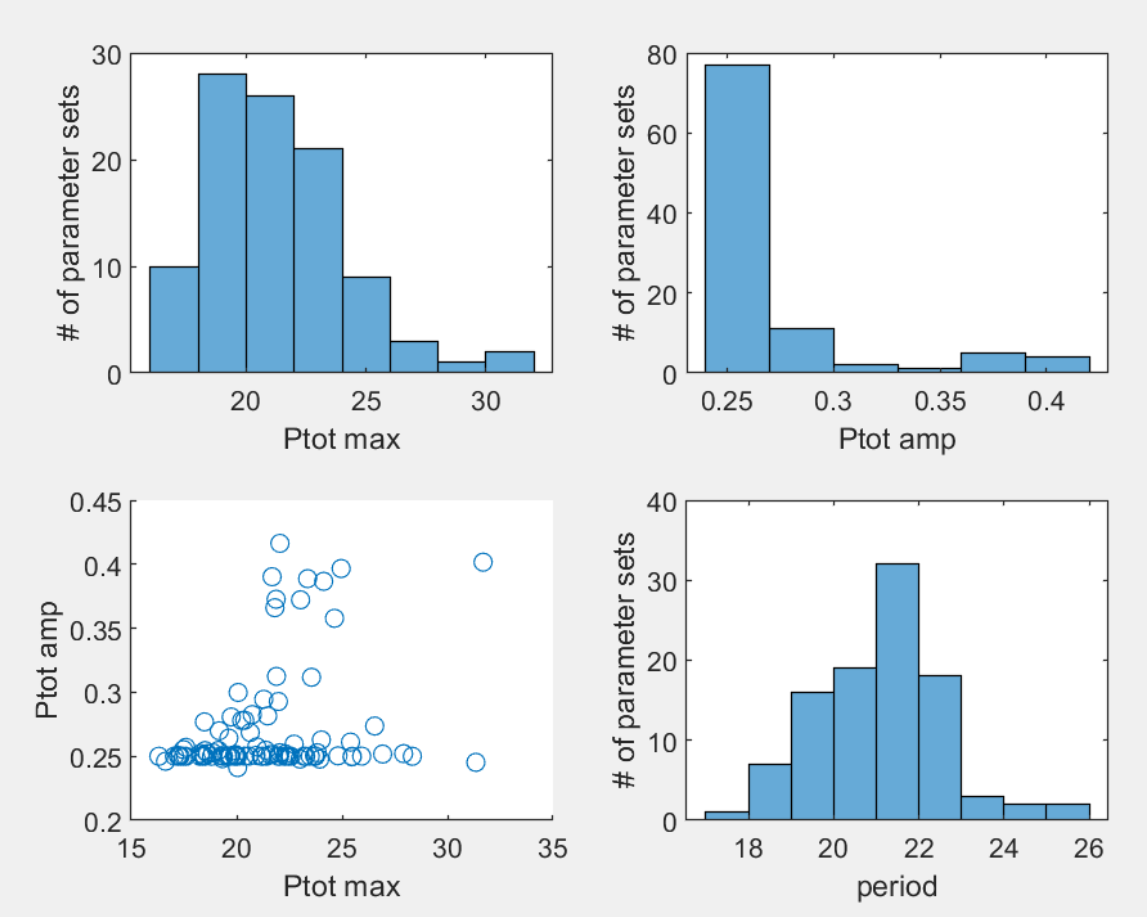
**Cost function:**

**Range of search:**

**Initial guesses:**

100 random samples with Latin hypercube in the range above for the logarithm values of the parameters.

**Results: (100 runs)**



**Best set (with lowest max(Ptot))**

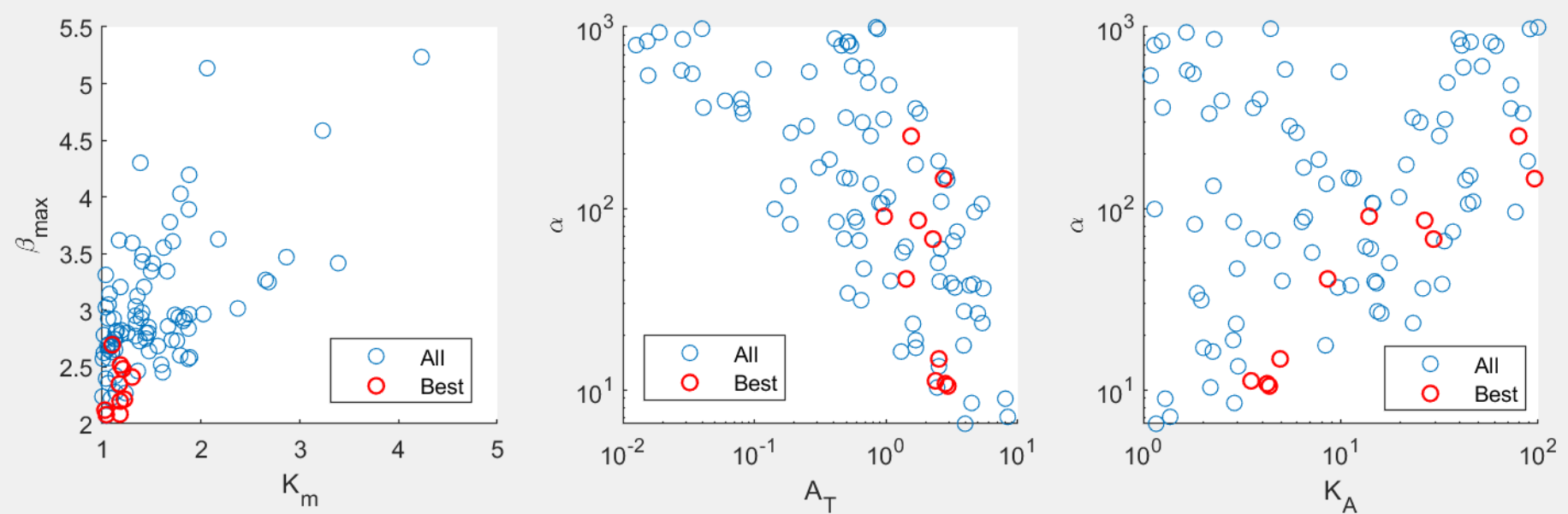
[At, KA, alpha, Km, beta\_max] = [2.7290 95.7827 145.9987 1.0268 2.1202];

period\_sim = 21.7500

Ptot\_max\_sim = 16.3082

Ptot\_amp\_sim = 0.2500

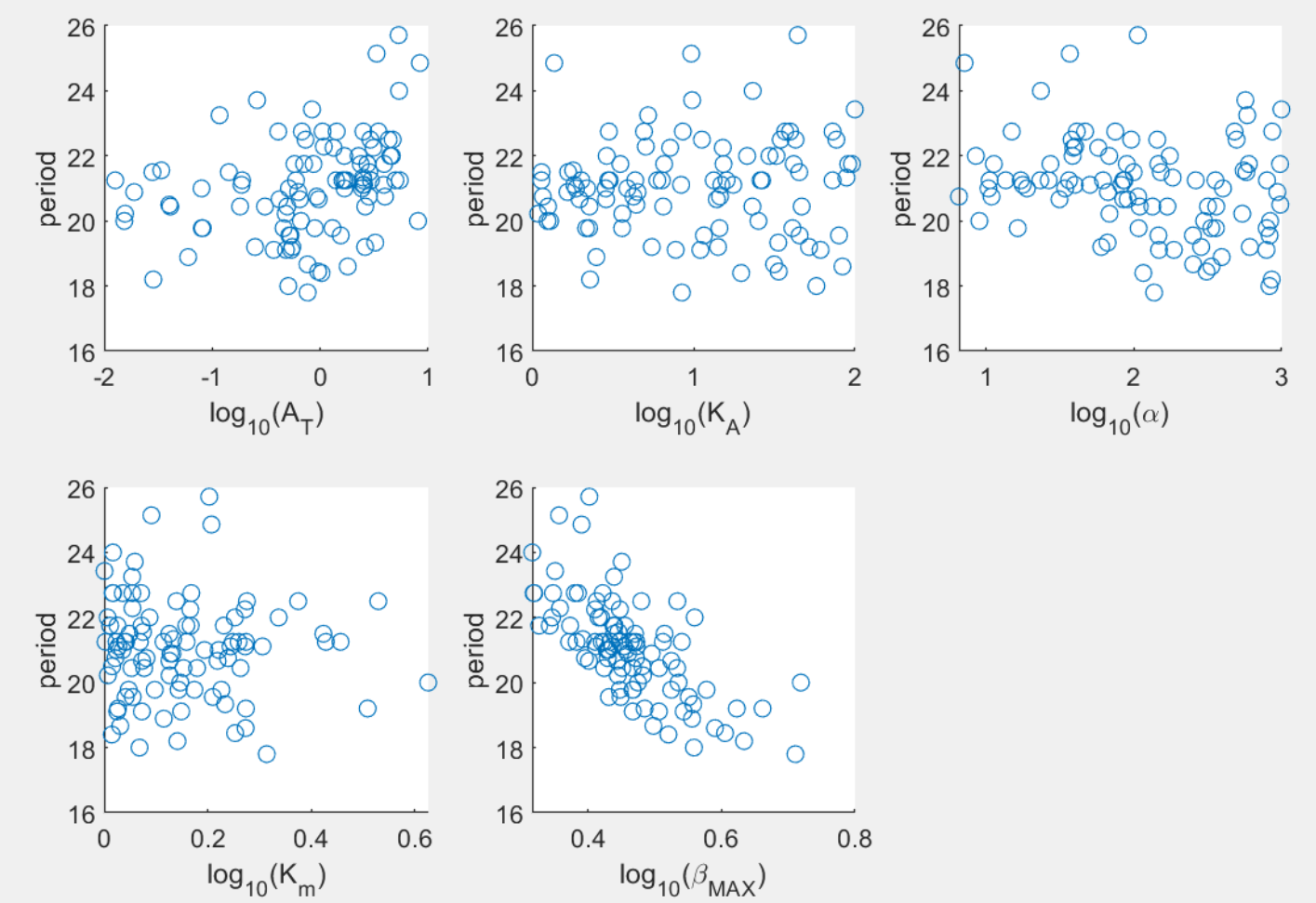
**Patterns for the top parameter sets**



Blue: all 100 sets from optimization. Red: 10 sets with lowest max(Ptot).

Main patterns:

1. Lower Km and beta\_max are preferred, which is not surprising, as lower values in both parameters slow down PER degradation and introduce time delay.
2. Alpha and AT are negatively correlated. This result is opposite to the trend in L models, although this comparison is not done between the same type of diagrams.
3. Alpha and KA positively correlated.
4. Period strongly correlated with beta\_max (figure below). This is not surprising, as beta\_max determines the time delay.



# NNF

**Task:** Optimize all 7 parameters: {delta, Amax, Vmax, Ka, alpha, Km, beta\_max}

**Criteria:**

1. Relative amp of Ptot > 0.25

2. max(Ptot) is minimized s.t Kd is maximized

~~3. BMAL (At) average level matches SNF model~~

4. Relative amp of BMAL > 0.2

~~5. Period of Ptot matches SNF~~

6. max(Rev) < 10

**Method**: simulated annealing with fmincon for the final step; Options: {'TemperatureFcn','temperatureboltz', 'AnnealingFcn','annealingboltz'}

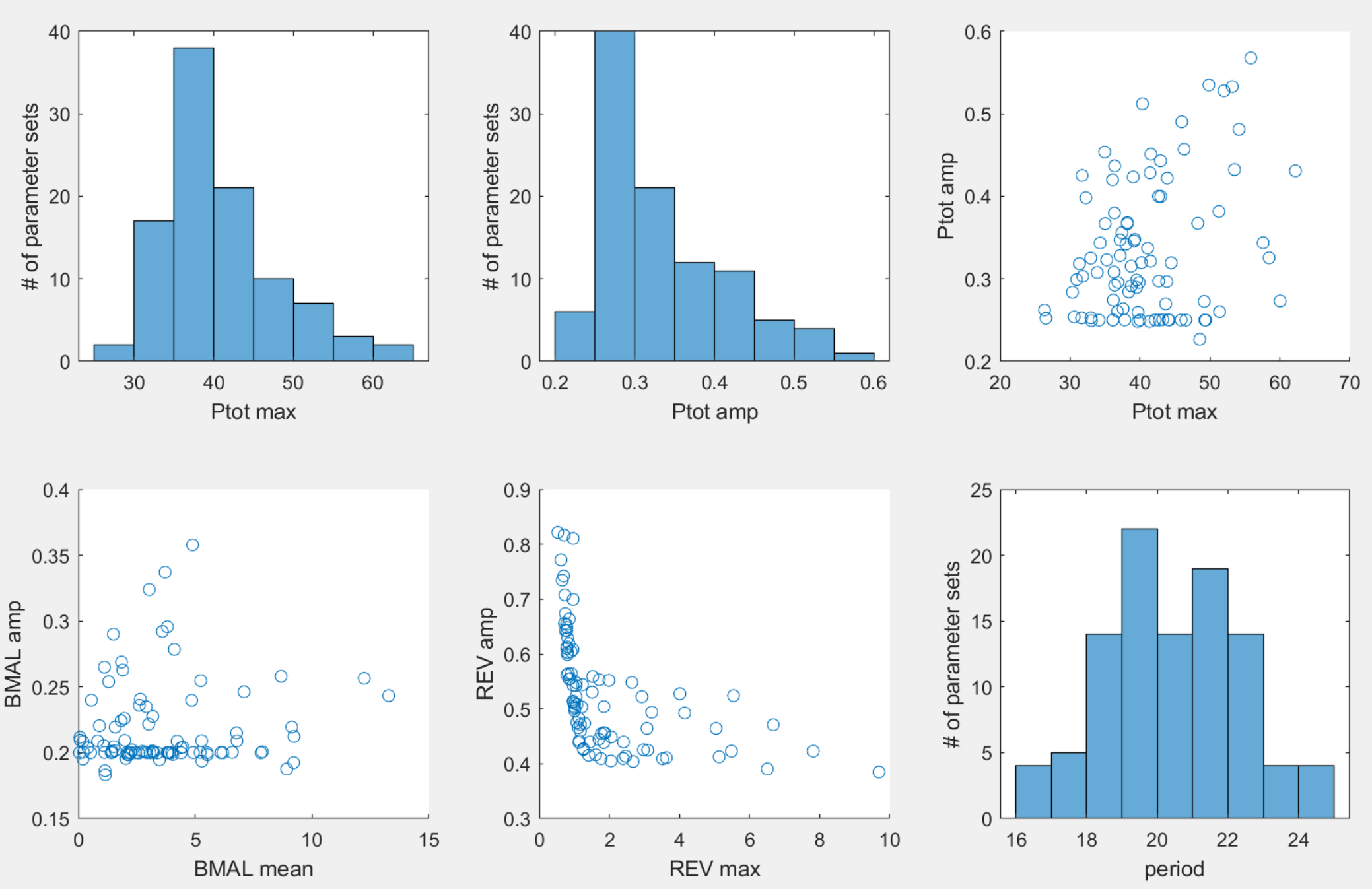
**Cost function:**

**Range of search:**

**Initial guesses:**

100 random samples with Latin hypercube in the range above for the logarithm values of the parameters.

**Results: (100 runs)**



NNF requires a moderately larger Ptot\_max, and decreases dimensional Kd? (may need to run more times to confirm?)

**Best set (with lowest max(Ptot))**

[delta, Amax, Vmax, Ka, alpha, Km, beta\_max] = [25.3886 5.3550 3.5109 1.2223 12.8716 1.3785 3.3049];

period\_sim: 22

Ptot\_max\_sim: 26.3520

Ptot\_amp\_sim: 0.2623

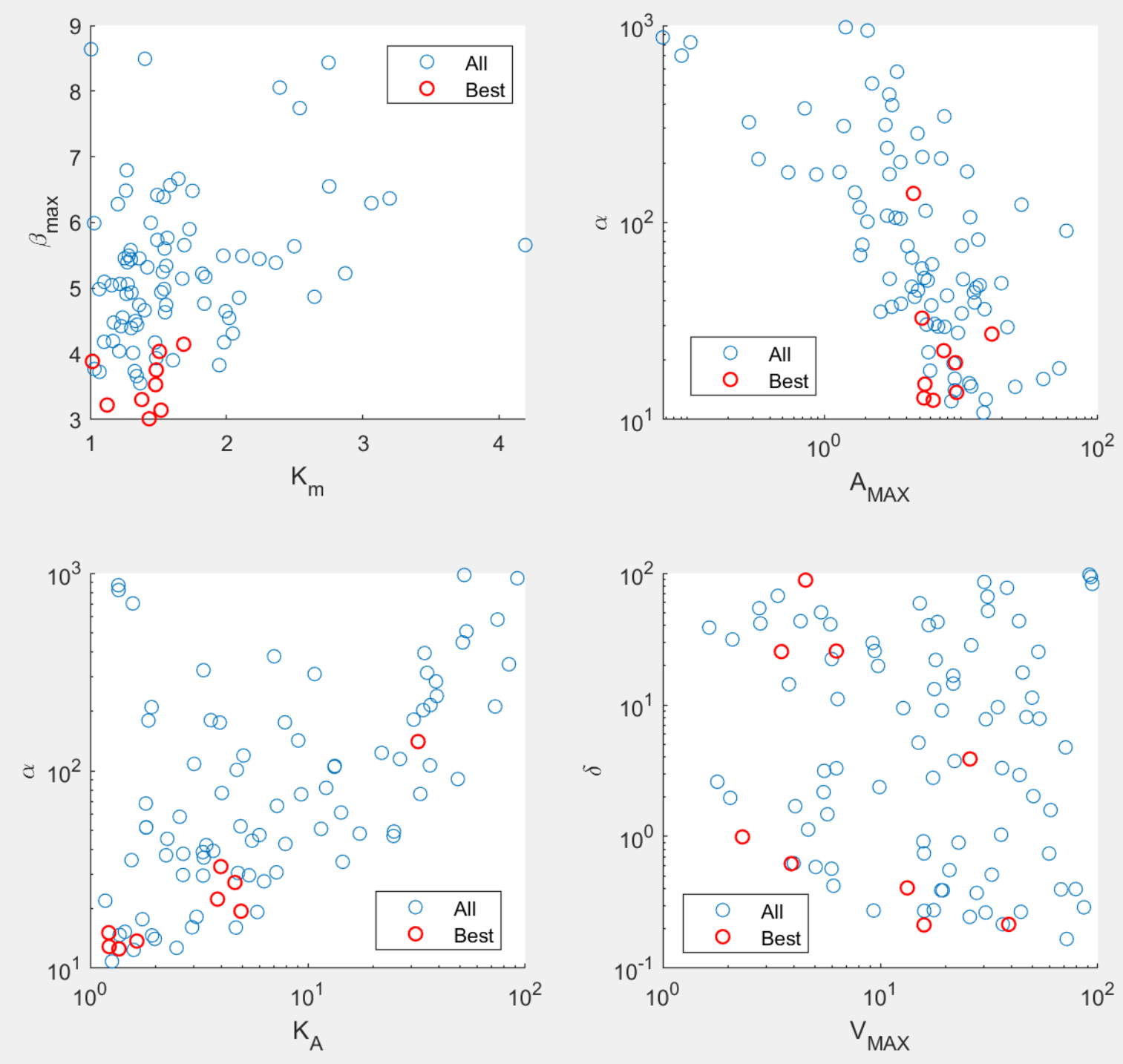
BMAL\_avg\_sim: 3.1690

BMAL\_amp\_sim: 0.2014

REV\_max\_sim: 1.1150

REV\_amp\_sim: 0.4659

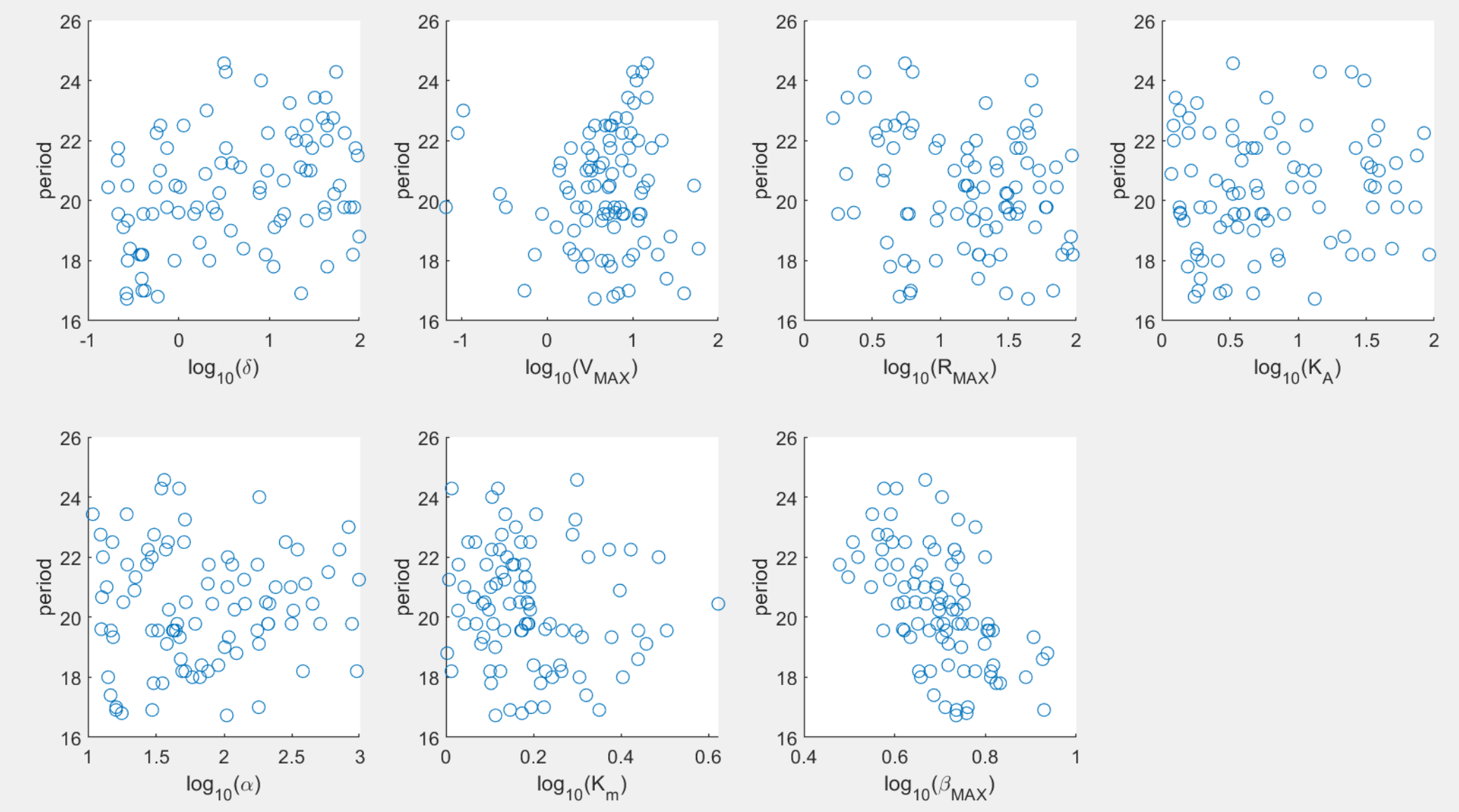
**Patterns for the top parameter sets**



Blue: all 100 sets from optimization. Red: 10 sets with lowest max(Ptot).

Main patterns:

1. Lower Km and beta\_max are preferred. The range is similar to SNF, with beta\_max slightly larger.
2. Alpha and AMAX are negatively correlated. Range of alpha is similar to SNF, but range of AMAX is lower than range of AT in SNF.
3. KA positively correlated with alpha.
4. Delta and Vmax are very flexible.
5. Period strongly correlated with beta\_max (figure below). This is not surprising, as beta\_max determines the time delay.



# PNF

**Task:** Optimize all 8 parameters: {delta, Amax, Rmax, Ka, alpha, Km, beta\_max, eps\*}

\* eps is the parameter that prevents zeros to be the steady state.

**Criteria:**

1. Relative amp of Ptot > 0.25

2. max(Ptot) is minimized s.t Kd is maximized

~~3. BMAL (At) average level matches SNF model~~

4. Relative amp of BMAL > 0.2

~~5. Period of Ptot matches SNF~~

6. max(Ror) < 5

**Method**: simulated annealing with fmincon for the final step; Options: {'TemperatureFcn','temperatureboltz', 'AnnealingFcn','annealingboltz'}

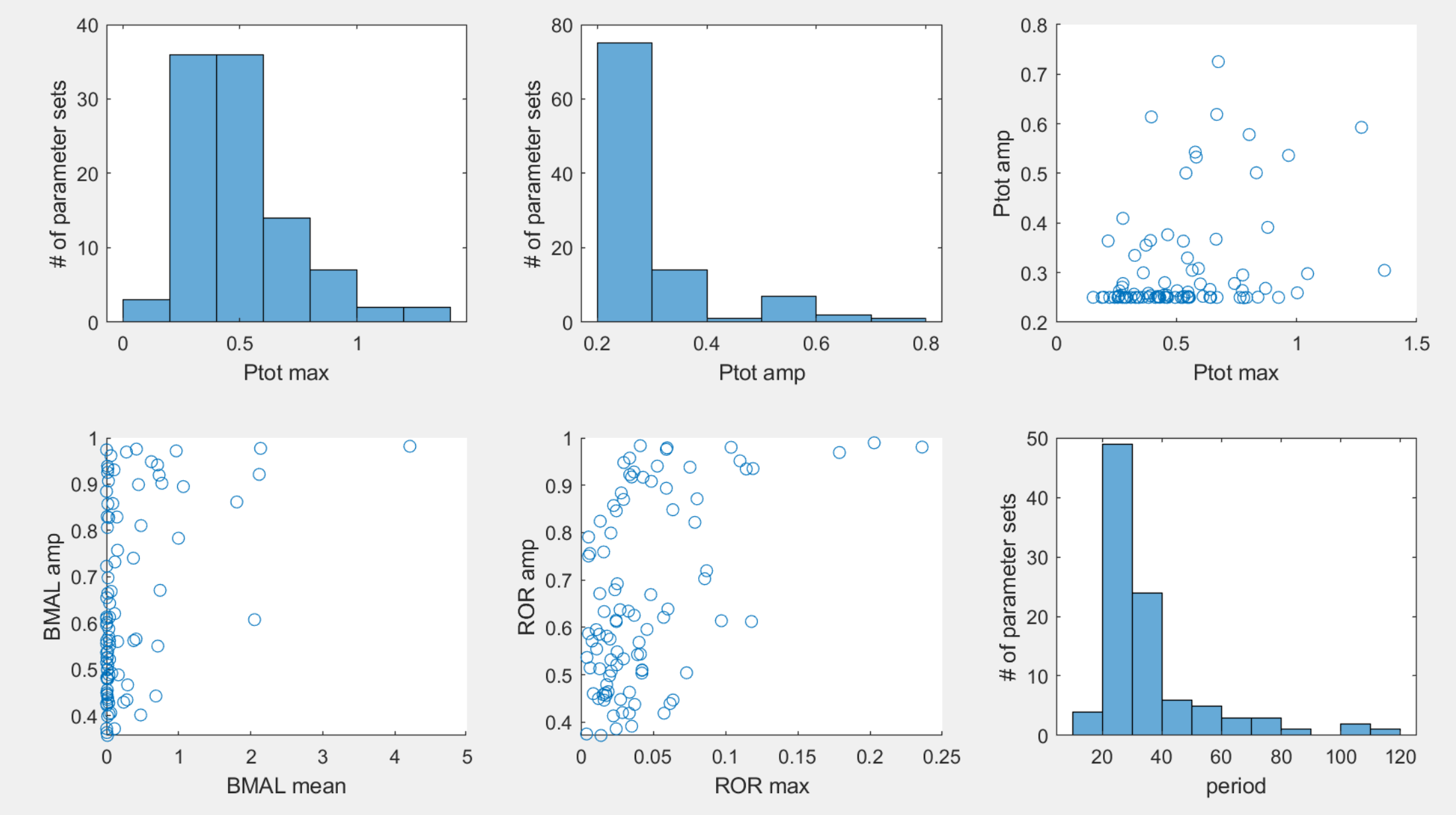
**Cost function:**

**Range of search:**

**Initial guesses:**

100 random samples with Latin hypercube in the range above for the logarithm values of the parameters.

**Results: (100 runs)**



PNF definitely lowers Ptot\_max, and hence increases dimensional Kd!

**Best set (with lowest max(Ptot))**

[delta, Amax, Rmax, Ka, alpha, Km, beta\_max, eps] = [55.1037 0.8578 41.1534 33.6073 41.3788 39.2248 10.0477 0.0001];

period\_sim: 22.8571

Ptot\_max\_sim: 0.1536

Ptot\_amp\_sim: 0.2501

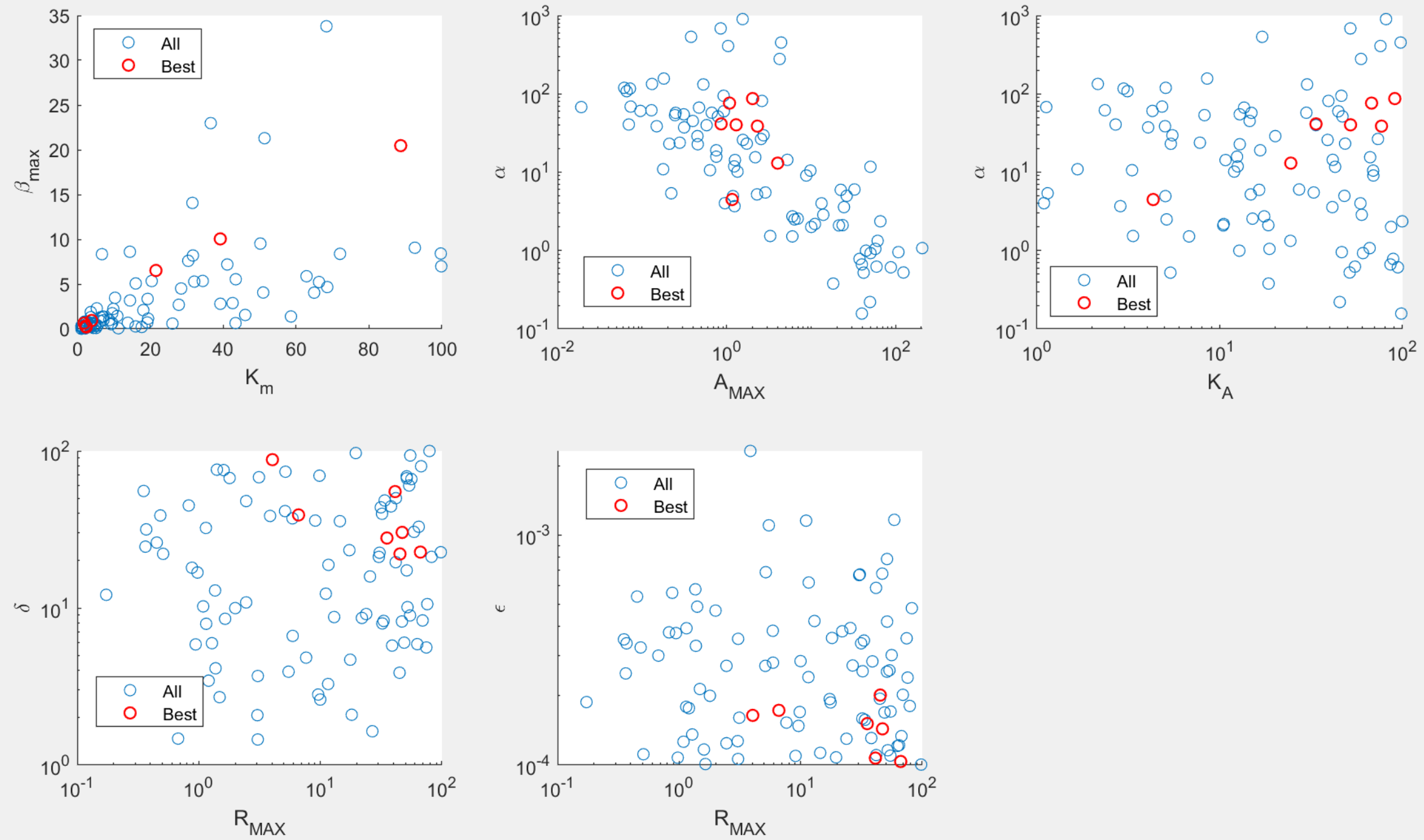
BMAL\_avg\_sim: 0.0109

BMAL\_amp\_sim: 0.4558

ROR\_max\_sim: 0.0188

ROR\_amp\_sim: 0.4643

**Patterns for the top parameter sets**

Blue: all 100 sets from optimization. Red: 10 sets with lowest max(Ptot).

Main patterns:

1. Km and beta\_max are restricted to a certain ratio?
2. Alpha and AT are negatively correlated. This pattern is similar to SNF.
3. KA does not seem very restricting.
4. Delta needs to be sufficiently high.
5. Eps needs to be sufficiently low.
6. Period strongly depends on more parameters, including beta\_max, delta, Amax, alpha, KA.

