

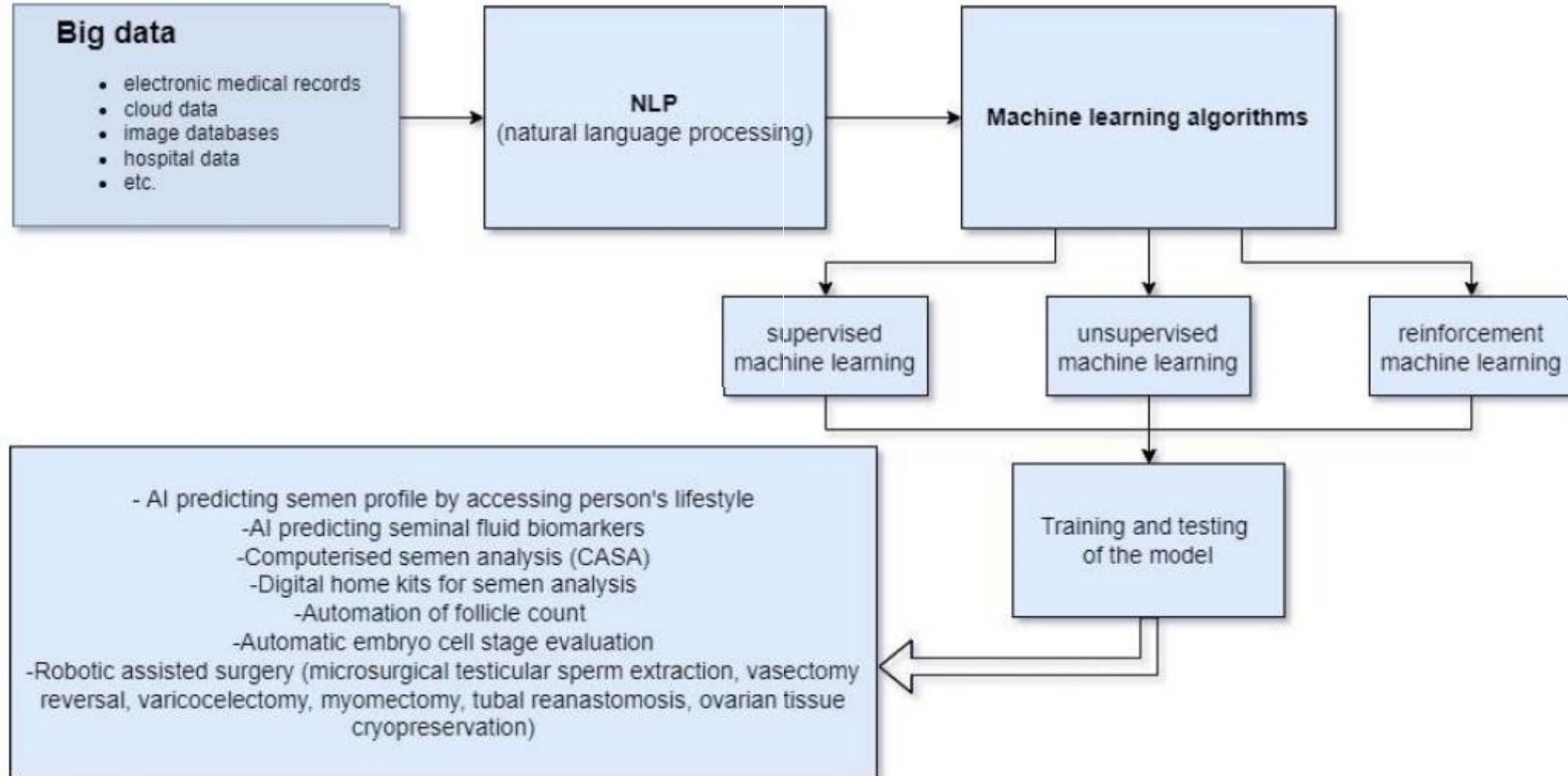
AI and Infertility



- AI will bring a great innovation to the field of reproductive medicine and to healthcare as a whole through the improvement of treatment options for infertile patients, better planning of the procedures, and ultimately, higher ART success rates, thus reducing the costs of the treatment.

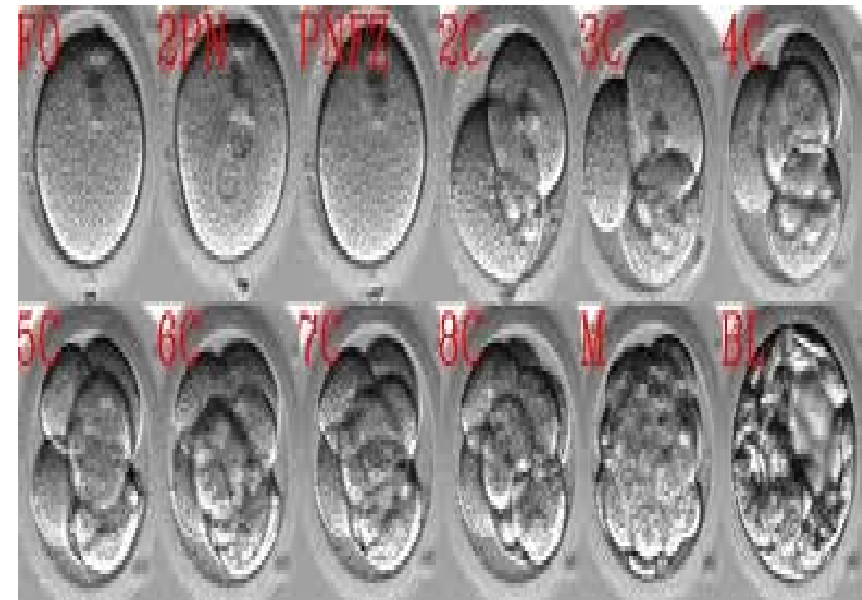
- The big data that electronic medical records (EMRs) and hospital data have within are perfect for AI to analyse and give some useful information. The current status of EMRs is that they are cumbersome and lack inter-record communication.

- In short, machine learning (ML) is classified in three main groups: ML capable of recognizing patterns (unsupervised ML), ML that has algorithms that perform classification and prediction based on previous examples (supervised ML), and ML that uses a system with reward and punishment methods to form a solution strategy to solve some problem (reinforcement learning)



- In reproductive medicine (RM), AI application started in the late twentieth century.
- Supervised learning methods are mostly used in non-surgical areas of RM, they are designed to categorise data from given information. The usage of this type of AI found its application in determining the morphokinetic parameters of the embryos that are most optimal, determining cost effectiveness in human oocyte cryopreservation, predicting IVF and ICSI outcomes, and classification of sperm cells.
- *Unsupervised learning models are not yet fully used in RM.*

- Artificial neural networks (ANN) borrow structures from neuronal connections are used in embryo segmentation ,to describe blastocyst expansion and rank-order blastocysts for transfer ,and to predict an overall outcome of IVF.



- Meanwhile, for robotic aspects of RM, reinforcement AI machine learning is more commonly used .Robotic surgery serves as a bridge between conventional open surgery and the minimally invasive laparoscopic surgery, and there are currently several different applications in this field. Examples are robotics-assisted myomectomy, tubal reanastomosis, endometriosis, ovarian tissue cryopreservation, and ovarian transposition.

Moon A.S., et al Robotic Surgery in Gynecology. Surg. Clin. North Am. 2020



- In addition, their applications include male infertility operations such as vasectomy reversal, subinguinal varicocelectomy, targeted spermatic cord denervation, and robotics-assisted microsurgical testicular sperm extraction (microTESE). These procedures, although costly and time consuming, have good results in terms of shorter hospital stay, decreased blood loss, less post-operative pain, and faster convalescence compared to open or laparoscopic surgeries .

Parekattil S.J., Gudeloglu A. Robotic assisted andrological surgery. Asian J. Androl. 2012

- Many machine learning algorithms, including traditional logistic regression, support vector machines, decision trees, and random forests which have been presented in order to improve the ART success rate, using parameters such as age, body mass index, endometrial thickness, estradiol and progesterone level on the day of embryo transfer, type of infertility, good-quality embryo rate, and others

Liu R., et al, Front. Endocrinol. 2021

The evaluation of ovarian reserve

- Using ultrasound (US), prediction of oocyte quality and pregnancy outcomes, variables such as ovarian follicular diameter and volume, number of follicles, and ovarian stromal blood flow index

Zhang C.-H., et al Front. Endocrinol. 2022

- Oocyte morphology assessment and adding oocyte morphology to AI may improve the precision of the algorithms. By including a total of 52 articles in this study, it has been shown that dark colour of the cytoplasm, homogeneous granularity of the cytoplasm, and ovoid shape of oocytes had no influence on treatment outcomes, but abnormalities such as refractile bodies, fragmented first polar body, dark zona pellucida, enlarged perivitelline space and debris were likely to affect the treatment outcome, whereas cytoplasmic vacuoles, centrally located cytoplasmic granularity, and clusters of smooth endoplasmic reticulum had negative impact on infertility treatment outcomes

Nikiforov D et al, A Systematic Review. Reprod. Sci. 2021

Idiopathic or unexplained infertility

- Environment and lifestyle factors, Obesity and metabolic syndrome have been pointed out as likely causes of idiopathic infertility.
- Bachelot et al. conducted a study in which they set forth a very promising machine learning model that can stratify infertile/fertile couples on basis of their bioclinical signature, thus helping the management of couples with unexplained infertility

Bachelot G., et al. Sci. Rep. 2021

- According to the Association for the Study of Reproductive Biology (ASEBIR) criteria and Gardner grading, inner cell mass, blastocyst expansion, and the trophectoderm are the best criteria for evaluating and selecting embryos on day five of development

Bori L., et al Fertil. Steril. 2020

- Mora-Sánchez and co. developed a methodology to analyze HLA haplotypes from couples with histories of either successful pregnancies or recurrent miscarriages in order to calculate the risk. This algorithm, called IMMATCH, is used to retrospectively predict recurrent miscarriage with an AUC = 0.71 ($p = 0.0035$)

Mora-Sánchez A., NPJ Digit. Med. 2019

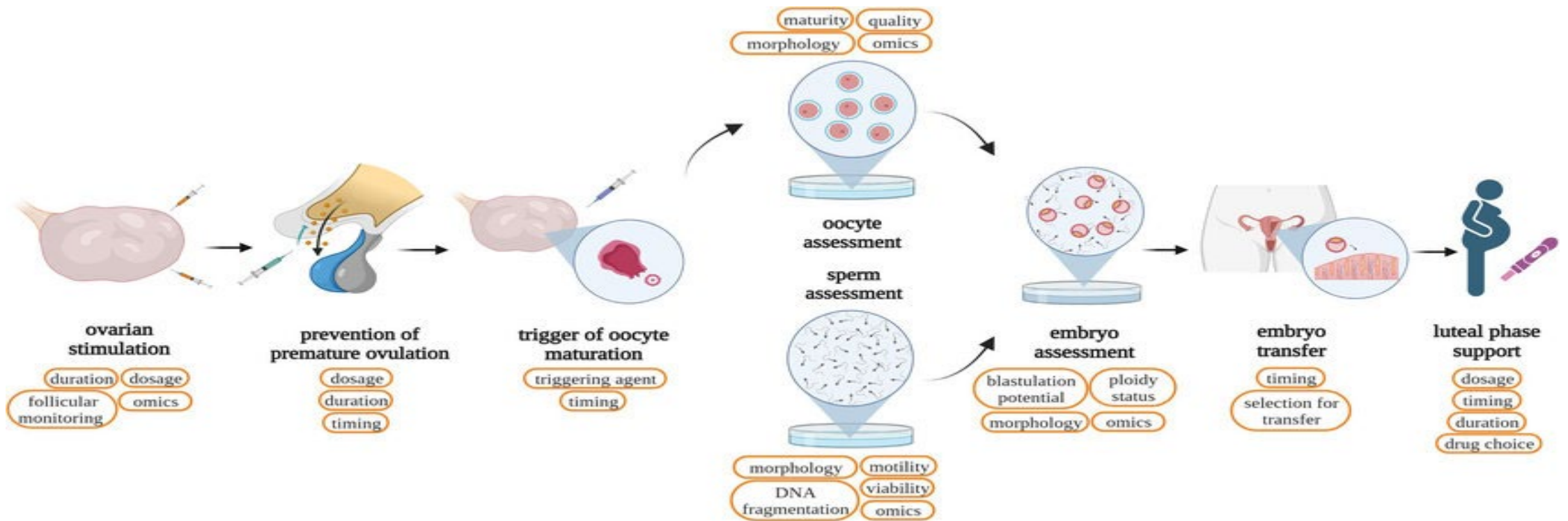
- Using a significant ET data set with enough records to train a model using powerful machine learning prediction techniques to increase the chances of a successful SET outcome. This data set included comprehensive and thorough aspects of patient demographics, embryo parameters, and cycle variables containing 82 features of IVF cycles. They discovered that among the six classification algorithms they used, random forest was the best classifier.

Raef B, Health Inform. J. 2019

- Recurrent implantation failure (RIF) is another big challenge for clinicians and a painful experience for couples that have experienced it. Shen et al. performed a study that provided a targeted and personalised treatment of RIF patients to help them achieve efficient and reliable pregnancy. They determined that among the four classification algorithms they used, the AdaBoost model obtained the best performance in the DET group, whereas the GBDT model proved to be the best in the SET group . It is worth stressing that clinical judgment cannot be replaced by an AI decision-making system.

Shen L, Front. Physiol. 2022

Potential target of AI for reproductive medicine



- Ultimately, such goals can only be achieved by preserving human control in order to make AI meet our needs, while at the same time operating transparently and achieving equitable outcomes.
- The legal aspects and ethics of the usage of this type of technology need to be clarified more in the future.

