Effects of modulating muscle contractions on embryo movement in early mouse pregnancy

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Background

- During early pregnancy, movement through the uterus is key for an embryo to find a receptive site for attachment.
- Uterine fluid movements aid in embryo transport (Eytan, 1999).
- Myometrial contractions of the uterine wall cause the fluid movements, allowing proper embryo spacing (Eytan, 1999).
- Disrupting embryo movement compromises pregnancy outcomes.

- When embryos were unable to access large areas of the uterus in pigs, even if embryos were spaced properly in the accessible areas of the uterus, pregnancy failure was observed (Dziuk, 1985).
- In the mare pregnancy, when sutures tied off parts of the uterus and prevented embryo access to more than two-thirds of the uterine area, pregnancy was lost (McDowell, 1988).

- Using a mouse model, we aim to understand the role of uterine myometrial contractions in embryo movement and establishing successful pregnancy.
- We have shown that in early mouse pregnancy, embryos first move unidirectionally as a cluster to the center of the horn (Gestation Day 3 [GD3] 6h-12h) and then move bidirectionally until they space out equally and attach (GD3 18h) (Flores, 2020).
- We also showed that while muscle contractions are essential for unidirectional clustered movement, they are dispensable for the bidirectional phase.

Research Questions

In this study we aim to:

a) Quantify muscle contractions and assess the affect of muscle relaxing drugs such as Salbutamol on uterine contractions.

b) Assess if uterine contractions are quantitatively different in the two phases of embryo movement (unidirectional and bidirectional).

References

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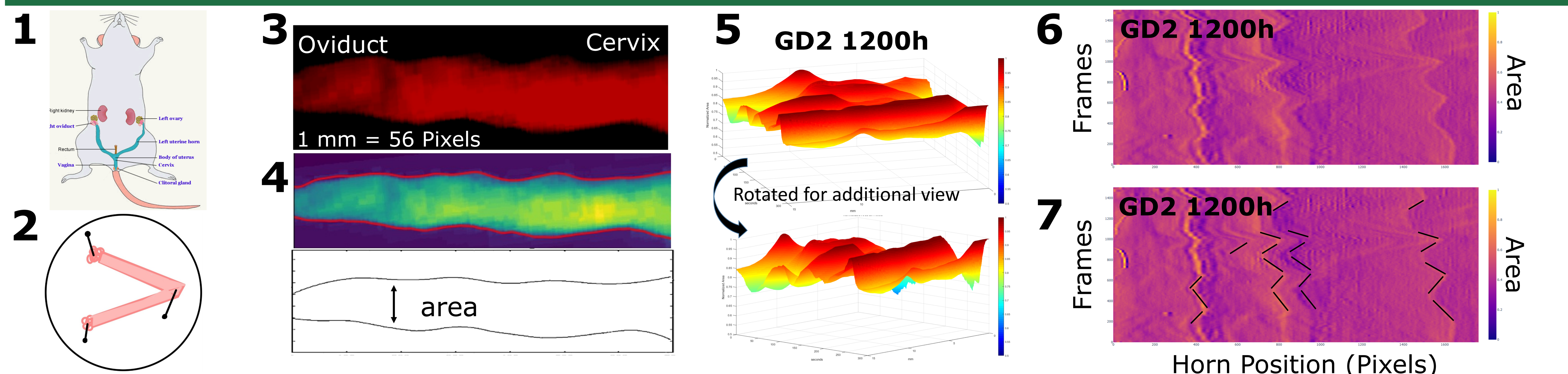
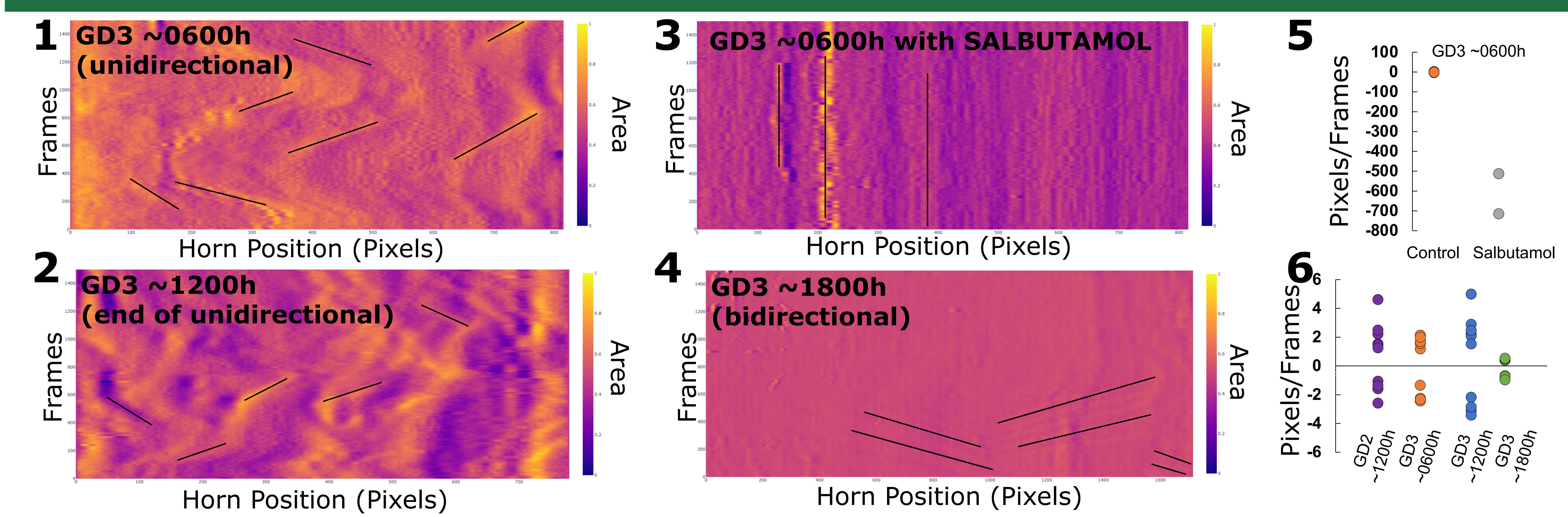
Methods



(1) mTomato expressing mice were dissected at different time points in early pregnancy. **(2)** The uterine horns were pinned in petri dishes with PBS. **(3)** Five-minute videos of the uterine contractions were recorded *ex vivo* (1 Frame/200msec). **(4)** A custom MATLAB script including a Sobel filter was used to detect the edges of the horns and analyze the uterine contractions. **(5)** A 3D graph was created by plotting the variables: position of the horn (x-axis), frames (time) (y-axis), and area between edges of the horn (z-axis). **(6)** The change in area between the uterine horn's M-AM axis was represented as varying colors to create a 2D graph. **(7)** The slopes on the 2D graph are analyzed to determine the velocity and directionality of the uterine contractions.

Results



(1-4) The direction of the line's slope determines the direction of the contraction. Contractions at GD3 1200h **(1)** are faster compared to GD3 ~0600h **(2)** and ~1800h **(4)**. Uterine contractions disappear with Salbutamol **(3)**. **(5-6)** The line's slope quantifies the velocity of the contraction.

Conclusions and Future Directions

- We were successful in establishing a method to quantify the direction and velocity of uterine contractions.
- The velocity of uterine contractions differs between non-pregnant (GD2), unidirectional (GD3 6h and 12h) and bidirectional embryo movement (GD3 18h) and uterine contractions disappear with Salbutamol treatment.
- We will now investigate how differential contraction velocity exerts its affect on embryo movement.