Green Simulation Assisted Reinforcement Learning with Model Risk for Biomanufacturing Learning and Control

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  - **faster convergence!**

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- More "personalized" bioprocess requires more advanced manufacturing protocols and automation (optimal policy from reinforcement learning);
- analytical testing time required by biopharmaceuticals of complex molecular structure is lengthy, and the process observations are relatively limited. (Bayesian dynamics model)

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- the bioprocess is in some state s_t, and the decision maker may choose any action a_t by following a policy $\pi_t(a_t|s_t)$.
- Then the process responds at the next time step $(t+1)$ by moving into a new state s_{t+1} following transition probability $P(s'|s,a)$, and giving the decision maker a corresponding reward or cost, denoted by $R_t(a_t, s_t)$.

Optimization

- Let $D^{\pi_\theta}_{P_{\omega^c}}(\tau) \equiv p(s_1;\omega^c)\prod_{t=1}^{H-1}\pi^t_{\theta}(a_t|s_t)p(s_{t+1}|s_t,a_t;\omega^c)$ denote the distribution of the trajectory $\tau \equiv (s_1, a_1, \ldots, s_{H-1}, a_{H-1}, s_H)$
- Given historical data $\mathcal{D}_p$, we have objective

$$\max_{\pi_\theta} \mu(\pi_\theta) = \mathbb{E}_{\omega\sim p(\omega|\mathcal{D}_p)}\left[\mathbb{E}_{\tau\sim D^{\pi_\theta}_{P_\omega}(\tau)}\left[\sum_{t=1}^{H-1}\gamma^{t-1}r_t \middle| \pi_\theta, s_1, \omega\right]\right]$$

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- Under some regularity conditions, we derived its gradient

$$\nabla_\theta \mu(\boldsymbol{\pi_\theta}) = \underbrace{\mathbb{E}_{\boldsymbol{\omega}}}_{(1)}\left[\underbrace{\mathbb{E}_{\boldsymbol{\tau}\sim D^{\boldsymbol{\pi}_{\bar{\boldsymbol{\theta}}}}_{P_{\bar{\boldsymbol{\omega}}}}}}_{(2)}\left[\frac{D^{\boldsymbol{\pi_\theta}}_{P_{\boldsymbol{\omega}}}(\boldsymbol{\tau})}{D^{\boldsymbol{\pi}_{\bar{\boldsymbol{\theta}}}}_{P_{\bar{\boldsymbol{\omega}}}}(\boldsymbol{\tau})}\sum_{t=1}^{H-1}\nabla_\theta \log(\pi_{\boldsymbol{\theta}}(a_t|s_t))\sum_{t'=t}^{H-1}\gamma^{t'-1}r'_t(a^{(i,j)}_{t'}, s^{(i,j)}_{t'})\right]\right]$$

where (1) accounts for parametric uncertainty (i.e. model risk) and (2) accounts for stochastic uncertainty.

Individual/Mixture Likelihood Ratio (ILR/MLR)

At the k-th iteration, given a posterior sample $\boldsymbol{\omega}_k \sim p(\boldsymbol{\omega}|\mathcal{D}_p)$ and policy $\boldsymbol{\pi}_{\boldsymbol{\theta}_k}$, the *likelihood ratio based policy gradient estimator*,

$$\widehat{\nabla_{\boldsymbol{\theta}}\mu}_{k,\mathbf{n}}^{ILR/MLR} = \frac{1}{k}\sum_{i=1}^{k}\frac{1}{n_i}\sum_{j=1}^{n_i}\left[L_k(\boldsymbol{\tau}^{(i,j)})\sum_{t=1}^{H-1}\nabla_{\boldsymbol{\theta}}\log(\pi_{\boldsymbol{\theta}_k}(a_t^{(i,j)}|s_t^{(i,j)}))\sum_{t'=t}^{H-1}\gamma^{t'-1}r_t'(a_{t'}^{(i,j)},s_{t'}^{(i,j)})\right]$$

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- MLR is bounded by $\frac{1}{\alpha_i^k}$ and has lower variance than ILR.

Algorithm

```
Input: the number of periods $P$ for real-world dynamic data collection; the number of
  iterations $K$; Initialize the set of sample trajectories $\mathcal{E}_1$, the set of transition model
  parameters $\boldsymbol{\Omega}_1$, and the set of policy parameters $\boldsymbol{\Theta}_1$ to be empty set.
for $p = 1, 2, \ldots, P$ (at each new real-world data collection point) do
    for $k = (p-1)K + 1, (p-1)K + 2, \ldots, pK$ do
        1. Generate posterior samples $\boldsymbol{\omega}_k \sim p(\boldsymbol{\omega}|\mathcal{D}_p)$ and build the transition model with
          new parameter $\boldsymbol{\omega}_k$, i.e., $p(s_{t+1}|s_t, a_t, \boldsymbol{\omega}_k)$ for $t = 1, 2, \ldots, H-1$ ;
        2. Generate $n_k$ trajectories following the policy $\pi_{\boldsymbol{\theta}_k}$ and model $\boldsymbol{\omega}_k$;
        3. Calculate $\widehat{\nabla_{\boldsymbol{\theta}} \mu}^{MLR}_{k,\mathbf{n}}$ and update $\boldsymbol{\theta}_{k+1} \leftarrow \boldsymbol{\theta}_k + \eta_k \cdot \widehat{\nabla \mu}^{MLR}_{k,\mathbf{n}}$ ;
        4. Record new generated trajectories $\mathcal{E}_{k+1} = \mathcal{E}_k \cup \{\boldsymbol{\tau}^{(k,j)}|j = 1, 2, \ldots, n_k\}$,
          transition model parameters $\boldsymbol{\Omega}_{k+1} = \boldsymbol{\Omega}_k \cup \{\boldsymbol{\omega}_k\}$ and policy parameters
          $\boldsymbol{\Theta}_{k+1} = \boldsymbol{\Theta}_k \cup \{\boldsymbol{\theta}_k\}$;
    end
    5. Collect new process real-world data $\mathcal{L}_p$ and update the historical data set
     $\mathcal{D}_{p+1} = \mathcal{D}_p \cup \mathcal{L}_p$ and the posterior distribution $p(\boldsymbol{\omega}|\mathcal{D}_{p+1})$.
end
```

A Biomanufacturing Problem

In this paper, we consider a biomanufacturing process control problem and mainly focus on chromatography in the downstream (Martagan et al.[1]).

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- **Action Space:** Let a_t denote the choice of pooling windows.
- **Reward:** Let $r_t = \frac{p_t}{p_t + i_t}$ denote the purity level. At each time step in downstream process, the reward is

$$\mathrm{r}(\mathrm{p}_t, i_t, t = 3) = \begin{cases} -c_f, & \text{if } r_t < r_d, \\ r(p_d), & \text{if } r_t \geq r_d, p_t \geq p_d, \\ r(p_t) - c_l(p_d - p_t), & \text{if } r_t \geq r_d, p_t \leq p_d. \end{cases}$$

$$\mathrm{r}(\mathrm{p}_t, i_t, t) = -\$8 \text{ with } t \in \{1, 2, 3\}$$

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    - uniform prior $\text{Unif}(0, 300)$ for all parameters.
- **Policy:** We use a 2-layer perceptron (MLP) of $D = 16$ dimensional first layer and 10 dimensional output layer with softmax activation function to parameterize our policy.

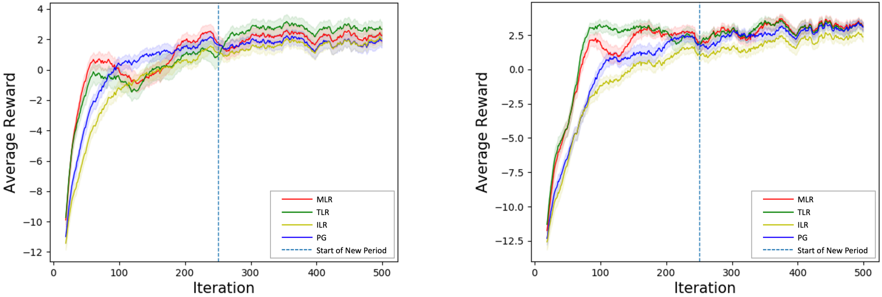
Benchmarks

We compare the performance of proposed green simulation assisted policy gradient with RL (MLR) with

- Likelihood ratio based policy gradient with mixture proposal distribution (MLR)
- Likelihood ratio based policy gradient with true transition model known (TLR)
- Individual likelihood ratio based policy gradient (ILR)
- Empirical policy gradient (PG): classical policy gradient method using the point estimator (mean) of state transition model parameter as the true one

Result: Faster Convergence

With $m = 20$ historical samples and $P = 2$ periods, $r_{test} = 200$ simulation runs and $M = 5$ macro replications, the simulation results shows faster convergence than other algorithms,



(a) $n_i = 50$

(b) $n_i = 25$

Figure: Convergence results of MLR, TLR, ILR and PG.

Conclusion

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- mixture likelihood ratio provides a new scheme for "experience reply" method for reinforcement learning;
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  - reduce policy gradient variance.

[1] Tugce Martagan, Ananth Krishnamurthy, Peter A. Leland, and Christos T. Maravelias. Performance guarantees and optimal purification decisions for engineered proteins. *Operations Research*, 66(1):18–41, January 2018.