Automating Treatment Planning in Radiation Therapy

Olalekan Ogunmolu

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Background – LINACs RT
MRI-LINACs
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Automating Treatment Planning in Radiation Therapy

Olalekan Ogunmolu

Perelman School of Medicine
University of Pennsylvania, Philadelphia, PA

Presented by **Lekan Molu** (`Lay-con Moh-lu`)

March 10, 2021

Funding Sources

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NIH NATIONAL CANCER INSTITUTE

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Talk Outline

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- Beam Orientation Optimization (BOO)
  - Monte Carlo Tree Search and Neuro-Dynamic Programming for BOO
  - Column Generation as Pretraining for MCTS for BOO
- Patient Head Motion Correction in External Beam Radiation Therapy (RT)
  - Intensity-Modulated RT (IMRT): Earlier PhD Work
  - Magnetic Resonance Imaging and Linear Accelerator Systems (MRI-LINACs)
- Robustness Margins and Robust Deep Policies for Nonlinear Control

Research Significance

2021 → 1,898,160 U.S. cancer cases[1] → 608,570 deaths → $246 billion in costs by 2030[1]

Cancer Treatment
- Chemotherapy/Radiosurgery.
- Radiation Therapy (RT).

RT Signif.
- Approx. 40% of all curative cancer treatment modality are performed with RT[1].
- Cost-effective -- accounting for only 5% of the total cost of cancer care[3].

Imaging
- CT images in RT = Low soft tissues contrast ⇒ OARs toxicity during treatment planning.
- MRI of brain, and head and neck (H&N) cancers provides exceptional soft tissues contrast and allows greater delineation of cancerous from non-cancerous tissues.

IMRT Treatment Planning (Beam Delivery)

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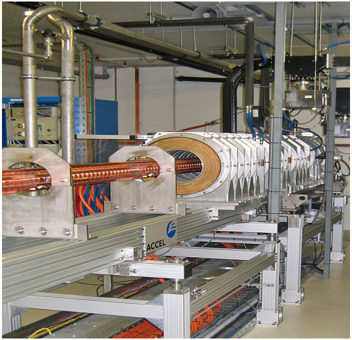
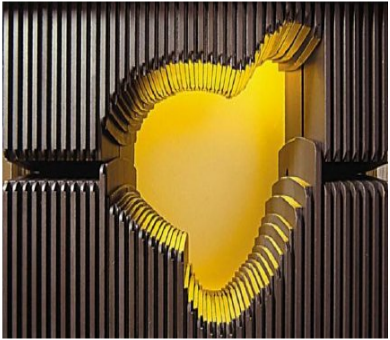


The Australian Synchrotron.


A Multi-leaf collimator, ©Varian.

Radiation Delivery Couch and Gantry

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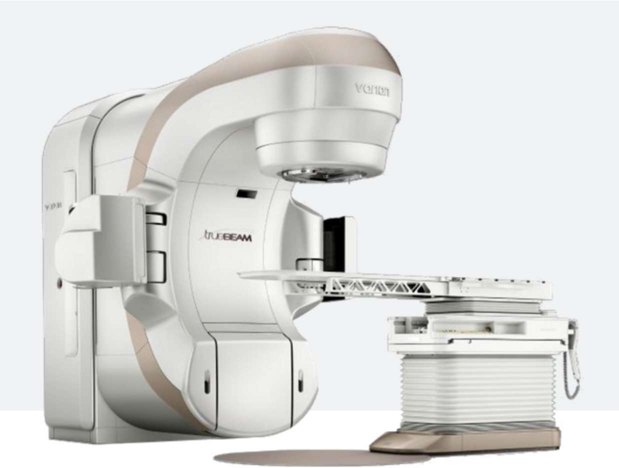

Varian's TrueBeam Radiotherapy System.

Part I.A: Beam Orientation Optimization (BOO)

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  - Monte Carlo Tree Search and Neuro-Dynamic Programming

Contributions

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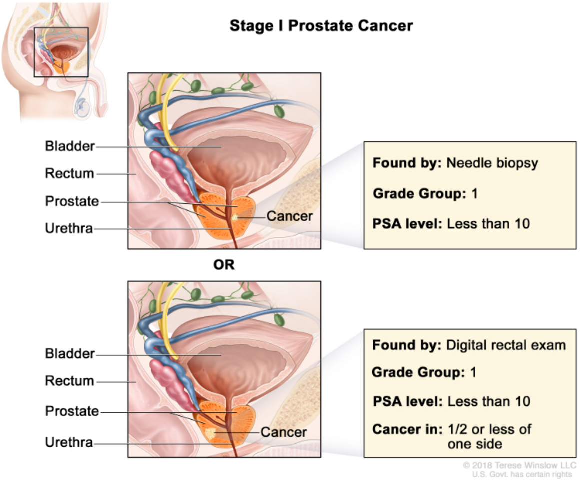
Relevant Publications

Ogunmolu, Olalekan, Michael Folkerts, Dan Nguyen, Nicholas Gans, and Steve Jiang. "Deep BOO! Automating Beam Orientation Optimization in Radiation Therapy." In *Algorithm Foundations of Robotics XIII*, Merida, Mexico. Published in *Springer's Proceedings in Advanced Robotics (SPAR) Book*, 2020.

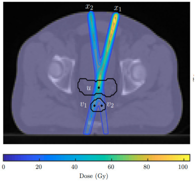
- A sparse tree lookout strategy for games with large state spaces guides transition between beam angle sets
- Tree lookout strategy guided by a deep neural network policy

Protate Cancer Example

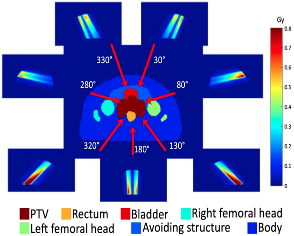


BOO Process: Fluence Map Optimization

Prostate CT slice



Prostate before BOO



Fluence Map

BOO Workflow

Manually Selection/Protocols Adoption

Laborious process; could take up to 5 days for head and neck cancer treatment.

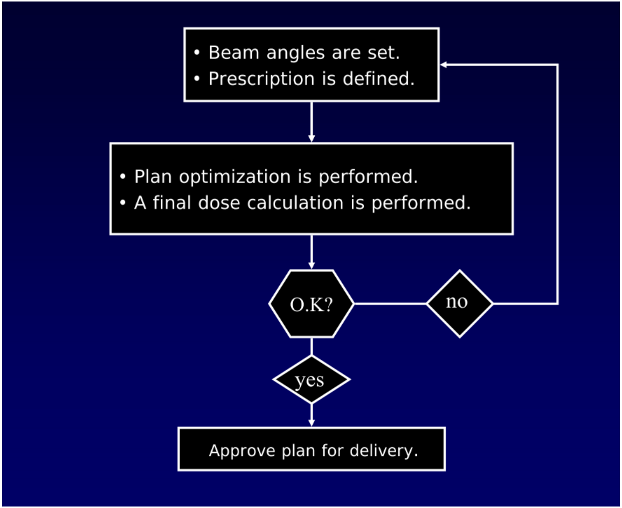
Pre-solve Large Sparse Dose Influence Matrix

Takes hours to solve for a single patient. Days/months for multiple patients.

Solve Fluence Map Optimization

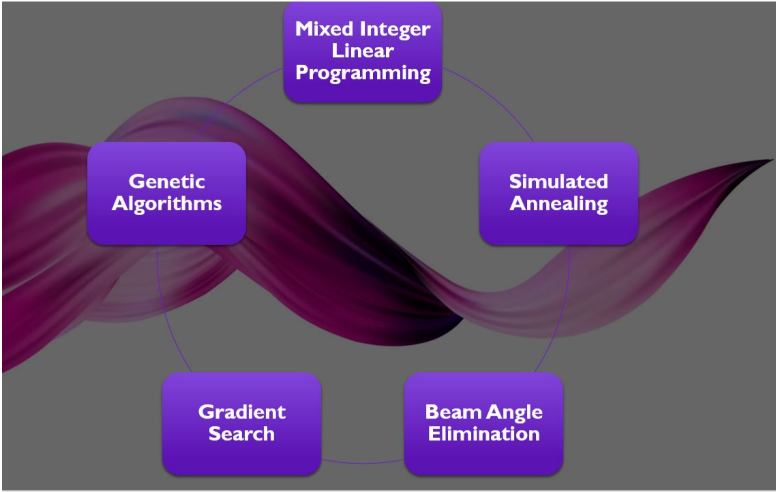
Time-consuming: Often takes minutes.

Treatment Plan Flowchart



Reprinted from "IMRT Optimization Algorithms. David Shepard. Swedish Cancer Institute. AAPM 2007."

Current Approaches and Limitations



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- A Tower Neural Network generates a policy that guides MCTS simulations for two players in a zero-sum Markov game
  - Produces a *utility (value) function* & a subjective *probability distribution*
- Each player in a two-player Markov game finds an alternating best response to the current player's average strategy
  - driving the neural network policy's weights toward an approximate **saddle equilibrium** [Heinrich et al. (2015)].
  - aids network in finding an *approximately optimal* beam angle candidate set that meets a dosimetric requirements.

State Encoding: Prostate Organ Masks

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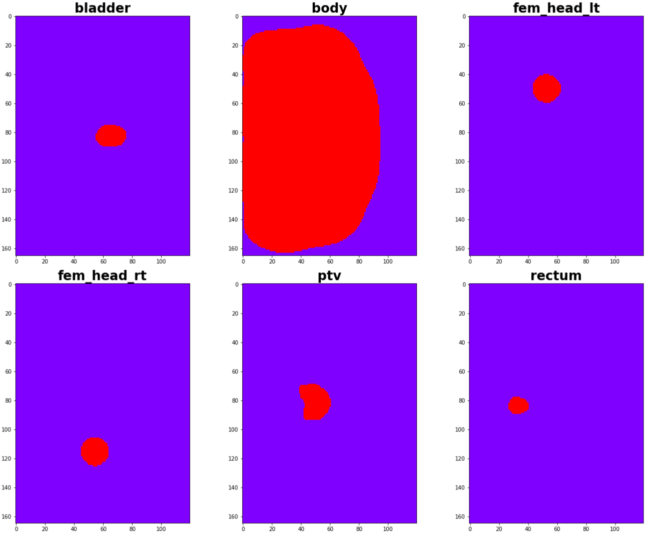
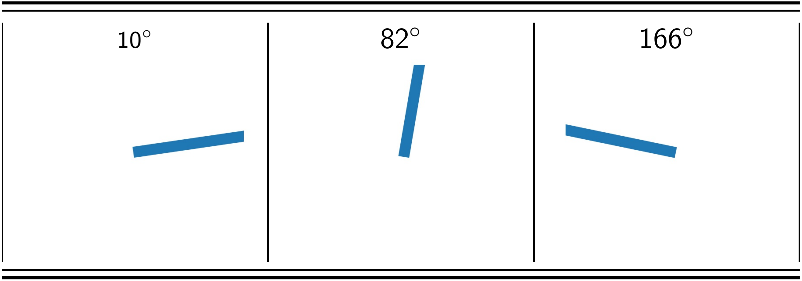
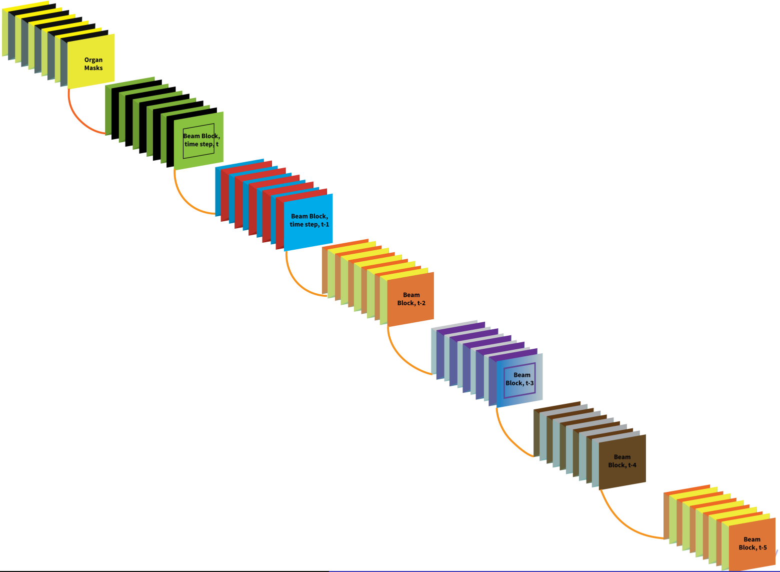


State Representation: Beam Angles



State Representation



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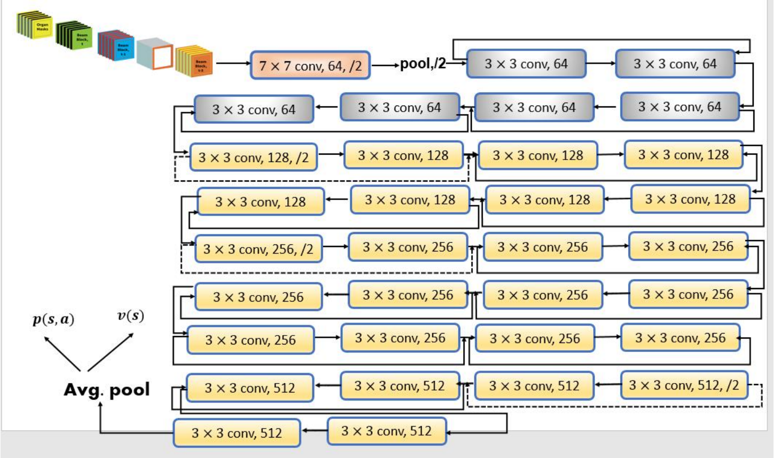
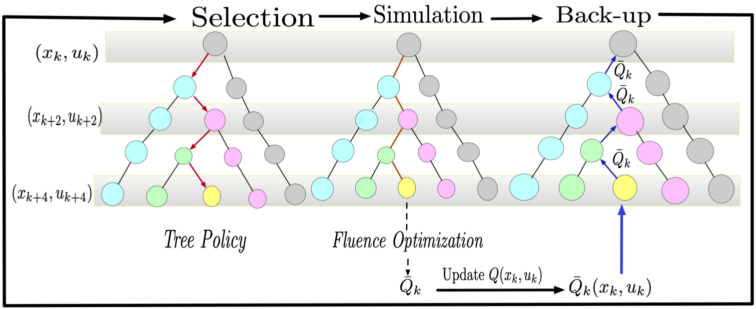
Two-player Fictitious network play with ResNet



Tree Representation and Game Simulation



Tree Composition

Every **node** of the tree, $\boldsymbol{x}$, has the following fields:

- a pointer to the parent that led to it, $\boldsymbol{x}.p$;
- the beamlets, $\boldsymbol{x}_b$, stored at that node; $b = \{1, \ldots, m\}$;
- a set of move probabilities prior, $p(s, a)$;
- a pointer $\boldsymbol{x}.\boldsymbol{r}$, to the reward r_t, for the state $\boldsymbol{x}_t$;
- a pointer to the state-action value $Q(s, a)$ and its upper confidence bound $U(s, a)$;
- a visit count $N(s, a)$, that indicates the number of times that node was visited; and
- a pointer $\boldsymbol{x}.child_i$ to each of its children nodes.

Saddle Point Strategy Formulation

- **Saddle point strategies** for optimal control sequence pair $\{a_t^{p_1^*}, a_t^{p_2^*}\}$ recursively obtained by optimizing, $V_t(s, a)$

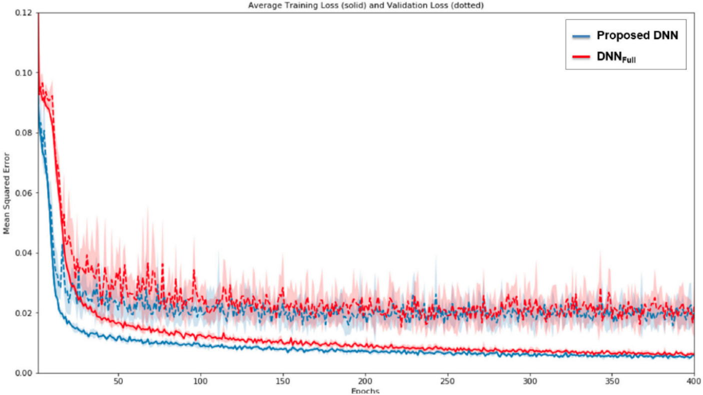
$$V_t^*(s) = Q_t^*(s_t, \pi_t^{p_1}, \pi_t^{p_2}) = \min_{\pi^{p_1} \in \Pi^{p_1}} \max_{\pi^{p_2} \in \Pi^{p_2}} Q_t^\star(s_t, \pi^{p_1}, \pi^{p_2})$$
$$\forall s_t \in \mathcal{S}, \pi^{p_1} \in \Pi^{p_1}, \pi^{p_2} \in \Pi^{p_2}.$$

such that

$$v_{p_1}^\star \leq v^\star \leq v_{p_2}^\star \quad \forall \{\pi_t^{p_1}, \pi_t^{p_2}\}_{0 \leq t \leq T}.$$

- p_1, p_2 respectively generating a **mixed strategy** via **averaging the outcome** of individual plays.

Training and Validation Loss



Average training (solid) and validation (dotted) loss function (MSE) values across six cross-validation folds for the network (blue) and full network.

BOO Results: Testing of self-play network

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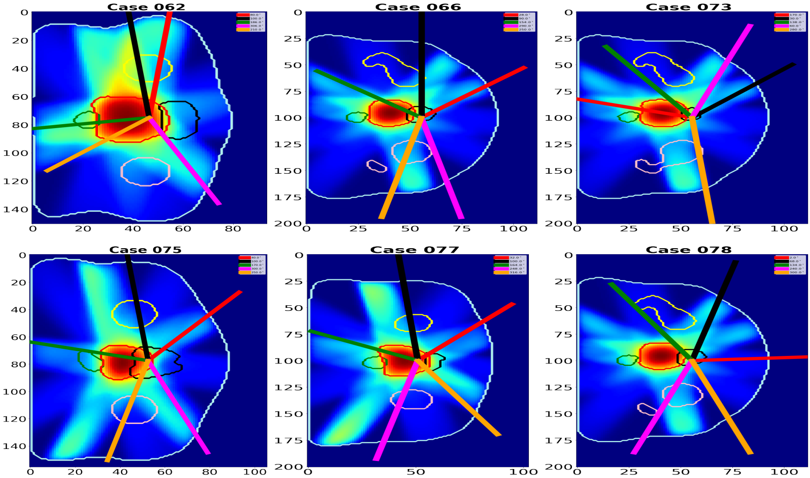
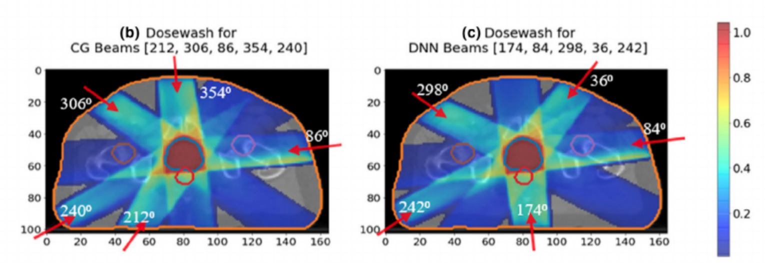


Column Generation vs Neural Network



Dose-Volume Histogram of CG vs DNN architectures [Sadeghnejad Barkousaraie, Azar and Ogunmolu, Olalekan and Jiang, Steve and Nguyen, Dan (2019)].

Conclusions

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- Deep Neural Network optimizes network weights in a separate multiprocessing thread; Network outputs probabilities used to guide search;
- Sparse lookahead search builds tree with nodes labeled by state-action pairs in an alternating manner; sample rewards stored on edges connecting state-action with state nodes;
- Beam angles prediction takes between 2-3 minutes with MCTS vs. $\sim$ 60 seconds with Column Generation Pre-training.

Head Stabilization in Radiation Therapy (RT)

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- Head Stabilization in Cancer Radiation Therapy
  - Intensity-Modulated RT (IMRT)

Robotic Radiosurgery

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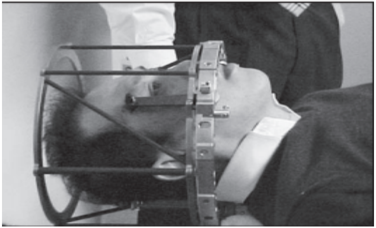
A Patient Head Motion-Correction Mechanism for MRI-LINAC RT

OLALEKAN OGUNMOLU

DEPARTMENT OF RADIATION ONCOLOGY, PENN SCHOOL OF MEDICINE

- Current Collaborators: Rodney Wiersma & Xinmin Liu (UChicago → UPenn)
- Past Collaborators: Steve Jiang, Xuejun Gu, (UT Southwestern); Nick Gans (UT Dallas, UT Arlington)

Correcting Head Motion: RT and MRI-LINACs

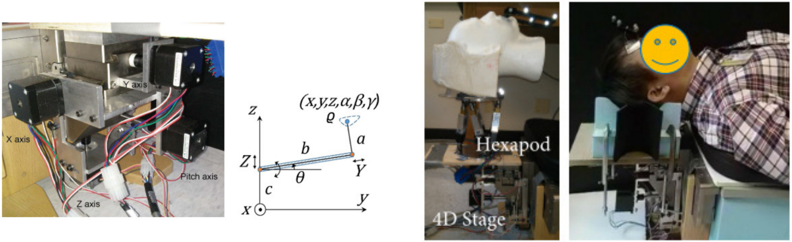


(a) The BRW SRS Frame [Chelvarajah et al. (2004)]

(b) Thermoplastic masks

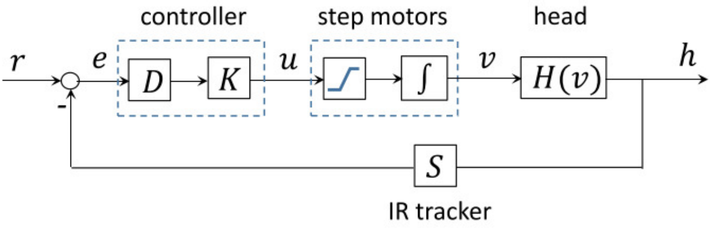
(c) Frame With MRI Coils (PSOM)

4-D Motion Correction Stage



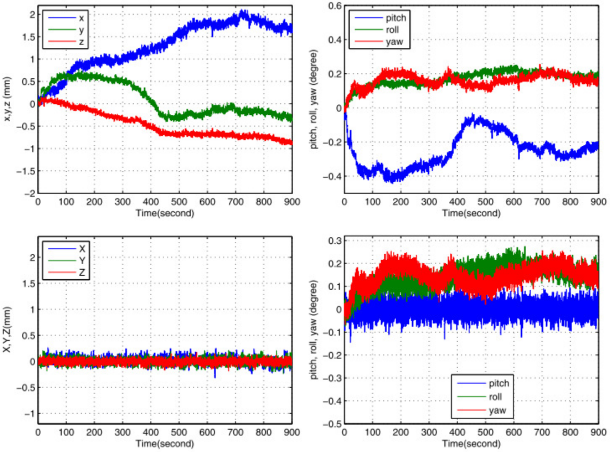
Liu et al. (2015)

4-DOF Motion Controller Block Diagram



Liu et al. (2015)

Phantom Feedback Motion Correction Results



Time response of feedback control without (left) and with (right) decoupling control [Liu et al. (2015)].

Human Volunteer Feedback Motion Correction Results

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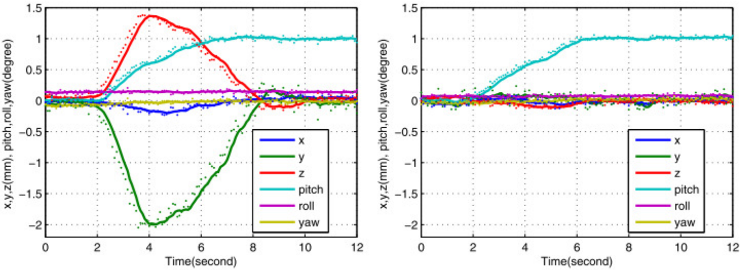
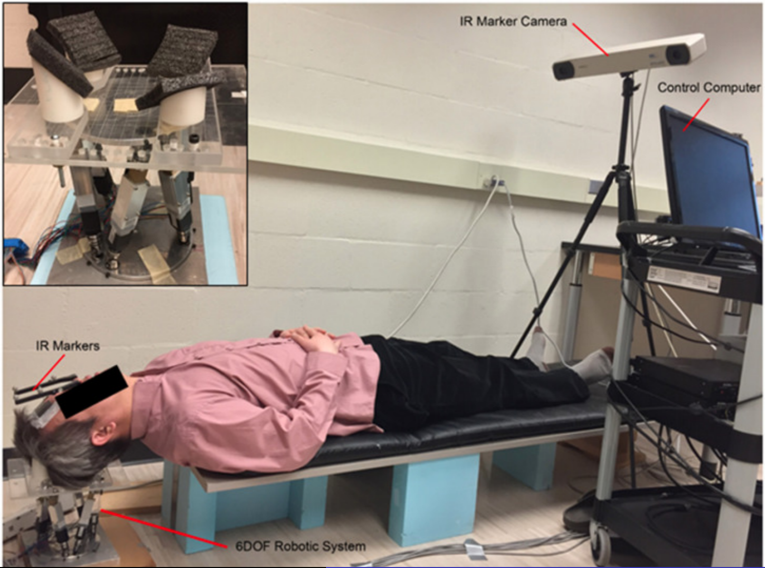
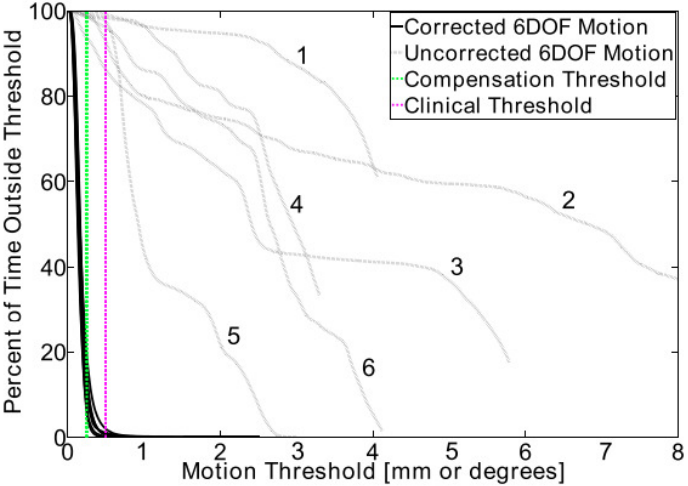


Head Motion Without and With Motion Correction. Left: Coupled Axes; Right: Decoupled Axes.

SRS: Wiersma Stewart-Gough Platform



6-DOF Motion Correction Results



Drawbacks of current solutions

- Rigid patient's body assumption
- Non-compliant immobilization devices
- Invasiveness during radiosurgery/RT
- Attenuation of photon beams

Radiation Delivery Couch and Gantry

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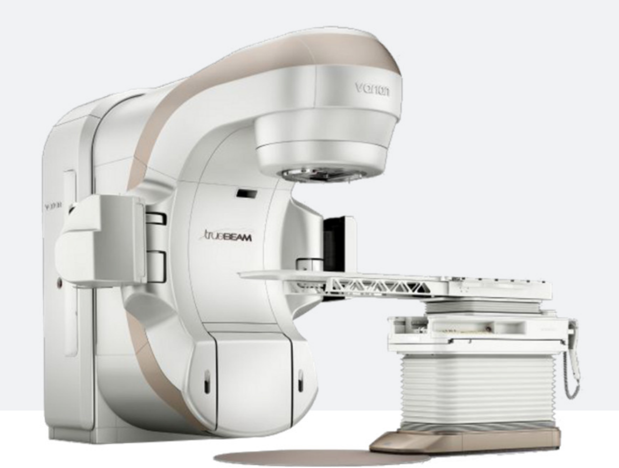

Varian's TrueBeam Radiotherapy System.

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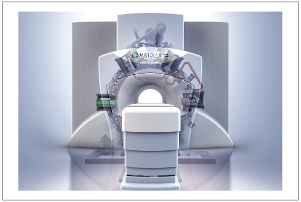
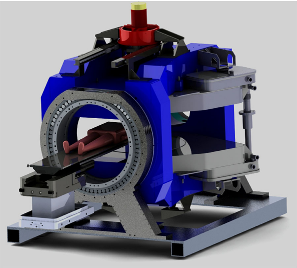
Next-Gen RT Treatment with MRI-LINACs

Elekta AB's (Sweden)

ViewRay's MRIdian



MagnetΓx (Canada) Aurora RT



Elekta AB's (Sweden)

Soft Robots for Head Motion Compensation

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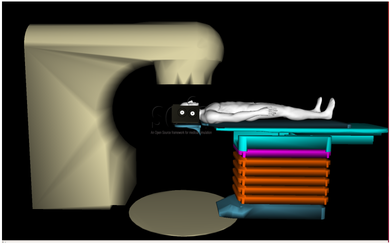
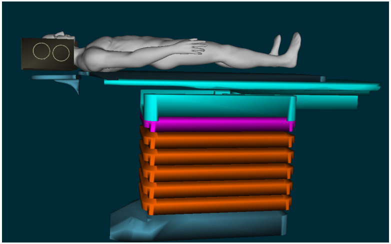
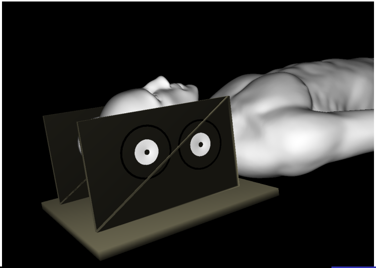
IMRT Setup



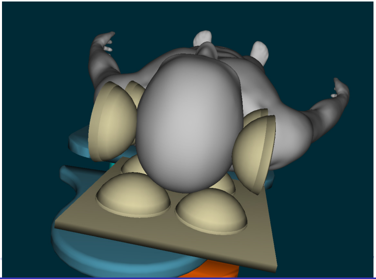
IMRT/MRI



Head and Robot Panel



Head-Robot Closeup



Morphing in Cephalopods

Morph Stage 1

Morph Stage 2

Morph Stage 3

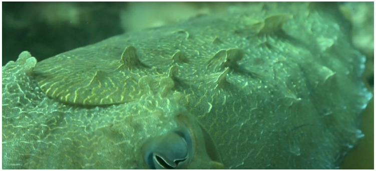
Morph Stage 4

Morph Stage 5

Morph Reversal

Cephalopods Neural-Controlled Physical Texture

Raises Periscope



Papillae

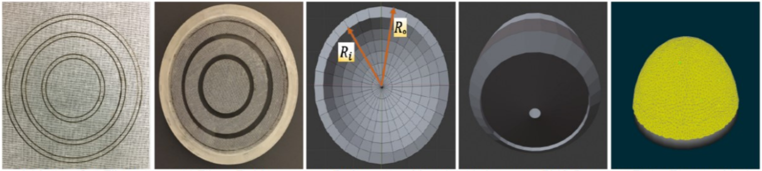
Papillae Up

Papillae × Papillae

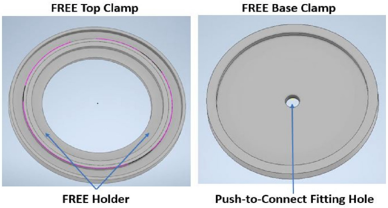
Cuttlefish' Morphin ©Roger Hanlon, YouTube.

Cephalopods-inspired Actuator Design

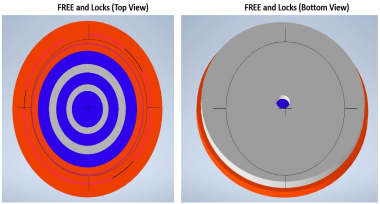
Circumferentially Constrained And Radially Symmetric Elastomers (CCOARSE).



(a) Laser-Cut Fiber (b) Fiber+Rubber (c) Deformation Model (d) Actuator+PVC Base (e) Finite Element Model



(f,g)



(h)

[Pikul et al. (2019)]

Nonlinear Elastic Deformation Analysis

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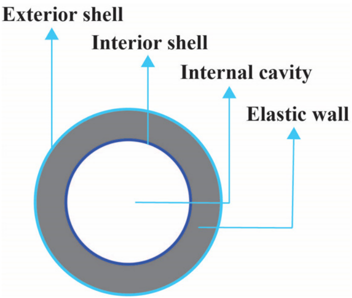
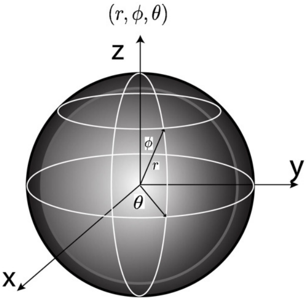
IAB SHELLS AND AIR CAVITY/DEFORMATION ANALYSIS





$r_i \leq r \leq r_o, \qquad 0 \leq \theta \leq 2\pi, \qquad 0 \leq \phi \leq \pi$

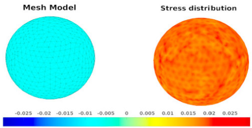
Soft IK via Boundary Value Problem

- With Cauchy's laws of motion, solve boundary volume problem of traction, and find that

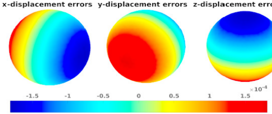
$$P(r) = \int_{r_i}^{r_0} \left[2C_1 \left(\frac{r}{R^2} - \frac{R^4}{r^5} \right) + 2C_2 \left(\frac{r^3}{R^4} - \frac{R^2}{r^3} \right) \right] dr \tag{1}$$

- *i.e.* Given a prescribed radius, find pressure to deform actuator between configurations

Volumetric Deformation Results (Simulation)



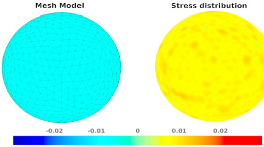
(a) **Left**: Mesh model. **Right**: Stress distribution on outer skin.



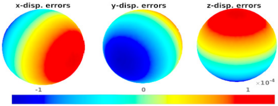
(b) Displacement errors along x, y, z coordinates.

Inputs					Outputs		
C_1	C_2	R_i	r_i	R_o	r_o	P	ΔV
$1.1e4$	$2.2e4$	.027	.03	.03	.033	.76	≈ 0

Fig. 6: Volumetric Deformation (Expansion).



(a) **Left**: Mesh model. **Right**: Stress distribution on outer skin.

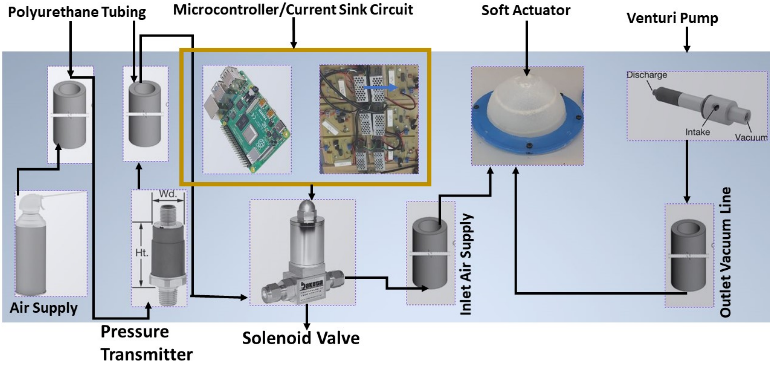


(b) Displacement errors along x, y, z coordinates.

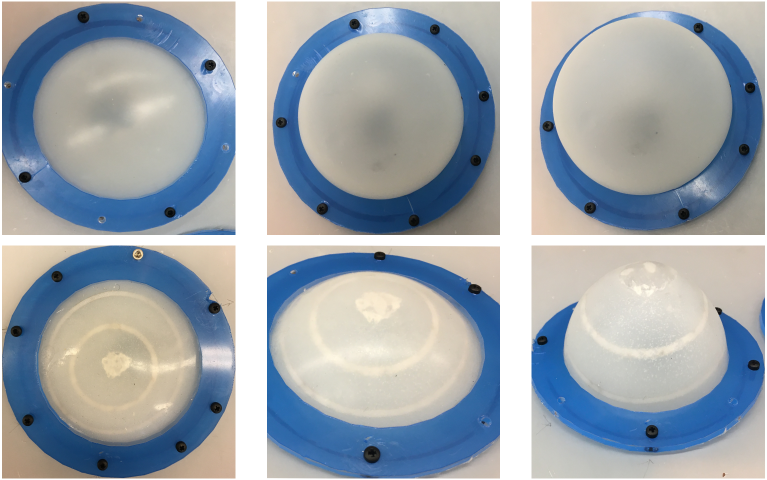
Inputs					Outputs		
C_1	C_2	R_i	r_i	R_o	r_o	P	ΔV
$1.1e4$	$2.2e4$	.025	.03	.03	.028	$-.34$	≈ 0

Fig. 7: Volumetric Deformation (Compression).

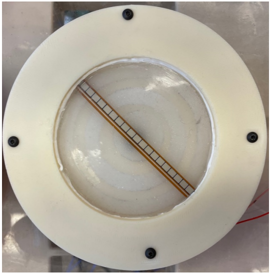
Pneumatic Control and Deformation Scheme



Volumetric Deformation Results (Actual)

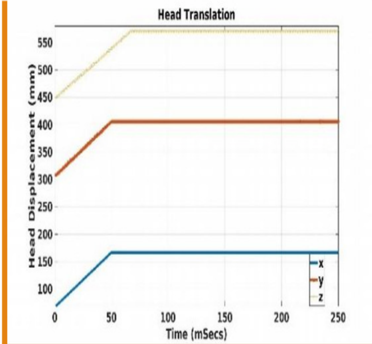


Actuator and Overall Mechanism with Phantom

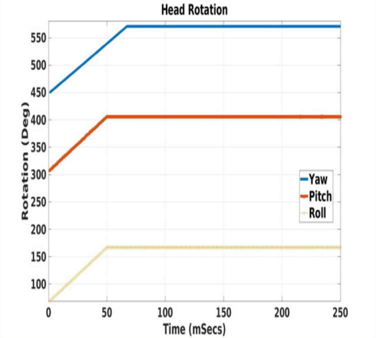


Head Motion Open Loop Control

Independent Actuation



Head Translation along x, y, z for a task of raising the head by a certain threshold above the table



Head rotation in Euler angles for a task of tilting the head about the x, y, z axes on the treatment table.

Ongoing Work: 6-DOF Closed-loop Control

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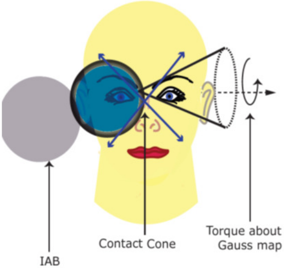
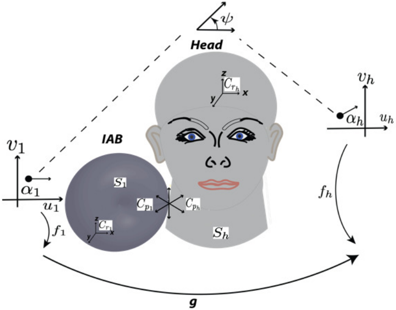
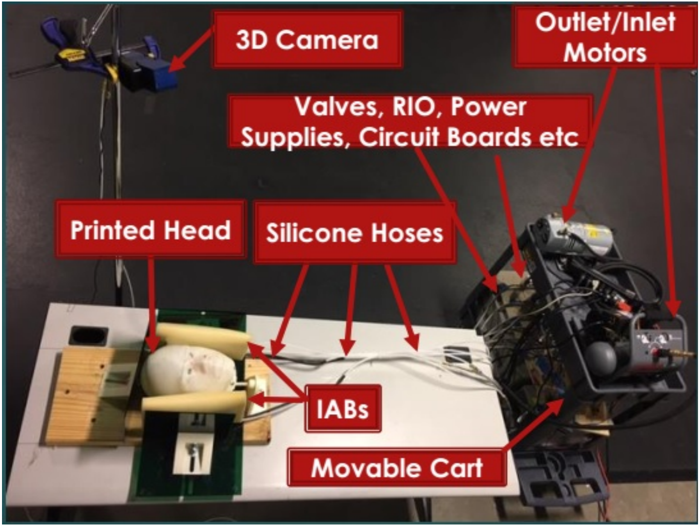
Continuum Mechanical Model Validation/Differential Geometry/Newton-Euler Dynamics





3-DOF Simulation Testbed



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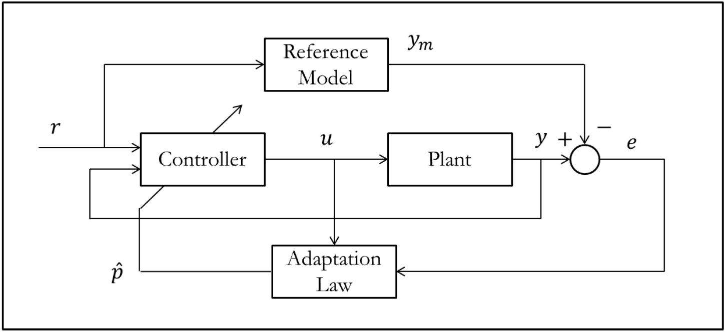
Model Reference Adaptive Control



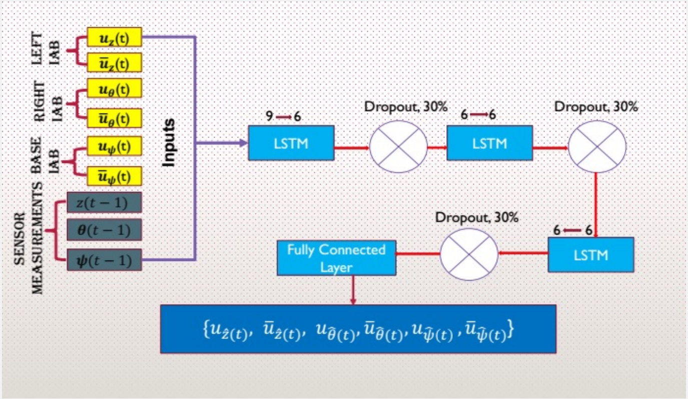
Indirect MRAC system. (Source mdpi.com)

3-DOF Model Reference Adaptive Control

- Model head and bladder dynamics as
  - $\dot{\boldsymbol{x}} = \mathbf{A}\boldsymbol{x} + \mathbf{B}\Lambda\left(\mathbf{u} - f(\boldsymbol{x}, \mathbf{u})\right) + \mathbf{w}(k)$
- Approximate $f(\boldsymbol{x}, \mathbf{u})$ by a neural network with continuous memory states
- Derive adaptive adjustment mechanism from Lyapunov analysis for Adaptive Control Parks (1966)
- $\mathbf{u} = \underbrace{\hat{\mathbf{K}}_x^{\mathbf{T}} \boldsymbol{x}}_{\text{state feedback}} + \underbrace{\hat{\mathbf{K}}_r^{\mathbf{T}} \mathbf{r}}_{\text{optimal regulator}} + \underbrace{\hat{f}(\boldsymbol{x}, \mathbf{u})}_{\text{approximator}}$

Neural Network Architecture

Neural Net Architecture

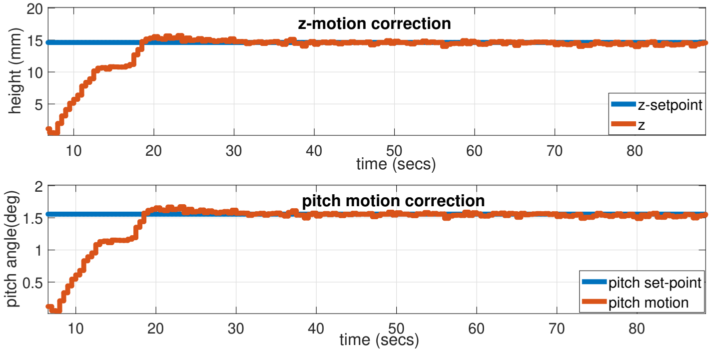


Lyapunov Redesign: Theorem

- For correct adaptive gains, $\hat{\mathbf{K}}_x$ and $\hat{\mathbf{K}}_r$, $\mathbf{e}(k)$ is ***uniformly ultimately bounded***, and the state $\boldsymbol{x}$ converges to a neighborhood of $\mathbf{r}$.
- Choose a $\mathbf{V}$ in terms of $\mathbf{e}$; $\tilde{\mathbf{K}}_x^T$, $\tilde{\mathbf{K}}_r^T$; and parameter error $\varepsilon_f(\boldsymbol{x}(k))$ space

$$\mathbf{V}(\mathbf{e}, \tilde{\mathbf{K}}_x, \tilde{\mathbf{K}}_r^T) = \mathbf{e}^T\mathbf{P}\mathbf{e} + \mathbf{tr}(\tilde{\mathbf{K}}_x^T\boldsymbol{\Gamma}_x^{-1}\tilde{\mathbf{K}}_x^T|\boldsymbol{\Lambda}|) + \mathbf{tr}(\tilde{\mathbf{K}}_r^T\Gamma_r^{-1}\tilde{\mathbf{K}}_r|\boldsymbol{\Lambda}|)$$

Results: Z and Pitch Motions



Goal command: $(z, \theta, \phi) = (14mm, 1.6^\circ, 45^\circ)^T$.

Results: Roll Motion

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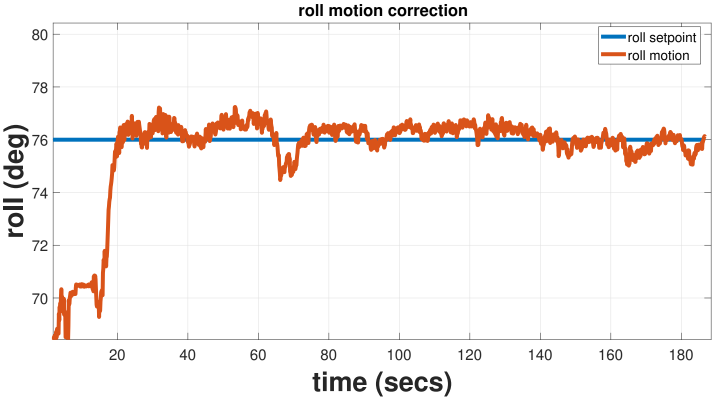

Head roll tracking.

Conclusions

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- Non-invasive soft robot for head motion compensation ✓
- Photons-transparent as opposed to rigid/electro-mechanical devices/robots ✓
- Adaptible under MRI coils for newer MRI-LINACs ✓

Part III: Robustness Margins and Robust Deep Policies

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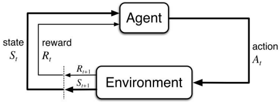
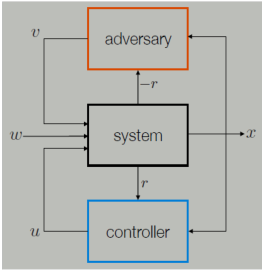
- Robustness Margins and Robust Deep Policies for Nonlinear Control

The robustness conundrum

- How to know *a priori* a policy's robustness limits?



- How to inculcate robustness into multistage decision policies?



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- To quantify the brittleness, we optimize the stage cost

$$\max_{\mathbf{v}_t \sim \psi \in \Psi} \left[\sum_{t=0}^{T} \underbrace{c(\mathbf{x}_t, \mathbf{u}_t)}_{\text{nominal}} - \gamma \underbrace{g(\mathbf{v}_t)}_{\text{adversarial}} \right]$$

- To mitigate lack of robustness, we optimize the *cost-to-go*

$$\mathcal{J}_t(\mathbf{x}_t, \pi, \psi) = \min_{\mathbf{u}_t \sim \boldsymbol{\pi}} \max_{\mathbf{v}_t \sim \psi} \left(\sum_{t=0}^{T-1} \ell_t(\mathbf{x}_t, \mathbf{u}_t, \mathbf{v}_t) + L_T(\mathbf{x}_T) \right),$$

- and seek a saddle point equilibrium policy that satisfies

$$\mathcal{J}_t(\mathbf{x}_t, \pi^*, \psi) \le \mathcal{J}_t(\mathbf{x}_t, \pi^*, \psi^*) \le \mathcal{J}_t(\mathbf{x}_t, \pi, \psi^*),$$

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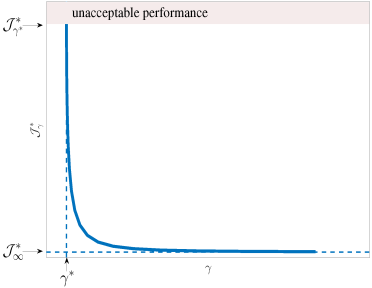
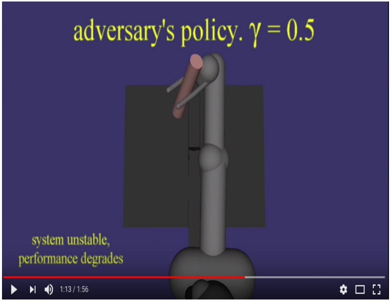
Results: Brittleness Quantification





Results: Iterative Dynamic Game

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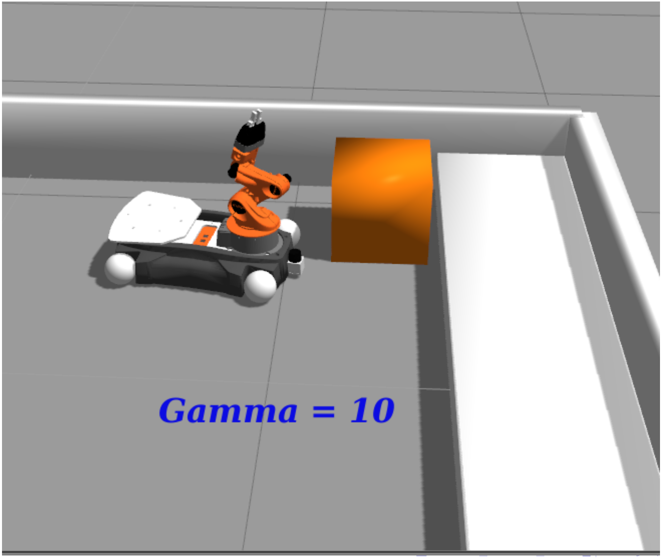

Future Work: MRI/RT Immobilization

- Explore multiple parallel robot mechanisms for head motion correction.
- Adopt iterative dynamic game approach [Ogunmolu et al. (2018)] for solving robust controller for head stabilization.
- Build on Freeman and Kokotovic's point-wise min-norm robust control lyapunov function to realize a meaningful value function in deep policies [Freeman and Kokotovic (1996)].

Constrained Robust Control Lyapunov Function (RCLF) Motion Planning

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Problem Definition

Find RCLF collision-free path $\sigma^\star : [0, 1] \to \mathcal{M}_{free}$ given a path planning problem $\left(\mathcal{Q}_{free}, \xi_i, \mathcal{Q}_{goal}\right)$, manipulation constraint, G, and cost function V such that $V(\sigma^\star) = \min_{\sigma \in \Sigma_{\mathcal{M}_{free}}} V(\sigma)$ if one exists.

- Leverage [Freeman and Kokotovic (1996),Ogunmolu et al. (2018)].
- Greedy approach using L-BFGS optimization algorithm with box constraints, in contrast to the quadratic nonlinear constrained optimization e.g. Khansari-Zadeh and Billard (2014).

Reproducing a Nonlinear Motion with GMM

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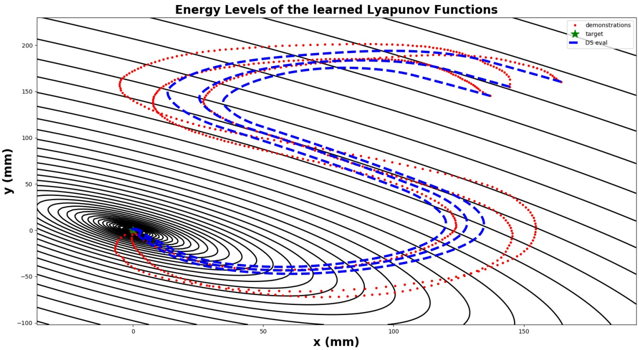
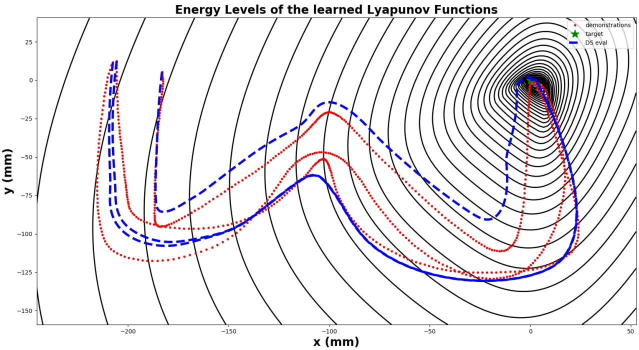


A CLF motion executor (red curves) that shows convergence to local attractors (green asterisks) and follows 3 different set trajectories (blue curves) for 2D nonlinear motion-trajectory problems on the WAM robot [Reproduced from Ogunmolu et al. (2020)].

Reproducing a Nonlinear Motion with GMM



A CLF motion executor (red curves) that shows convergence to local attractors (green asterisks) and follows 3 different set trajectories (blue curves) for 2D nonlinear motion-trajectory problems on the WAM robot [Reproduced from Ogunmolu et al. (2020)].

Conclusions

- Designed a non-invasive soft robot for head motion compensation in IMRT/emerging MRI-LINACs ✓
- Photons-transparent; Adaptible under MRI coils for newer MRI-LINACs ✓
- Fast inference of beam orientations in treatment planning: Approx 60 secs beams prediction time✓
- Adapted H-∞ control methods for quantifying the brittleness of deep policies✓
- Devised a min-max-trained deep saddle policy for mitigating model mismatch, transfer errors, and policy sensitivity e.t.c. ✓

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