Lecture 1: Introduction to Hybrid AI and Formal Methods in Medical Imaging

Course: Formal and Hybrid Methods for Medical Imaging
Date: September 15, 2025
Duration: 2 hours
Instructor: Vincenzo

Learning Objectives

By the end of this lecture, students will be able to: - Understand the concept of hybrid AI and its relevance to medical imaging - Distinguish between symbolic, subsymbolic, and hybrid approaches - Recognize the role of formal methods in medical image analysis - Understand the basic principles of VoxLogica and spatial model checking - Appreciate the ethical considerations in AI-driven medical imaging

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1. Introduction: The Landscape of AI in Medical Imaging (30 minutes)

1.1 Traditional Approaches vs. Modern AI

Medical imaging has evolved from purely manual interpretation to sophisticated automated analysis. Today's landscape includes:

Traditional Image Processing: - Rule-based algorithms - Mathematical morphology - Feature extraction based on domain knowledge - Deterministic, interpretable results

Modern Machine Learning: - Deep neural networks (CNNs, U-Net, nnU-Net) - Data-driven feature learning - High performance on specific tasks - Often "black box" with limited interpretability

The Gap: - Traditional methods: interpretable but limited in complex scenarios - ML methods: powerful but lack transparency and domain knowledge integration

1.2 What is Hybrid AI?

Hybrid AI combines the strengths of different AI paradigms:

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Hybrid AI = Symbolic AI + Subsymbolic AI + Human Knowledge
```

Key Characteristics: - **Complementarity:** Different methods handle different aspects of the problem - **Interpretability:** Formal methods provide explainable reasoning - **Robustness:** Multiple approaches reduce single-point failures - **Domain Integration:** Incorporates medical expertise and constraints

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2. The Three Pillars of AI in Medical Imaging (45 minutes)

2.1 Symbolic AI (Formal Methods)

Definition: AI based on explicit representation of knowledge using symbols and logical rules.

In Medical Imaging: - Spatial logic for describing anatomical relationships - Rule-based segmentation using geometric constraints - Formal verification of image analysis pipelines

Example: "A brain lesion is a connected region with intensity $>$ threshold AND distance from ventricles $<$ 5mm"

2.2 Subsymbolic AI (Machine Learning)

Definition: AI that learns patterns from data without explicit symbolic representation.

In Medical Imaging: - Convolutional Neural Networks for segmentation - Deep learning for classification - Generative models for image synthesis

Example: A CNN trained on 10,000 brain scans learns to segment tumors without explicit rules.

2.3 Hybrid Approaches

Definition: Integration of symbolic and subsymbolic methods to leverage both data-driven learning and domain knowledge.

Strategies: 1. **Sequential:** ML preprocessing → Formal verification 2. **Parallel:** Multiple methods vote on results 3. **Integrated:** Formal constraints guide ML training 4. **Hierarchical:** Different methods at different scales

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3. Introduction to Formal Methods and Model Checking (30 minutes)

3.1 What are Formal Methods?

Definition: Mathematical techniques for specification, development.

Verification of software and hardware systems.

Key Components: - **Formal specification:** Mathematical description of system behavior - **Formal verification:** Mathematical proof of correctness - **Model checking:** Automated verification of finite-state systems

3.2 Model Checking in Medical Imaging

Traditional Model Checking: - Verifies software/hardware systems - Checks if system satisfies temporal logic properties - Example: "The system never enters an unsafe state"

Spatial Model Checking: - Verifies spatial properties of images - Checks if image regions satisfy spatial logic formulas - Example: "All tumor regions are connected and have high intensity"

3.3 Why Formal Methods in Medical Imaging?

Advantages: - **Precision:** Exact mathematical specification of requirements - **Verification:** Proof that analysis meets specifications - **Interpretability:** Clear reasoning about results - **Reliability:** Reduced errors in critical medical applications

Challenges: - **Complexity:** Requires mathematical expertise - **Scalability:** May be computationally intensive - **Flexibility:** Less adaptable than learning-based methods

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4. VoxLogica: Spatial Model Checking for Medical Images (45 minutes)

4.1 What is VoxLogica?

VoxLogica is a spatial model checker specifically designed for medical image analysis.

Key Features: - **Spatial Logic:** Describes spatial relationships in images - **3D Support:** Handles volumetric medical data (MRI, CT) - **Declarative:** Specify what to find, not how to find it - **Verification:** Proves properties about image regions

4.2 Spatial Logic Fundamentals

Basic Concepts: - **Atomic Propositions:** Basic properties (e.g., "high intensity") - **Spatial Operators:** Describe spatial relationships - **Logical Connectives:** AND, OR, NOT, IMPLIES

Spatial Operators: - `near( , d)`: Points within distance d of regions satisfying - `surrounded( , )`: Regions completely enclosed by regions - `connected( )`: Connected components satisfying

Example Formula:

```
tumor := intensity > 150 AND connected(true)
edema := near(tumor, 10) AND intensity > 100
```

4.3 VoxLogica in Practice

Workflow: 1. **Image Loading:** Import medical images (DICOM, NIfTI) 2. **Property Definition:** Write spatial logic formulas 3. **Model Checking:** Verify properties against image 4. **Result Analysis:** Examine satisfied/violated regions

Example Use Cases: - **Lesion Detection:** Find connected high-intensity regions - **Anatomical Validation:** Verify organ relationships - **Quality Control:** Check image acquisition artifacts

Aspect	Traditional	VoxLogica

4.4 VoxLogica vs. Traditional Methods

Aspect	Traditional	VoxLogica
Specification	Procedural code	Declarative logic
Verification	Testing	Formal proof
Interpretability	Code inspection	Logical reasoning
Flexibility	High	Medium
Correctness	Empirical	Mathematical

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5. The ISOLA24 Paper: "Towards Hybrid-AI in Imaging Using VoxLogicA" (20 minutes)

5.1 Paper Overview

Publication Details: - **Title:** "Towards Hybrid-AI in Imaging Using VoxLogicA" - **Authors:** Gina Belmonte, Laura Bussi, Vincenzo Ciancia, Diego Latella, Mieke Massink - **Venue:** ISoLA 2024 (International Symposium on Leveraging Applications of Formal Methods) - **Pages:** 205-221 - **DOI:** 10.1007/978-3-031-75387-9_13

5.2 Research Context and Significance

ISOLA 2024 Focus: - Premier venue for bridging formal methods theory and practical applications - Emphasis on real-world impact of formal verification techniques - Platform for demonstrating innovative applications in critical domains

Paper's Contribution to Hybrid AI: This paper represents a significant step toward integrating formal methods with AI in medical imaging, addressing the critical need for: - **Interpretable AI:** Making AI decisions explainable to medical professionals - **Reliable automation:** Combining data-driven learning with domain knowledge - **Clinical validation:** Providing mathematical guarantees for medical applications

5.3 Key Research Contributions

Methodological Advances: - **Hybrid Architecture:** Novel integration of VoxLogica spatial model checking with machine learning pipelines - **Spatial Logic Extensions:** New operators specifically designed for medical imaging applications - **Performance Optimization:** Efficient algorithms for real-time medical image analysis

Practical Applications: - **Medical Image Segmentation:** Combining CNN-based segmentation with formal geometric constraints - **Quality Assurance:** Automated verification of imaging analysis results - **Clinical Decision Support:** Providing explainable reasoning for diagnostic assistance

5.4 Hybrid AI Framework

The VoxLogicA Approach: 1. **ML Preprocessing:** Neural networks handle noise reduction and initial feature extraction 2. **Formal Specification:** Spatial logic defines anatomical and pathological constraints 3. **Model Checking:** VoxLogicA verifies that ML results satisfy medical requirements 4. **Hybrid Validation:** Combined confidence from both statistical and logical reasoning

Example Workflow:

```
Medical Image → CNN Segmentation → VoxLogicA Verification → Validated Results
                        ↓                         ↓
              Statistical Confidence    Logical Certainty
                        ↓                         ↓
                    Combined Hybrid Confidence Score
```

5.5 Clinical Impact and Future Directions

Immediate Benefits: - **Increased Trust:** Medical professionals can understand and verify AI decisions - **Reduced Errors:** Formal constraints catch ML mistakes that violate medical knowledge - **Regulatory Compliance:** Mathematical verification supports medical device approval

Future Research Directions: - **Scalability:** Extending to larger, more complex medical imaging datasets - **Real-time Processing:** Optimizing for clinical workflow integration - **Multi-modal Integration:** Combining different imaging modalities with unified formal specifications

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6. Recent Advances: Medical Imaging Applications (15 minutes)

6.1 Contemporary Research in Medical Imaging

Recent Work by Course Instructor: Building on the theoretical foundations established in previous work, recent research has focused on practical applications of formal methods in clinical medical imaging scenarios.

Key Research Areas: - **Clinical Validation:** Real-world testing of VoxLogica in hospital environments - **Multi-modal Integration:** Combining MRI, CT, and ultrasound data analysis - **Performance Optimization:** Scaling formal methods for large medical datasets - **Regulatory Compliance:** Meeting FDA and CE marking requirements for medical AI

6.2 Practical Applications in Medicine

Current Medical Imaging Challenges: - **Diagnostic Accuracy:** Reducing false positives and negatives in automated analysis - **Workflow Integration:** Seamlessly incorporating AI tools into clinical practice - **Interpretability Requirements:** Meeting regulatory demands for explainable AI - **Multi-institutional Validation:** Ensuring methods work across different hospitals and equipment

Formal Methods Solutions: - **Spatial Logic Specifications:** Encoding medical knowledge as verifiable constraints - **Hybrid Validation:** Combining statistical and logical confidence measures - **Quality Assurance:** Automated detection of analysis errors and artifacts - **Documentation:** Providing audit trails for regulatory compliance

6.3 Impact on Medical Practice

Clinical Benefits: - **Enhanced Diagnostic Confidence:** Doctors can verify AI reasoning - **Reduced Training Time:** Formal specifications capture expert knowledge - **Standardization:** Consistent analysis across different institutions - **Risk Mitigation:** Mathematical guarantees reduce liability concerns

Research Contributions: - **Methodological Advances:** New spatial operators for medical imaging - **Performance Studies:** Comparative analysis of hybrid vs. pure ML approaches - **Clinical Validation:** Real-world testing in medical environments - **Tool Development:** User-friendly interfaces for medical professionals

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7. Ethics and Human-Centric AI in Medical Imaging (20 minutes)

6.1 Ethical Considerations

Key Principles: - **Transparency:** AI decisions must be explainable to medical professionals - **Accountability:** Clear responsibility for AI-assisted diagnoses - **Fairness:** Avoiding bias in training data and algorithms - **Privacy:** Protecting patient data and medical information

6.2 The Human-Centric Approach

Human-in-the-Loop: - AI assists but doesn't replace medical expertise - Doctors maintain final decision authority - Continuous feedback improves system performance

Hybrid AI Benefits: - **Interpretability:** Formal methods provide clear reasoning - **Validation:** Multiple approaches increase confidence - **Flexibility:** Adapts to different clinical workflows - **Trust:** Transparent processes build user confidence

6.3 Regulatory and Professional Considerations

Medical Device Regulation: - AI systems must meet safety and efficacy standards - Formal verification can support regulatory approval - Documentation and traceability requirements

Professional Standards: - Integration with existing clinical workflows - Training requirements for medical professionals - Quality assurance and continuous monitoring

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8. Course Preview and Next Steps (10 minutes)

7.1 Course Journey

Weeks 1-4: Foundations - Image generation and preprocessing - Traditional image processing - Programming with ITK/SimpleITK

Weeks 5-8: Formal Methods - Deep dive into VoxLogica - Spatial logic programming - Case studies and applications

Weeks 9-12: Hybrid Approaches - Machine learning integration - Performance evaluation - Real-world applications

7.2 Learning Approach

Theory + Practice: - Conceptual understanding of methods - Hands-on programming exercises - Real medical imaging datasets

Progressive Complexity: - Start with basic concepts - Build to sophisticated hybrid systems - Culminate in individual projects

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Summary and Key Takeaways

1. **Hybrid AI** combines symbolic and subsymbolic approaches for robust medical imaging solutions
2. **Formal methods** provide mathematical precision and verification capabilities
3. **VoxLogica** enables declarative specification of spatial properties in medical images
4. **Ethics and transparency** are crucial in medical AI applications
5. **Integration** of multiple approaches addresses individual method limitations

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Preparation for Next Lecture

Reading: - Review basic concepts of medical imaging modalities - Familiarize yourself with Python programming basics - Install required software (instructions will be provided)

Questions to Consider: - How might formal verification improve trust in medical AI? - What spatial relationships are important in your area of medical interest? - How can we balance automation with human expertise in medical imaging?

References and Further Reading

1. **Belmonte, G., Bussi, L., Ciancia, V., Latella, D., Massink, M.** (2024). "Towards Hybrid-AI in Imaging Using VoxLogicA." *ISoLA 2024: Leveraging Applications of Formal Methods*, pp. 205-221. DOI: 10.1007/978-3-031-75387-9_13

2. **Ciancia, V., et al.** (2024). "[Recent Medical Imaging Paper Title]." *[Medical Imaging Journal]*, [Volume], [Pages]. DOI: [DOI] *Note: Please update with specific details of your recent medical imaging publication*

References and Further Reading (2)

3. **Ciancia, V., Latella, D., Loreti, M., Massink, M.** (2014). "Specifying and verifying properties of space." *Theoretical Computer Science*, 550, 25-41.
4. **Nenzi, L., Bortolussi, L., Ciancia, V., Loreti, M., Massink, M.** (2015). "Qualitative and quantitative monitoring of spatio-temporal properties." *Runtime Verification*, pp. 21-37.
5. **Bartocci, E., Bortolussi, L., Loreti, M., Nenzi, L.** (2018). "Monitoring mobile and spatially distributed cyber-physical systems." *ACM Computing Surveys*, 51(4), 1-29.

References and Further Reading (3)

5. **Medical Imaging Ethics Guidelines:** IEEE Standards for Medical Device Software, FDA Guidelines for AI/ML-Based Medical Devices
6. **VoxLogicA Tool and Documentation:** Available at the official VoxLogicA repository and ISTI-CNR research pages
7. **Recent Advances in Hybrid AI:** Survey papers on neuro-symbolic AI and explainable AI in healthcare applications