A Deep Learning Approach for Prediction of IVF Implantation Outcome from Day 3 and Day 5 Time-lapse Human Embryo Image Sequences

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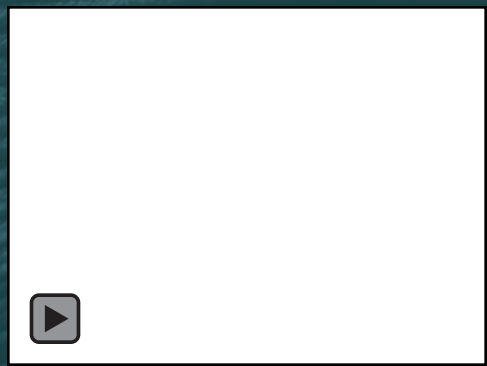

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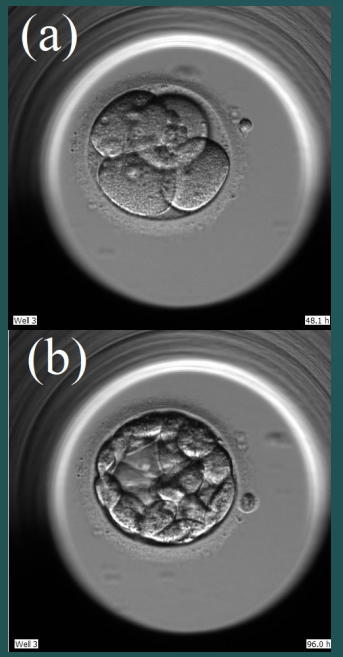
In Vitro Fertilization

- One of the most common practices.
- OVAs are fertilized in a lab environment.
- Incubated for 3 or 5 days.
- Embryo grading :
  - Day 3 (a) [1].
    1. Number of cells.
    2. Quality of cells.
  - Day 5 (b) [2].
    1. ICM quality.
    2. TE quality.
    3. Blastocyst expansion.
- 30% Success rates [3]



Artificial Intelligent Assisted Embryo Selection

- Automatic embryo grading.
  - Compared against the accumulated decision of multiple embryologists.
  - Not completely indicative of the outcome.
- Implantation or Live-birth prediction.
  - Hard to gather data.
  - Mostly focused on single image analysis.
  - Few methods based on time-lapse analysis.
    - ! Frames are assumed to have the same deciding attributes.
    - ! Different time windows, different attributes.

Our Proposals

- Time-lapse analysis.
- Separated time window analysis.
  - Day 3.
  - Day 5.
- Combined final prediction.
- Data Length Scheduler (DLS)
  - Regulates the training process.
  - Suppresses the adverse effects of training on variable-length image sequences.

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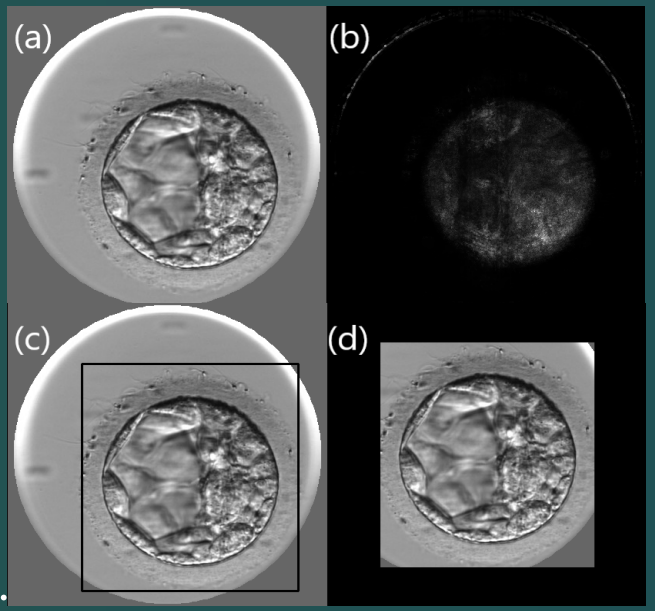
Data

- Time-lapse image sequences of 130 transferred embryos with known outcome.
- 15-minute interval frame capture.
- 5-Fold cross-validation.
- Day 3:
  - Between 48-72nd Hour.
  - 96 Frames.
  - Training frames = 9984.
  - Test frames = 2496.
- Day 5:
  - Pass the 96th Hour.
  - Varied lengths (70 - 96).
  - Varied number of Train/test frames.
- Image preparation.
  - Cell crop & center:
    a) Input b) Optical flow median
    c) Detected ROI* d) Output
  - Resize from 500x500 to 224x224



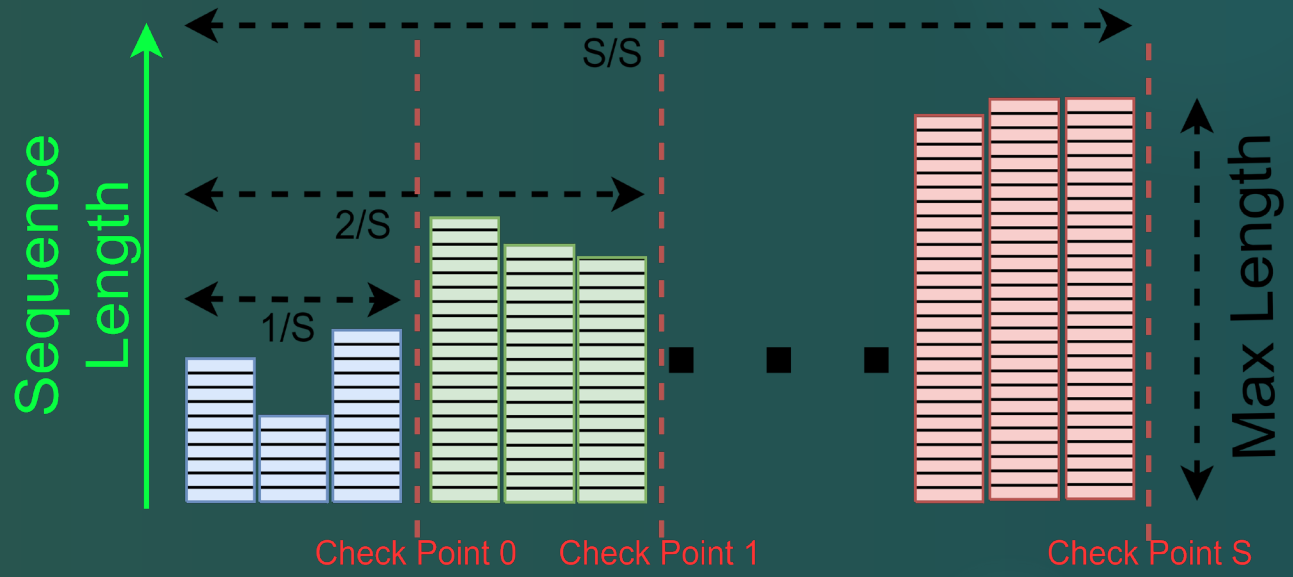
*Region Of Interest

Data Length Scheduler

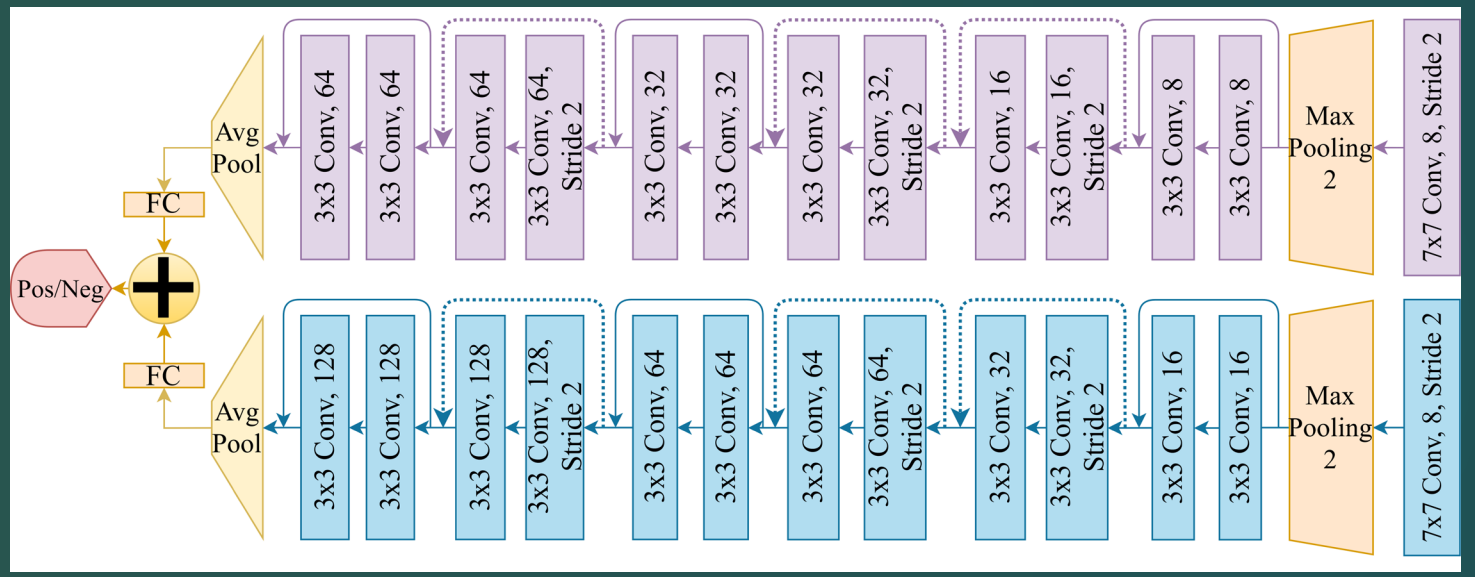
- Different development speeds, different sequence lengths.
- Slower developing embryos:
  - Similar frames ~ repeated samples.
  - Unbalanced training.
- A data regularization method.
- Regulating the training data based on sample's lengths.

Data Length Scheduler

- *S* percentile groups of sequences based on the length.
- Training starts with the first group.
- Group replacing checkpoints.
- Checkpoint modes:
  1. Passage of *n* epochs.
  2. No validation loss decrease after *p* epochs



Model's Structure



- Top path = Day 3 model.
- Bottom path = Day 5 model.

Model's Structure

- Training:
  - Independent path training.
  - Automatic extraction of Day 3 and Day 5 sequences.
  - Sequences are divided into frames.
  - Batch construction: only one frame per sequence.
- Testing:
  - Automatic extraction of Day 3 and Day 5 sequences.
  - Each sequences passes through its respective path.
  - Score are averaged over the temporal dimension.
  - Day 3 and Day 5 averaged together.
- Data Length Schedular (DLS) used in Day 5 training:
  - Mode 1.
  - $S = 4$.
  - $n = 10$.

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- DLS improves Day 5 model accuracy by 1.6%.
- Applying DLS to Day 3+ Day 5 model = 4.6% accuracy increase.
- Comparison against state of the art:
  - 6% accuracy increase in implantation prediction.
  - 2.6% accuracy improvement against live-birth predictor model.

Table 1: Performance comparison on Embryo outcome prediction

Row No	Model	Label format	Precision	Recall	Jaccard-Index	Accuracy
1	Day 3 model	Implantation	63.9	67.4	50.6	68.5
2	Day 5 model	Implantation	70.6	69.0	52.6	69.2
3	Day 5 model + DLS	Implantation	72.6	70.4	54.2	70.8
4	Combined Day 3 and Day 5	Implantation	72.6	72.3	56.7	72.3
5	Combined Day 3 and Day 5 + DLS	Implantation	**79.6**	**76.4**	**61.8**	**76.9**
6	Image CNN classifier [4]	Implantation	63.6	63.6	46.7	62.8
7	Image + Segmentation CNN classifier [4]	Implantation	71.1	72.7	56	70.9
8	Handmade feature classifier [5]	Live-birth	61.5	60.5	44.0	62.0
9	Image + Morphological factors CNN [6]	Live-birth	70.2	71.4	55.3	74.3

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Conclusions & Future Work

- Our approach:
  - A deep-learning based system.
  - Capable of processing time-lapse embryo image sequences.
  - Predict embryo implantation outcome.
  - Individual Day 3 and Day 5 analysis.
  - More accurate than using only one of the stages or only single images.
- DLS algorithm is a way to suppress the adverse effects of training on length variant image sequences.
- Future works:
  - Time window range analysis.
  - AI-based time series analysis of embryo sequences.

Thank You.

References

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