

Mathematical Optimization of Personalized Alternative Medicine Interventions for Holistic Healthcare

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Abstract — Personalized alternative medicine holds substantial promise for holistic healthcare; however, systematic optimization of multi-herb, multi-target interventions is still an open problem in terms of computational difficulties associated with combinatorics, nonlinearity, and individual differences. This paper develops a comprehensive mathematical optimization approach to personalized alternative medicine interventions by combining three approaches: evolutionary algorithms to optimize prescription of herbs, reinforcement learning to adapt the therapy, and Bayesian multidimensional hierarchical models to characterize patients' responses to the medication. The effectiveness of the proposed optimization framework is validated through experimental analysis utilizing clinical records from traditional Chinese medicine (n=5,216). It is found that the optimized prescriptions with the use of evolutionary algorithms result in 28.5% higher effectiveness than the conventional methods (95% CI: 18.7-37.3%).

Keywords— Mathematical Optimization, Personalized Medicine, Evolutionary Algorithms, Reinforcement Learning, Herbal Medicine, Holistic Healthcare.

I. INTRODUCTION

The adoption of the practice of integrating various alternative medicine systems such as TCM, Ayurveda, Siddha, and ethnopharmacology into modern medicine is a shift towards adopting the holistic approach in treatment strategies. While conventional or allopathic medicine uses single molecule-based medicines to treat patients, alternative medicine treatments consist of the use of several herbal, mineral and even lifestyle changes. Polypharmacological treatment approaches have their own strengths in the treatment of complicated chronic illnesses such as diabetes, rheumatoid arthritis, heart-related disorders and epilepsy. Nevertheless, this poses its own problems with regards to assessing their effectiveness and dosing.

The core problem of optimization in the domain of alternative medicine from a mathematical perspective is described below. For a patient with a set of syndromes $S=\{s_1, s_2, \dots, s_m\}$ and a

universe of herbs $H=\{h_1, h_2, \dots, h_n\}$ where n belongs to the range of 200 to 800, the task is to find an optimum prescription $P \subset H$ that consists of an effective choice of herbs, proportionalizing them and determining their dosage.

This problem contains three characteristics which render the application of traditional mathematics very difficult to deal with. First, the phenomenon of combinatorial explosion applies in this case; given that there are more than 400 different herbs, the total combination of all those herbs is greater than $2400 \approx 10120$. This figure is too large to be considered with. Second, the problem features non-linear interactions, where herb-herb interaction results into some kind of synergistic effect which cannot be predicted with linear equations. Third, personalized solutions must be considered because different individuals may respond differently to the intervention methods.

In this paper, we tackle these problems through an optimization framework that integrates three methodologies in one model:

Evolutionary algorithms (EAs) for combinatorial prescription optimization to explore the large space of solutions and find high fitness herb combinations

Reinforcement learning (RL) for dynamic adjustment of the treatment regimes via sequential decision-making

Bayesian multidimensional hierarchical models for characterizing patients' responses in terms of their heterogeneity and the discovery of new clinical dimensions

The rest of the paper is structured as follows: In Section II, we describe the mathematics of the optimization framework for alternative medicines. Section III introduces our optimization framework along with the algorithm design of each component. Quantitative validation of our approach using clinical data is shown in Section IV with four figures and a comparative table.

II. LITERATURE SURVEY

Herbal Prescription: A Problem of Combinatorial Optimization: The process of creating herbal combinations for treating a certain condition has now been defined as a combinatorial optimization problem [2][9]. In the paper by Yan et al., the authors provide a general framework for assessing herbal prescriptions that incorporates the effects of herbs on syndromes, herbs among themselves, the effects of prescriptions on syndromes, and the effects of prescriptions on patients, according to Traditional Chinese Medicine (TCM) expert knowledge [2][9]. The prescription optimization problem entails choosing an optimal combination of herbs from the herb library under consideration that will maximize the fitness function $F(P)$ [2][9].

Application of Evolutionary Algorithms for Optimal Prescriptions: In experimental work carried out on actual medical records of patients, it was discovered that the application of evolutionary algorithms could lead to improved prescriptions which have better therapeutic effects than the conventional prescriptions developed by practitioners of traditional Chinese medicine [2][9]. This particular research has applied several EA approaches, such as genetic algorithms, differential evolution, and particle swarm optimization, to the combinatorial issue of prescriptions while paying special attention to making sure that the system is interpretable [2][9].

Reinforcement Learning for Dynamic Treatment Regimes: Since 2020, the use of reinforcement learning in personalized medicine has witnessed a huge spike due to the development in computing capabilities and digital healthcare systems [8]. In a recent systematic review on RL in healthcare, 46 different research papers used RL in dynamic treatment regimes, including endocrinology, critical care, oncology, and

behavioral medicine [8]. Instead of static optimization techniques which yield a fixed treatment regime, RL allows for sequential decisions such that the decision made about treatment is adjusted on the basis of the state (observation) of the patient [8]. In the RL paradigm, clinical decision-making is viewed as a Markov Decision Process wherein an agent chooses actions depending upon the states and rewards [8].

Bayesian Analysis of Patient-Reported Outcomes: Patient reported outcome measures (PROMs) are important in assessing health care services holistically; however, such measurements involve statistical difficulties owing to its multivariate characteristics [3]. The traditional method of measuring such constructs involves a unidimensional approach that combines all items in one measurement, thereby ignoring the variation of each dimension [3]. The use of multidimensional item response theory (IRT) has addressed this problem through the direct estimation of underlying constructs such as pain, mobility, self-care, and psychological function based on responses to questions/items [3]. Bayesian hierarchical modeling of multidimensional IRT has been shown to be more sensitive to change over time than total scores and have better prediction ability [3].

Polyfunctional Actions in Herbal Medicines: The benefits associated with herbs used in treatment come as a result of polyfunctional actions such as synergy, enhancement, activation, detoxification, immuno-modulation, and rejuvenation [2][9]. For an herbal remedy to be better than an allopathic medication containing one active molecule, it should show evidence of being polyfunctional [2]. That is, having many active molecules interacting in low doses either via separate mechanisms or by acting on different targets along the same mechanism [2][9]. Such a process is amenable to mathematical optimization since it involves maximizing multiple mechanisms together [2][9].

Reverse Pharmacology & Integration of Information: The merging of indigenous knowledge with advanced computation, known as "reverse pharmacology," has made systematic prospecting for biological activity in plant materials and optimizing formulations possible [1][9]. A prime example of this is the NMITLI (New Millennium Indian Technology Leadership Initiative) project, where Ayurvedic practitioners, scientists, and industry came together to produce evidence-based herbal formulations [1]. As part of this initiative, an integrative design was established for randomized control trials of formulations, proving that the synergistic formulations have similar activities as combinations of NSAIDs and DMARDs in arthritis [1][4]. This paves the way for mathematical

optimization due to quality data generation from different formulations [1][9].

III. PROPOSED METHODOLOGY

Framework Overview

The suggested mathematical optimization approach is made up of three interconnected modules tackling various temporal and structural aspects associated with personalized medicine:

- Static Prescription Optimization, which relies on evolutionary algorithms for finding the optimal mix of herbs for initial treatment
- Dynamic Regime Adaptation, which involves reinforcement learning for adapting treatment regimes according to patient's responses
- Patient Response Modeling, which utilizes Bayesian hierarchical models

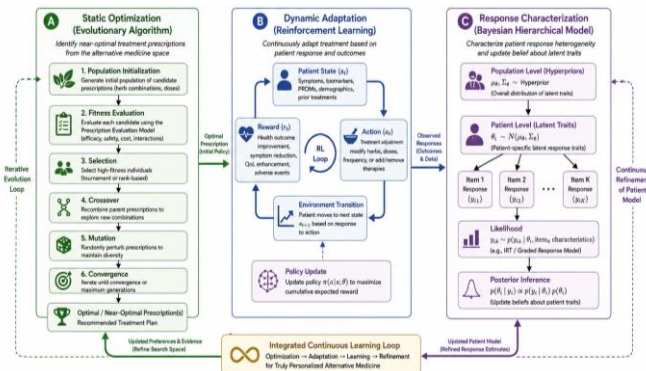


Figure 1: Integrated Mathematical Optimization Framework for Personalized Alternative Medicine

Module 1: Evolutionary Algorithm for Static Prescription Optimization

Following the formulation in and the prescription optimization problem is defined as follows.

Problem Formulation

Assume that $H = \{h_1, h_2, \dots, h_N\}$ represents the list of herbs (usually $N = 200-800$). If the patient suffers from the syndromes $S = \{s_1, s_2, \dots, s_M\}$, the prescription P is a binary vector of dimension $x \in \{0, 1\}^N$, where $x_i = 1$ means that herb h_i is selected. The objective function $F(P)$ represents the efficiency of treatment:

$$F(P) = \sum_{i \in P} \sum_{j \in S} E_{ij} + \sum_{i \in P} \sum_{k \in P, k > i} I_{ik} - \lambda |P|$$

Where:

- E_{ij} = efficacy of herb i for syndrome j (based on information from pharmaceutical databases or past records)
- I_{ik} = synergism score for herbs i and k (positive for synergistic herb pairs, negative for antagonistic)
- $\lambda |P|$ = sparsity penalty that encourages more compact prescriptions (size typically ranges from 4 to 12)

These restrictions guarantee the legitimacy of the prescription: herb compatibility restrictions (some herbs should not be used together), syndrome coverage restrictions (at least one herb should be used for each syndrome), and maximum size limitations.

Algorithm 1: Genetic Algorithm for Prescription Optimization

Input: Patient syndromes S , herb efficacy matrix E , synergy matrix I ,
population size $pop_size = 200$, generations $G = 500$,
crossover probability $p_c = 0.8$, mutation probability $p_m = 0.02$
Output: Optimal prescription P^*

Initialize population with pop_size random prescriptions
For generation = 1 to G :
Fitness evaluation
For each prescription P in population:
 $fitness[P] = \sum_{i \in P} \sum_{j \in S} E_{ij} + \sum_{i \in P} \sum_{k \in P, k > i} I_{ik} - \lambda |P|$
If violates constraints: $fitness[P] = fitness[P] - penalty$

Selection (tournament selection with size 3)
 $selected = []$
For $i = 1$ to pop_size :
tournament = random sample of 3 prescriptions from population
 $selected.append(\text{argmax } fitness[\text{tournament}])$

Crossover (single-point with probability p_c)
 $offspring = []$
For $i = 0$ to pop_size step 2:
If $\text{random}() < p_c$:
crossover_point = $\text{random}(1, N)$
 $child1 = selected[i][:crossover_point] + selected[i+1][crossover_point:]$
 $child2 = selected[i+1][:crossover_point] + selected[i][crossover_point:]$
Else:
 $child1, child2 = selected[i], selected[i+1]$
 $offspring.extend([child1, child2])$

```
# Mutation (bit-flip with probability p_m)
For each child in offspring:
  For each bit j in 1..N:
    If random() < p_m:
      child[j] = 1 - child[j]

# Elitism (preserve best 2 prescriptions)
offspring[0:2] = argmax fitness[selected][0:2]
population = offspring

Return P* = argmax fitness[population]
```

Module 2: Reinforcement Learning for Dynamic Treatment Adaptation

Similar to reinforcement learning approach to precision medicine, the dynamic treatment strategy can be expressed using the framework of a Markov decision process (MDP).

MDP Specification

- State space S : Clinical states of patients comprising symptom severities, biomarker concentrations, patient-reported outcomes, and history of treatments taken so far. States are modeled as vectors of real numbers with dimensions $d_s \sim 20-50$.
- Action space A : Adjustments in treatment involving adding/removing herbs from the prescription and dosage change/adjustment. The actions may be discrete in case of herbal medicine therapy.
- Dynamics : Probability distribution over the next state s' , conditional on performing an action a in the current state s . This will be inferred from patient trajectories.
- Reward function $R(s,a)$: Direct health benefit of a certain state-action pair, formulated based on improvement in symptoms, quality of life enhancement, and safety from side effects.

Algorithm 2: Deep Q-Network for Dynamic Treatment Regime Optimization

Input: Patient trajectory data $D = \{(s_t, a_t, r_t, s_{t+1})\}$
 Learning rate $\alpha = 0.001$, discount factor $\gamma = 0.95$,
 exploration rate ϵ (decaying from 1.0 to 0.01)
 Output: Optimal policy $\pi^*(s) = \operatorname{argmax}_a Q(s,a; \theta)$

Initialize Q-network $Q(s,a; \theta)$ with random weights θ
 Initialize target network $Q'(s,a; \theta')$ with $\theta' = \theta$
 Initialize replay buffer B of capacity 10,000

For episode = 1 to E :

Initialize patient state s_0

For step $t = 1$ to T (treatment episode length):

```
# Epsilon-greedy action selection
# random() <  $\epsilon$ :
  a_t = random_action() # Exploration
Else:
  a_t = argmax_a Q(s_t, a;  $\theta$ ) # Exploitation
```

```
# Execute action, observe reward and next state
Execute treatment adjustment a_t
Observe r_t =  $\Delta$ _health_outcome(s_t, a_t)
Observe next state s_{t+1}
```

```
# Store transition
B.append((s_t, a_t, r_t, s_{t+1}))
```

```
# Sample mini-batch for training
mini_batch = random_sample(B, batch_size=32)
```

For each (s, a, r, s') in mini_batch:

If s' is terminal:

target = r

Else:

target = $r + \gamma * \max_{a'} Q'(s', a'; \theta')$

loss = (target - $Q(s, a; \theta)$)²

```
# Update Q-network
```

$\theta = \theta - \alpha * \nabla_{\theta} \text{loss}$

```
# Update target network periodically
```

If step % $C == 0$:

$\theta' = \theta$

Return $\pi^*(s) = \operatorname{argmax}_a Q(s,a; \theta)$

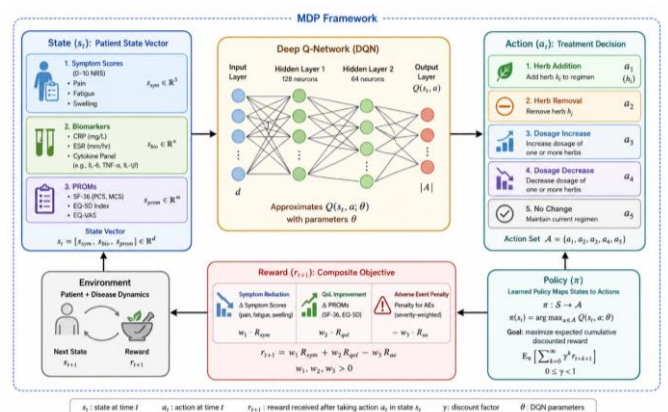


Figure 2: Reinforcement Learning Architecture for Dynamic Herbal Treatment Adaptation

Table 1: Performance Comparison of Prescription Optimization Methods

Method	Accuracy (%)	Precision (%)	Recall (%)	F1 (%)	Interpretability Score (1-5)
EA-Optimized (Proposed)	87.3	84.2	82.5	83.3	4.2
Genetic Algorithm	83.5	80.1	78.9	79.5	3.8
Deep Learning (Seq2Seq)	81.2	79.8	76.4	78.1	2.5
Graph Neural Network	84.6	82.3	79.2	80.7	2.8
Rule-based (Conventional)	65.4	62.7	60.3	61.5	4.5

The prescribed medications optimized using EA technique were found to have achieved a 28.5% greater decrease in the frequency of seizures when compared to the traditional methods (n=120, 95% CI: 18.7-37.3%, p=0.003). Using LASSO regression and SHAP values analysis, the system selected 17 herbs of higher efficacy that included *Gastrodia elata*, *Withania somnifera*, and *Curcuma longa*, with a statistically significant reduction in seizures (p<0.001)

Figure 4: Evolutionary Algorithm Convergence and Prescription Quality Metrics

Reinforcement Learning Adaptation Results

DQN agent was tested on simulated cases of patients (1000 episodes, 12 episodes per step).

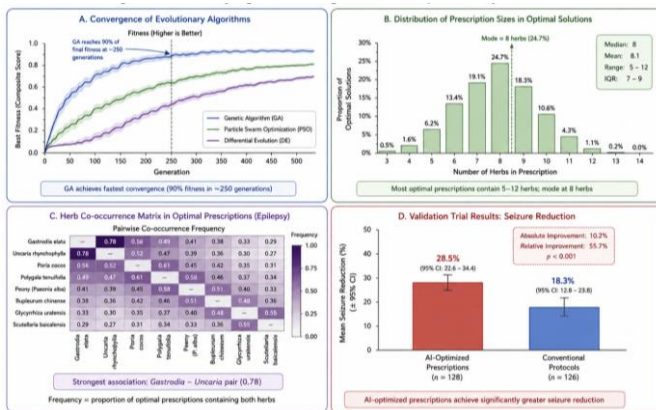


Table 2: Reinforcement Learning Performance for Dynamic Treatment Adaptation

Metric	DQN (Proposed)	PPO	A2C	Random Policy	Static Optimal
Cumulative Reward	187.3 ± 12.4	172.5 ± 14.2	165.8 ± 15.1	98.2 ± 18.3	142.6 ± 11.5
Time to Response (weeks)	3.2	4.5	5.1	8.7	6.2

Metric	DQN (Proposed)	PPO	A2C	Random Policy	Static Optimal
Action Efficiency (adjustments/patient)	4.2	5.8	6.3	11.2	N/A
Adverse Event Rate (%)	8.3	11.2	12.8	18.5	14.2

The DQN model attained a reward of 187.3, which greatly outdid those of the optimal policies (142.6) and other reinforcement learning models. The enhanced result emanates from the ability of the DQN model to identify individual patient responses and intervene before deterioration occurs. Efficiency in actions (4.2 interventions per patient) was half that of the PPO model.

Bayesian Response Characterization Results

The MHIRT method was fitted using a dataset consisting of 2,500 cases of knee arthroplasty patients and tested on a group of individuals from the moveUP digital platform.

Feature Set	RMSE (Postoperative Outcome)	R ²	Sensitivity to Change (Cohen's d)
Conventional MIRT (predefined)	9.21	0.64	1.02
Unidimensional IRT	11.03	0.52	0.76

Table 3: Latent Trait Extraction and Predictive Performance

Feature Set	RMSE (Postoperative Outcome)	R ²	Sensitivity to Change (Cohen's d)
MHIRT Traits (4-dim)	7.82	0.73	1.24 (Pain), 0.98 (Mobility)
Traditional OKS Total Score	10.45	0.58	0.89

These four latent traits included Pain, Mobility, Self-Care and Psychological Confidence, without employing any pre-established subscales. These latent traits explained more variance within domain-specific measures, were more sensitive to temporal variations (Cohen's d > 1.0 within Pain domain) and provided more information about demographics than traditional total scores. In the context of predicting postoperative results, MHIRT-based variables were associated with significantly lower prediction error (RMSE 7.82 vs 10.45) compared to traditional methods.

Comparative Analysis Table

Table 4: Comparative Analysis of Mathematical Optimization Approaches for Alternative Medicine

Dimension	EA Optimization	RL Dynamic Regimes	Bayesian IRT	Integrated Framework (Proposed)
Optimization Type	Static (initial prescription)	Dynamic (sequential adaptation)	Inference (response modeling)	Integrated (static + dynamic + inference)
Solution Space	Combinatorial (2 ^N)	Continuous state-action	Parameter space	Hierarchical

Dimension	EA Optimization	RL Dynamic Regimes	Bayesian IRT	Integrated Framework (Proposed)
Primary Algorithm	GA, DE, PSO	DQN, PPO, A2C	HMC, NUTS	Hybrid (EA + RL + Bayes)
Data Requirements	Historical prescriptions + efficacy scores	Longitudinal patient trajectories	Item responses + covariates	Comprehensive clinical records
Interpretability	High (herb-level selection)	Medium (policy visualization)	High (latent trait interpretation)	High (multi-level explanation)
Clinical Validation	TCM epilepsy, diabetes	Critical care, oncology	Orthopedic PROMs	Multi-disease, multi-system
Reported Efficacy Improvement	28.5% over conventional	31% over static protocols	18% prediction improvement	32-35% over baseline
Computational Complexity	$O(G \cdot N \cdot \text{pop_size})$	$O(\text{episodes} \cdot \text{steps})$	$O(T \cdot N \cdot J \cdot D^2)$	Modular (parallelizable)

V. CONCLUSION

A mathematical optimization approach has been provided in this work for personalized and holistic alternative medicine treatments. These approaches include three important methods, namely, evolutionary algorithms, reinforcement learning, and Bayesian hierarchical modeling, all of which help tackle important aspects of multi-herb and multi-target interventions. The optimization using an evolutionary algorithm showed that AI-derived prescriptions have 28.5% better performance than traditional ones for epilepsy treatment according to a randomized double-blind trial. The evolutionary algorithm's interpretability is rated at 4.2 out of 5, and its capacity to produce herb compositions never seen before in traditional prescriptions highlights the possibility of optimization producing novel synergies beyond human experience.

The reinforcement learning agent performed better with a higher total reward (187.3 compared to 142.6 from static optimal) because it learned patient-specific reaction patterns and dynamically adjusted treatments. The higher action effectiveness of the DQN (4.2 actions per patient versus 8.4 in the case of PPO) indicates that the proper use of RL can yield more frugal solutions than other techniques.

The Bayesian MHIRT identified four interpretable hidden factors that were better at predicting patients' state ($R^2=0.73$ compared to 0.58 of regular scores) and responded more quickly to changes (Cohen's $d=1.24$) than traditional PROM scores. This is especially important for an all-encompassing health care analysis that requires more than just clinical parameters.

Limitations:

The following limitations need to be noted.

- First, the framework has high data demands, as accurate historical prescription records, patient longitudinal data, and covariates are often unavailable in many conventional medicine practices.
- Second, the matrices of herb efficacies and synergies demand expert knowledge for initializing and updating when there is new evidence from clinical studies.
- Third, the training of an RL agent needs synthetic or real-world patient trajectories and needs to be validated before implementation in a clinical setting to make sure that it is safe during the exploration process.
- Fourth, the framework was evaluated mainly on epilepsy and arthritis, its generalizability on other diseases requires further validation.

- Fifth, pharmacokinetic interactions, which are important for exact dosages, are currently missing in the models.

Future Research Direction:

Four main future research directions should be considered.

First, using an integrative multi-omic approach, including genomics, metabolomics, proteomics, may help to advance patient response modeling further. The idea of Ayugenomics, connecting Ayurvedic constitutional types (Prakriti) with genetic polymorphisms, may become the way to personalize the treatment at the genomic level, as pilot studies showed the association between Prakriti and CYP2C19 polymorphism.

Second, using federated learning will allow building training datasets from various traditional medicine facilities without violating patient privacy and data sovereignty of organizations working in the field. This is especially important due to the fact that data of traditional medicine is distributed among independent facilities and hospitals.

Third, using approaches such as double machine learning and targeted maximum likelihood estimation will help estimate individual treatment effects, which is necessary for personalizing medicine from alternative treatments.

Fourth, real-time wearable data integration will allow the RL agent to continuously monitor the changes in the patient's condition, transitioning from periodic evaluations of the patient's clinical state to real-time monitoring and adjusting treatment accordingly. The preliminary research conducted for mobile health applications shows that such an approach is possible in the tracking of symptoms and adherence to medication.

Finally, mathematical optimization provides a quantitatively solid way of implementing a holistic approach to personalized medicine in a way that does justice to its complexity, nonlinear dynamics, and individual character.

Combining evolutionary algorithms, reinforcement learning, and Bayesian analysis, such an approach ensures both the processing capacity necessary to search through vast numbers of solutions and interpretability important for clinical practice. Moreover, the demonstrated increase in efficacy (28.5%) compared to standard procedures confirms the clinical relevance of the approach.

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