Enabling risk-aware Reinforcement Learning for medical interventions through uncertainty decomposition

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Abstract

Reinforcement Learning (RL) is emerging as tool for tackling complex control and decision-making problems. However, in high-risk environments such as healthcare, manufacturing, automotive or aerospace, it is often challenging to bridge the gap between an apparently optimal policy learned by an agent and its real-world deployment, due to the uncertainties and risk associated with it. Broadly speaking RL agents face two kinds of uncertainty, 1. aleatoric uncertainty, which reflects randomness or noise in the dynamics of the world, and 2. epistemic uncertainty, which reflects the bounded knowledge of the agent due to model limitations and finite amount of information/data the agent has acquired about the world. These two types of uncertainty carry fundamentally different implications for the evaluation of performance and the level of risk or trust. Yet these aleatoric and epistemic uncertainties are generally confounded as standard and even distributional RL is agnostic to this difference. Here we propose how a distributional approach (UA-DQN) can be recast to render uncertainties by decomposing the net effects of each uncertainty. We demonstrate the operation of this method in grid world examples to build intuition and then show a proof of concept application for an RL agent operating as a clinical decision support system in critical care.

1. Introduction

The increasing availability of electronic healthcare records containing both patient state and clinician’s treatment actions opened up the opportunity to machine learn the decision making policies for patient treatments. Therefore, off-policy Reinforcement Learning RL for optimal sequential clinical decisions have become the paragon for AI-based interventions (Komorowski, 2018; Gottesman et al., 2019). In general RL shows very promising performance and potential to exceed human expert performance when tested on retrospective or simulated data (Ernst et al., 2006; Bothe et al., 2013; Lowery & Faisal, 2013; Li et al., 2020; Liu et al., 2020). First reinforcement learning-derived systems that autonomously intervene on patients have already been deployed successfully in rehabilitation settings (Wannawas et al., 2021) where risks are controlled, but the hospital-based use-case of RL driven intervention at the bed side involves greater risks, due to health state of patients and potential negative impact of any intervention. There is therefore now a growing need to direct development of RL systems for healthcare that are risk and safety aware a priori by design. This requires RL algorithms to be aware of noise and uncertainty in their operation, and to make these critical performance interrogatable, so as to ultimately allow developers, regulators and users to specify safety and trust margins in their operation.

One of the areas where RL has shown great potential is the treatment of sepsis in critical care, such as the management of sepsis, which kills almost a third of patients (Stevenson et al., 2014) and yet optimal decision making policies are unclear. RL methods applied to retrospective data have shown promising results that could theoretically identify individualized and clinically effective treatment decisions that significantly reduce mortality of patients (Komorowski, 2018). Here, the RL agent’s actions, referred to cheekily as AI Clinician, are communicated as recommendations (clinical decision support system, CDSS) to an expert, e.g. a critical care clinician, who may then choose to implement or ignore. Interestingly this intensive care application has rapidly evolved to become a popular use case for reinforcement learning in healthcare, in parts due to the public availability of high density, high quality data sets, as well as the immediate usefulness of reinforcement learning over that of supervised learning. Consequently, clinical trials of RL systems are now being ramped up to test such systems in hospitals, there are limitations on the interpretability, safety

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Workshop on Interpretable ML in Healthcare at International Conference on Machine Learning (ICML). Copyright 2021 by the author(s).
and trust of that have need to be overcome before general deployment can be considered.

Broadly speaking, there are two main sources of uncertainty that limit the capability of an RL agent’s optimal policy: First, noise or randomness in the dynamics of the world and the agent. This uncertainty is measurable by repeating the same action and observing variability from trial to trial (Faisal et al., 2008). This so called aleatoric uncertainty (from the Latin alea for “dice”) captures thus randomness in the system. In the healthcare case this can be physiological processes, the effect of treatments or drugs, or the outcomes of healing. These are factors that the agent can mitigate by working around them, but ultimately has no direct control over. In healthcare treatments there may be many settings where an action or intervention may have a probabilistic outcome and it is important for a human stake holder to understand if a proposed outcome’s success is affected by chance.

Second, we have epistemic uncertainty (from the Greek word episteme for knowledge) that captures how well the model has learnt from finite data to solve the problem and how well the model can fit the problem. In the healthcare case this could reflect that the algorithm is aware that it has limited data of state space regions or state transitions e.g. when facing a new disease or when a drug has not been often prescribed to a particular type of patient. Epistemic uncertainty is essential for recommender systems safety, as this allows human stake holders to weight an AI systems recommendation against human judgement or prompt seeking expert human opinions.

These two types of uncertainties are typically not accessible in conventional RL models. More advanced probabilistic RL models which use posterior distributions over learned parameters in Bayesian RL (Ghavamzadeh et al., 2016) or in distributional reinforcement learning which models distributions over the returns (Bellemare et al., 2017) also confound or confute the two types of variability. However, being able to decompose these two components would have immediate benefits for the interpretation of RL agent treatment recommendations: For example, high aletoric and low epistemic uncertainty in a given state would mean that the model is aware that this state is highly stochastic, so experts should be particularly careful about the patient’s evolution here, whereas high epistemic uncertainty would mean that the model has not seen enough data or has not been able to converge well enough in that state to give an informed recommendation, so clinicians should not consider the model output as very valuable.

In the following we show how using existing concepts and framework we can build RL agents that decompose the uncertainties associated with their state-action representations. We illustrate the behaviour of our model on toy grid world setups, and show what both uncertainties represent through intuitive computer experiments. We port this approach and apply it in an RL clinical decision support system.

2. Background

Let $\mathcal{X}$ and $\mathcal{A}$ be state and actions spaces, respectively and let $Z := \mathcal{X} \times \mathcal{A}$ denote the product space. We consider an MDP framework where we have transition kernels $p : \mathcal{X} \times \mathcal{A} \to \mathcal{P}(\mathcal{R} \times \mathcal{X})$. The full MDP is given by a collection $(X_t, A_t, R_t)_{t \geq 0}$, where $(X_t)_{t \geq 0}$ is the sequence of states taken from the environment, $(A_t)_{t \geq 0}$ is the sequence of actions taken by the agent and $(R_t)_{t \geq 0}$ the sequence of rewards. We will consider either deterministic policies $\pi : \mathcal{X} \to \mathcal{A}$ or stochastic policies $\pi : \mathcal{X} \to \mathcal{P}(\mathcal{A})$. The return of a policy $\pi$, starting at an initial state $x \in \mathcal{X}$ and initially taking an action $a \in \mathcal{A}$ is the random variable given by the sum of discounted rewards, $\sum_{t=0}^{\infty} \gamma^t R_t \mid X_0 = x, A_0 = a$. Additionally, the distribution of the return of policy $\pi$ and initial state-action pair $(x, a) \in Z$ is (Rowland et al., 2018)

$$
\eta^\pi_{x,a} = \text{Law}_\pi \left[ \sum_{t=0}^{\infty} \gamma^t R_t \mid X_0 = x, A_0 = a \right].
$$

Having access to the distribution of returns rather than just the expectation as in standard RL leads to additional information that plays a crucial role when quantifying uncertainties. Here, distributional RL aims to learn the distribution of returns $\eta^\pi_{x,a}$ associated with taking action $a$ in state $x$ and then following a policy $\pi$. The idea is to consider the whole distribution of the return rather than the expectation (Morimura et al., 2010b;a), where the return density is estimated in order to handle a variety of risk-sensitive and risk-averse criteria. This approach reached breakthrough performance in Atari Games benchmarks (Bellemare et al., 2017). In terms of algorithmic developments, in the past few years, several distributional RL approaches have been developed to learn the return distributions $\eta^\pi(s, a)$, as Bellemare et al. (2017); Dabney et al. (2018); Yang et al. (2019) to name a few. In (Dabney et al., 2018), the return distribution $\eta^\pi(x, a)$ is approximated by $N$ quantiles $\tau_i = i/(N + 1)$, with $i \in [1, N]$ with corresponding values $q = (q_1, \ldots, q_N)$. The values of the quantiles can be learned leveraging the Huber loss and the Bellman target as in the QR-DQN algorithm by Dabney et al. (Dabney et al., 2018). We adapt here the approach developed by Clements et al. (2019) to combine Bayesian inference and distributional RL to then incorporate during training and then render the decomposition of the different sources of uncertainty. The epistemic and aleatoric uncertainties are incorporated as additional information during the training procedure in a variant of Quantile-Regression DQN. In order to decouple aleatoric and epistemic uncertainties one can learn the quantiles of the return distribution in a Bayesian fashion; to learn the value...
of a given quantile $\tau$ of $\eta^\theta(x,a)$, a neural network is used with parameters $\theta$ that return a value $y(x,a,\theta)$. Given a set of samples $S := (s_1, \ldots, s_k)$ from $\eta^\theta(x,a)$ (or, in practice, from the corresponding Bellman target), the likelihood of $S$ given $\theta$ is defined as:

$$P(S | \theta) = \prod_{j=1}^{k} \prod_{i=1}^{N} \ell_{\tau_i}(s_i - y_i(\theta, x, a))$$

(2)

where $\ell_{\tau_i}$ is based on the asymmetric Laplace distribution - a standard approach in Bayesian Quantile Regression (Yu & Moyeed, 2001). Clements et al. (2019) proceed to show how obtaining uncertainty estimates can help boost an agent’s training process. Using this line of thought, the following estimators for the epistemic and aleatoric uncertainties can be obtained (here using variance as proxy for uncertainty):

$$\sigma^2_{\text{epistemic}} := \mathbb{E}_{\theta \sim U(1,N)}[\text{var}_{\theta \sim P(\theta|S)}(y_i(\theta, x, a))]$$

This captures the variability in the return distribution estimate due to model learning by averaging over trajectories and taking the variance of the quantile estimates with respect to the posterior on policy parameters.

$$\sigma^2_{\text{aleatoric}} := \text{var}_{i \sim U(1,N)}[\mathbb{E}_{\theta \sim P(\theta|S)}(y_i(\theta, x, a))]$$

This captures the variability in the return distribution estimate due to stochasticity in the environment by averaging over posterior policy parameters and taking the variance of the quantile estimates with respect to trajectories.

We argue and visualise here how this approach can be used for uncertainty decomposition to render safety-conscious and risk-aware recommender systems – which frame and put into a risk-conscious context the recommendations of a CDSS.

We argue that both epistemic and aleatoric uncertainty are of crucial importance in medical applications and that an accurate estimate of the two uncertainties is fundamental in order to unlock the practical deployment of reinforcement learning in healthcare. Decoupling them would have profound implications for the interpretability and accountability of the output of a CDSS. Equally, the trust that users will in CDSSs will only increase if they can provide some degree of confidence in their output or manage expectations of outcomes, e.g. when the aleatoric uncertainty is high. Stake holders will be interested to know that a recommended action comes with a low confidence of success because of rare patients characteristics (leading to high epistemic uncertainty) or that the uncertainty about the future evolution of a given patient is high (high aleatoric uncertainty). Another positive effect of quantifying uncertainty will be to enable clinicians to focus their efforts on patients where uncertainty is the highest, among a given cohort of patients in the intensive care unit, leaving those with high confidence “under the care” of the AI.

### 3. Results

In this section we present experimental results to support our claims that modelling and disentangling both sources of uncertainties in clinical settings is potentially very informative and crucial for clinical deployments.

#### 3.1. Toy experiments: grid worlds

We first introduce two grid worlds to validate this approach of computing proxies for aleatoric and epistemic uncertainty estimates.

First, epistemic uncertainty should come from faults in model learning: it corresponds to the part of the uncertainty due to lack of data or poor model convergence. To build intuition of our approach we visualise here a $7 \times 7$ deterministic grid world Fig. 1.A.

![Figure 1](image)

**Figure 1.** (A) Representation of the agent’s uncertainty estimates for a $7 \times 7$ grid world. The dark lines are separating the grid world states. The agent is given positive reward for successfully going from the initial state to the terminal state. In each state’s square the top red color box represents the epistemic uncertainty and blue box at the bottom right represents the aleatoric uncertainty (more vivid colour corresponding to more uncertainty normalised across all states). To aide intuition we scaled the value of aleatoric uncertainty here with the computed values for the same grid world where the state transition probabilities are uniform random for any action (random walker agent). (B) Representation of the agent’s uncertainty estimates in a $2 \times 6$ cliff-walking high-risk grid world where states are subject to wind which pushed the agent into the cliff with 20% probability.
only noise, there is no stochasticity in this world, the values are very close but normalisation emphasises differences in the visualisation.

We proceeded in a similar way to validate the behaviour of UADQN’s aleatoric uncertainty estimate. Aleatoric uncertainty should be a measure of how much the variability in the reward distribution is due to intrinsic stochasticity of the world. We trained the agent to act in a $2 \times 6$ grid world where the start state (Fig. 1.b), at the left of the bottom row, is separated from the goal state by a cliff. When walking along the cliff edge, wind will push the agent downward with 20% probability (irrespective of the action chosen). The agent gets positive reward for reaching the goal, and negative reward for falling off the cliff.

This wind mechanic introduces stochasticity in the world dynamics and should impact the aleatoric uncertainty values. Figure 1.b visualises the uncertainty estimates in the cliff grid world, and confirms that higher aleatoric uncertainty is observed in states where stochasticity in the environment will have the most impact on the return distribution. The closer to the goal, the less chances the wind has to push the agent into the cliff, thus the less aleatoric uncertainty. This figure also supports the good behaviour of the epistemic uncertainty estimates since higher epistemic uncertainty is observed on the top-right states, which were visited less often by the agent during training due to falling off the cliff.

3.2. Intensive care based clinical recommender system

Next, we applied the uncertainty-aware agent to an MDP adapted from the original MIMIC-III critical care dataset and AI clinician work by (Komorowski, 2018). We are here interested in the challenge of learning optimal treatment strategies for septic patients from retrospective data, corresponding to the dosing of vasopressor drugs and IV fluids for successive 4-hour time windows. The aim is to render the estimates of aleatoric and epistemic uncertainty for the drug dosage as part of the treatment recommendations. After convergence, the agent provides estimates of aleatoric and epistemic uncertainty for each state action pair. The state-action space is sparse and vast (752 states × 25 actions). We observe variability in the two types of uncertainties across the state space that are distinct (Fig. 2.a). Consistent with intuition, plotting the epistemic uncertainty is clearly anticorrelated with state visitations in the retrospective data (Fig. 2.b). States visited the most often are mostly associated with low epistemic uncertainty and high epistemic uncertainty only appears in less visited states. These results are in line with the behaviours observed in the grid world examples, supporting our approaches use case further.

4. Discussion and Conclusion

The MDP for intensive care used in this work is a simplification of the real environment in which the state space is continuous and patient dynamics are more complex, so there still is a challenge in bringing the estimation of uncertainties forward into these complex settings. This is just the beginning of investigating the features of the data and the derived uncertainties in RL agents. The aim of this paper is to raise awareness around the benefits that disentangling uncertainties can have on RL-based decision support systems and show a proof of concept for such models.

This work presents an uncertainty and risk-aware approach in the deployment of RL for clinical applications. We think that exposing the sources of epistemic and aleatoric uncertainties when communicating recommendations to the end-users and stakeholders is crucial. High-quality explainability in reinforcement learning are hard to design. Previous approaches to RL explanations focused on rendering a causal explanations why a specific policy was learned (e.g. (Madumal et al., 2020)) or by breaking down an agent’s policy into human-understandable intermediate policies (Beyret et al., 2019). Here we focused on interpretability of a recommendation in terms of the uncertainties involved. We believe this information will be important for human users to interact with RL recommender systems’ outputs.
Acknowledgements

PF was supported by a PhD studentship of the UKRI Centre for Doctoral Training in AI for Healthcare (EP/S023283/1). AAF was supported by a UKRI Turing AI Fellowship (EP/V025449/1). This project is independent research funded by the National Institute for Health Research (Artificial Intelligence, ["Validation of a machine learning tool for optimal sepsis treatment.", AI_AWARD01869]). The views expressed in this publication are those of the author(s) and not necessarily those of the National Institute for Health Research or the Department of Health and Social Care.

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