Interactive learning for Neurosciences: Between Simulation and Reality

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A popular topic



Deisenroth, M. P., Rasmussen, C. E., & Fox, D. (2011). Learning to control a low-cost manipulator using data-efficient reinforcement learning. Robotics: Science and Systems VII, 7, 57-64.





Reinforcement Learning (RL)



Environment



Reinforcement Learning (RL) Agent Action a_t given state s_t $\mathbf{\bullet}$



Environment



Reinforcement Learning (RL)



Reinforcement Learning (RL)



Episodic learning

1 episode = 1 game

• Game 1:



Game 2: ullet





Defeat!

• Game *N*:

... Victory!







Episodic learning

History $\begin{bmatrix} s_1, a_1, r_1, s_2 \\ s_2, a_2, r_2, s_3 \end{bmatrix}$







Recall Supervised Learning

Dataset

Cats:

Dogs:









Training

Predictive model

* https://sandeep-bhuiya01.medium.com/disadvantages-of-cnn-models-95395fe9ae40



Predictive model

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Exploration / Exploitation

Exploitation: Using knowledge to maximize collected rewards

Exploration: Improving knowledge about the problem (better understanding the impacts of actions) possibly at the cost of rewards

Example: Learning the optimal path

Galbrun, E., Pelechrinis, K., & Terzi, E. (2016). Urban navigation beyond shortest route: The case of safe paths. Information Systems, 57, 160-171.

- Goal: Get from S to T as fast as possible
- Optimal path (unknown): Path 2
- Shortest path currently known: Path 5
- Exploitation: Follow Path 5
- Exploration: Deviate from Path 5
 → Could allow to discover Path 2

How to achieve this with RL?

https://medium.com/@xaviergeerinck/the-markov-property-chain-reward-process-and-decision-process-4f63f7922401

Planning for the future

Example: Structured bandits

- Action $a \in \mathscr{A}$ is associated with features $x \in \mathscr{X}$
- Simple case: Discrete set $\mathscr{X} \subset \mathbb{R}$
- Expected reward function: $f: \mathcal{X} \mapsto \mathbb{R}$
- Reward $r_t = f(x_t) + \varepsilon_t$ with $\varepsilon \sim \mathcal{N}(0, \sigma^2)$
- Assumption: Actions nearby in ${\mathcal X}$ have similar expected reward
- Assumption: $f(x) = \langle \phi(x), \theta \rangle$ with unknown θ and known $\phi(\cdot)$

Kernel regression

- Kernel $k(x, x') = \langle \phi(x), \phi(x') \rangle$
- σ^2

Gaussian prior
$$\theta \sim \mathcal{N}_d(0, \Sigma)$$
 with $\Sigma = \frac{\partial}{\lambda} I$ for $\lambda > 0$
 $\mathbf{K}_N = [k(x_i, x_j)]_{1 \le i,j \le N}$ and $\mathbf{k}_N(x) = (k(x, x_i))_{1 \le i,j \le N}$
 $\mathbb{P}[f | x_1, \dots, x_N, y_1, \dots, y_N] \sim \mathcal{N}\left((f(x)_{x \in \mathcal{X}}), [k_N(x, x')]_{x, x' \in \mathcal{X}}\right)$
Posterior mean: $f_N(x) = \mathbf{k}_N(x)^{\top}(\mathbf{K}_N + \lambda I)^{-1}\mathbf{y}_N$
Posterior covariance: $k_N(x, x') = k(x, x') - \mathbf{k}_N(x)^{\top}(\mathbf{K}_N + \lambda I)^{-1}\mathbf{k}_N(x)$

Kernel regression

- Kernel $k(x, x') = \langle \phi(x), \phi(x') \rangle$
- Gaussian prior $\theta \sim \mathcal{N}_d(0,\Sigma)$ with $\Sigma = \frac{\sigma^2}{\lambda} I$ for $\lambda > 0$

Example: Posterior distributions after 1, 10, and 100 observations (x_t, r_t)

Kernel regression + Thompson Sampling (TS)

Example: Decision making at t = 4

- Compute posterior distribution given previous observations •
- Sample function \tilde{f} from the posterior
- Select $x_t = \arg \max_{x \in \mathcal{X}} \tilde{f}(x)$

STED Microscopy Optimization

Excitation laser Depletion laser

Flavie Lavoie-Cardinal et Theresa Wiesner

Difficult to configure to acquire good images

SLM_595 Alignment ×	Pulse Calib ×	Hardware Acquisition Timing ×	Experiment Control	×	Configurations
	Corr Inv Width 185nm -2.188ns 8.000ns on 518nm -1.406ns 8.000ns on • 518nm -1.406ns 8.000ns on • N.C. 15.39ns 10.00ns off • 561nm 4.687ns 8.000ns off • 640nm 13.13ns 10.00ns off • N.C. 9.844ns 10.00ns off • GFP 19.38ns • • • • YFP -19.30ns • • • •	Bapeed Time n.a. Estimated Remaining Time n.a. Axis details Step details Measurement details Sync and update Measurement Setup × Scan Axes: Sync: 1: ExpControl X • Frame •	ху ▼ Range Off X 1.94µm 5.64µm Y 1.70µm -13.0µm Z 3.17µm 0.00m T N/A Une Accu Lock Aspect	Eliptical Scan ≠ Pixel Pix. Size 97 20.0nm 85 20.0nm 62 51.2nm 512 N/A 1 ✓ Lock Pixel Size ✓ Square Pixels	Stack Display
Offset X 20 43 Offset Y -29 -28 Grating X 4.88/mm 4.78/mm Grating Y -0.0100/m -0.0100/m ► Advanced	CY3 11.64ns CY5 16.64ns STED_ 0.000s STED_ 0.000s OlympusIX X Observation method none Current Measurement Current Measurement Apply measurement values now Usis Rode 2 (meas) = 4 Shutter	2: ExpControl Y 3: None 4: None 5 Bidirectional Scan Permanent Add TimeLapse X Enable timer measurement Timesteps Length 0.000s	Global Offset Coarse Fine X 0.00m Y 0.00m Z -3.06µm Frame Trigger Dwell Time 10.0µs Lin	Orientation Rat 0.00 Tilt 0.00 Ral 0.00 Use Autofocus	Stack Display Display Orientation Kno values2 Hidden Axis Mode <no <no="" axis="" data="" display<="" flim="" graph="" hidden="" mode="" range="" rescue="" td="" values2=""></no>
	Main Deck 2 (none) ▼ ✓ Shutter Aux. Deck 2 (none) ▼ ✓ Shutter Light Path scanner ▼ ✓ Shutter Light Path scanner ▼ ✓ Shutter Trans Illum 0.00 □ □ Lens 100X NA1.4(oil) [UPLSAPO1 ▼ ✓ Stage pos. global Local offset X X -180.000nm 0.000m ■ Y 320.000nm 0.0000m ■ Z 0.00000m 0.0000m ■ Z 0.00000m ■ ■ Focus Search Continuous AF ✓ DM in Focus offset lens position 0 ■ SLM_775 Alignment ×	Count 1 Ignore Timer Overflow Wait 1 timestep before restart Use Sequence Scheduler Gating × Delay Width ✓ Ch1 781.3ps % Ch2 781.3ps ✓ Ch3 781.3ps ✓ Ch4 781.3ps Ø Delay Output Ø Upout 0 Ø Ch4 781.3ps Ø Ch4 781.3ps Ø Ch4 781.3ps Ø Delay Output Ø Upout 0 Ø Upout 0 Ø Upout 0 Ø LP2 0.000s 513nm Ø LP3 0.000s 640nm	Lasers and Channels Detector ✓ Ch1 PMT refi ✓ Ch2 PMT refi ✓ Ch3 PMT refi ✓ Ch3 PMT refi ✓ Ch4 PMT refi ✓ L1 Exc_485 ✓ L2 Exc_518 ✓ L2 Exc_518 ✓ L3 STED_595 ✓ L4 Exc_561 ✓ L5 Exc_640 ✓ L6 STED_775 L7 L8	X Gain Rescue 28.00% 28.00% 28.00% 28.00% 28.00% 28.00% 10.00% 10.00% 10.00% 10.00% 10.00%	Line Steps
	Mode L 2D R 3D Offset X 41 31 </th <th>Steps 1 Scan Calib × Range Scale Pos Ramp X 85.0µm 13.35V -800.0C 700µs Y 85.0µm 13.35V -800.0C 700µs Y 85.0µm 13.94V 200.00 700µs Z 200µm 10.00V 5.0000' 200µs Delay Drag Global Data Delay X X 140µs 135.0µs 0.00s Y Y 140µs 140.0µs - - Z 30.0ms 100.0µs - - PupI correction </th> <th>Puise Steps Pool St ✓ Puise Gates Power Distribution STED 775 20 STED 595 20 ✓ Laser On Set value ✓ C. Power 800.0mW C. Current 0.000A Trig. Source Internal Frequency 35.00MH SHG Temp. 57.47°C Status warming up STED 775</th> <th>eps ✓ Line Steps 3D 0.00% 3D 0.00% × • Measured value / 0.000W 0.000A ▼ Level 0.00V z Shutdown ×</th> <th>1 1 1 1 55 56 1 1 Camera Live video Start Stop FPS Exposure time </th>	Steps 1 Scan Calib × Range Scale Pos Ramp X 85.0µm 13.35V -800.0C 700µs Y 85.0µm 13.35V -800.0C 700µs Y 85.0µm 13.94V 200.00 700µs Z 200µm 10.00V 5.0000' 200µs Delay Drag Global Data Delay X X 140µs 135.0µs 0.00s Y Y 140µs 140.0µs - - Z 30.0ms 100.0µs - - PupI correction	Puise Steps Pool St ✓ Puise Gates Power Distribution STED 775 20 STED 595 20 ✓ Laser On Set value ✓ C. Power 800.0mW C. Current 0.000A Trig. Source Internal Frequency 35.00MH SHG Temp. 57.47°C Status warming up STED 775	eps ✓ Line Steps 3D 0.00% 3D 0.00% × • Measured value / 0.000W 0.000A ▼ Level 0.00V z Shutdown ×	1 1 1 1 55 56 1 1 Camera Live video Start Stop FPS Exposure time
	SLM_775 Aberrations × Defocus L 0.0500 R 0.000 Astigmatism X 0.000 Y 0.000 Coma X 0.000 Y 0.05000 Spherical 0.01000 Trefoil Vert. 0.000 Obl. 0.000 Status connected Vert.	SLM_595 Aberrations × Defocus L -0.0500 R -0.0500 Astigmatism X 0.05000 Y 0.000 Coma X 0.000 Y 0.000 Spherical 0.000 Vert. 0.000 0bl. 0.000 Trefoil Vert. 0.000 Obl. 0.000 0.000	Power 1.251W 1. Current 10.06mA Temp 48.00°C Status Emission on Error no errors	249W V On Shutdown	Ingger Source Source STED_595 • Delay 30.0ns Pinhole In Measurement 1.0AU • Current 1.0AU • Current position: 9895

Imspector Software – Abberior Instruments

Parameters:

- Power of lasers
- Time spent per pixel
- Number or repetitions

Objectives:

. . .

- Signal to noise ratio
- Photobleaching
- Resolution
- Quality

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Bandit problem!

Imaging parameters

Durand et al. (2018) "A machine learning approach for online automated optimization of super-resolution optical microscopy". Nature Communications.

Bandit problem!

Imaging parameters

Durand et al. (2018) "A machine learning approach for online automated optimization of super-resolution optical microscopy". Nature Communications.

What is good image quality?

Avoiding images likes these:

Acquiring more images likes these:

Multiple objectives to consider

Maximize image quality: Being able to acquire *good* images

Optimizing multiple objectives

Automated multi-objective optimization

Experiments

Three parameters (1000 configurations):

- Excitation laser power
- Depletion laser power
- Duration of imaging per pixel

Acquire:

- Confocal (low resolution image)
- First STED
- Second STED

From abberior-instruments.com

Goal: 1 1st STED quality and 1 photobleaching

Beginning of optimization \rightarrow

End of optimization \rightarrow

Bottom left corner: Confocal Not super-resolution

Beginning of optimization \rightarrow

End of optimization \rightarrow

Bottom left corner: Confocal Not super-resolution

Beginning of optimization \rightarrow

End of optimization \rightarrow

Bottom left corner: Confocal Not super-resolution

Beginning of optimization \rightarrow

End of optimization \rightarrow

Bottom left corner: Confocal Not super-resolution

Bandits formulation

Steps t = 1, 2, ...

New problem:

. . .

. . .

. . .

New problem:

New problem:

. . .

. . .

\rightarrow Good parameters for *this* sample

. . .

 \rightarrow Good parameters for *this* sample

... vs RL formulation

Steps t = 1, 2, ...

Episode 1

. . .

. . .

. . .

Episode 2

Episode 3

. . .

. . .

Parameter tuning policy

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Turcotte et al. (2022) "pySTED : A STED Microscopy Simulation Tool for Machine Learning Training". AAAI workshop on AI to Accelerate Science and Engineering.

Simulated imaging of a dendritic spine

Simulated image

Evaluating an acquisition

- Identifying nanostructures on a STED image: •
 - Identify local intensity maxima + 2D Gaussian fit
 - Gaussian standard deviation (2 directions) < 250 nm (diffraction limit) \rightarrow nanostructure
- Associating identified locations with true locations \rightarrow Hungarian algorithm
- Comparing with true locations (ground truth) : $\bullet TP \bullet FP$ FN TΡ F_1 -score = - $TP + \frac{1}{2}(FP + FN)$ Ground Truth

RL formulation

Episode:

T images

State S_t :

- **Excitation laser power** \bullet
- STED laser power
- Time spent per pixel

Last confocal-STED pair and associated objective values

- Signal to noise ratio
- Resolution
- Photobleaching

Current confocal

╋

PPO (Proximal Policy Optimization)

CNN

Visual information:

Previous confocal and STED +

Current confocal

Previous objective values:

- Signal to noise ratio
- Resolution
- Photobleaching

Experiments

- Episodes of T = 10 images
- 20 000 episodes

Rewards that do not depend on ground truth

Expert image databank:

Acquired image:

Reward r_t : Ranking between 0 (worst) and 1 (best)

Experiments

- Episodes of T = 10 images
- 20 000 episodes

A fully automated parameter tuning strategy!

Thanks!

Questions?

