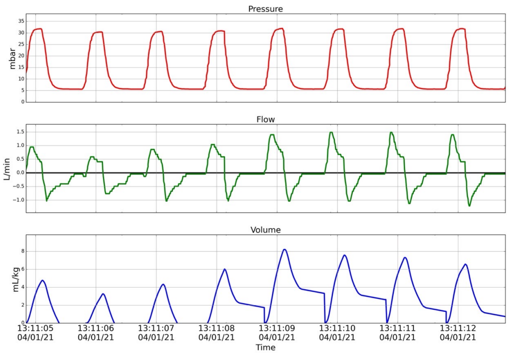
Patient-ventilator interactions in infants. The "dark matter" of neonatal ventilation



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Rosie Hospital, Cambridge, UK

18th Hot Topics in Neonatal Medicine, Jeddah, 14/02/2024

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Short Bio and Declarations

- Consultant Neonatologist in Cambridge (UK) since 2010
- Interest and active research in neonatal ventilation
- Downloaded years of data from neonatal ventilators
- Developed computational methods to analyse and interpret ventilator "Big Data"
- Advisor to Vyaire Medical and Dräger Medical
- In this talk I am presenting my own knowledge, experience and research findings as a clinician

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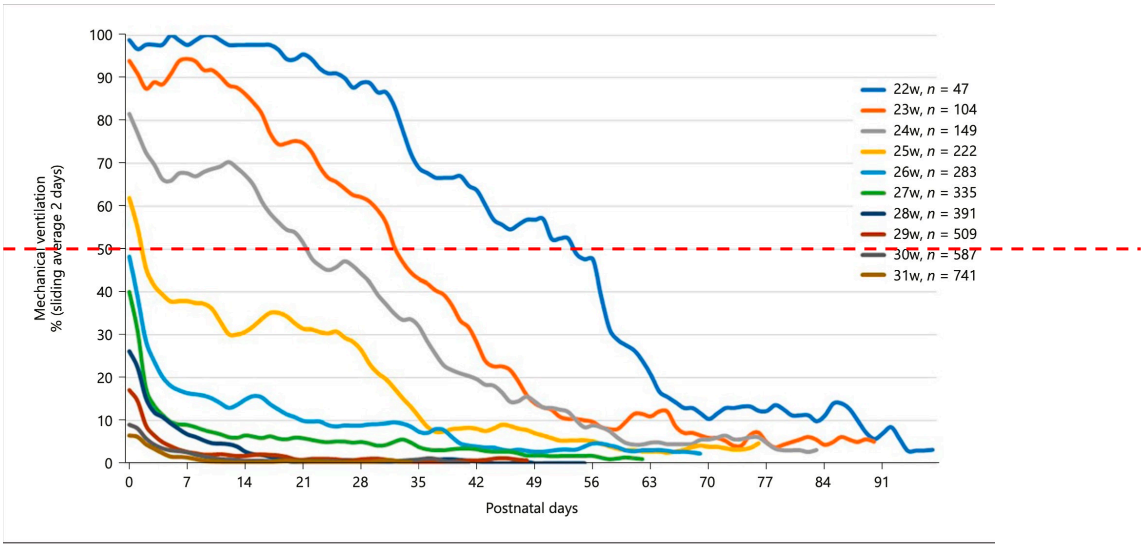

Fig. 1. Proportions (%) of very preterm survivors with mechanical ventilation per postnatal day and stratified by gestational age in weeks (22–31) up to a postmenstrual age of 36 weeks (*N* = 3,368).

Norman M, et al,. Patterns of Respiratory Support by Gestational Age in Very Preterm Infants. *Neonatology,* 2023

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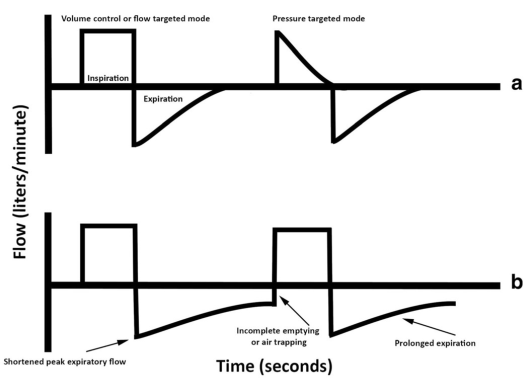
Ventilator waveforms in books and review articles



Emrath E et al, Current Pediatrics Reports (2021)

Mammel M et a,l Seminars in Fetal & Neonatal Medicine 20 (2015)

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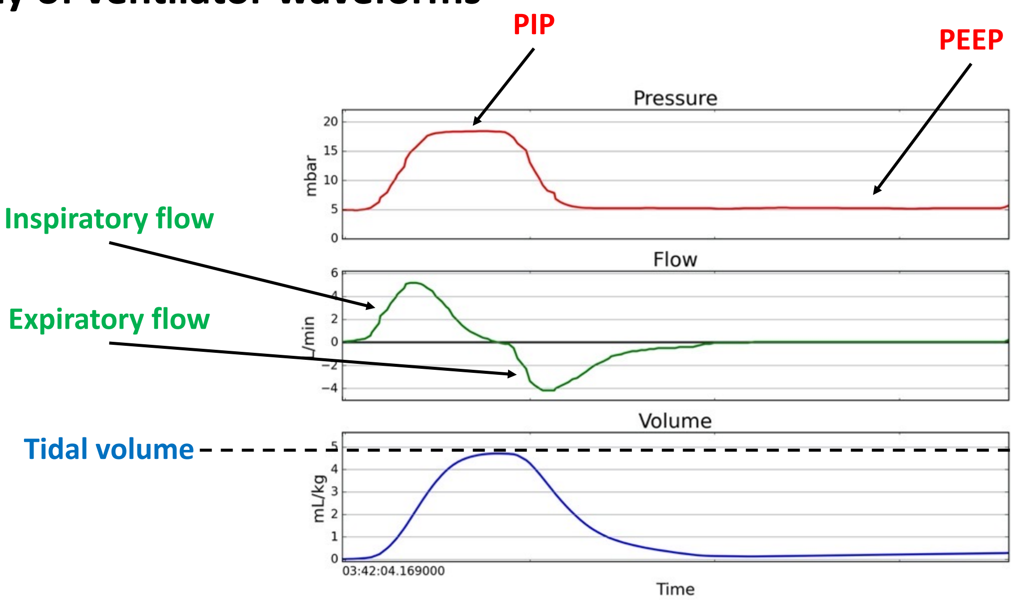
Anatomy of ventilator waveforms



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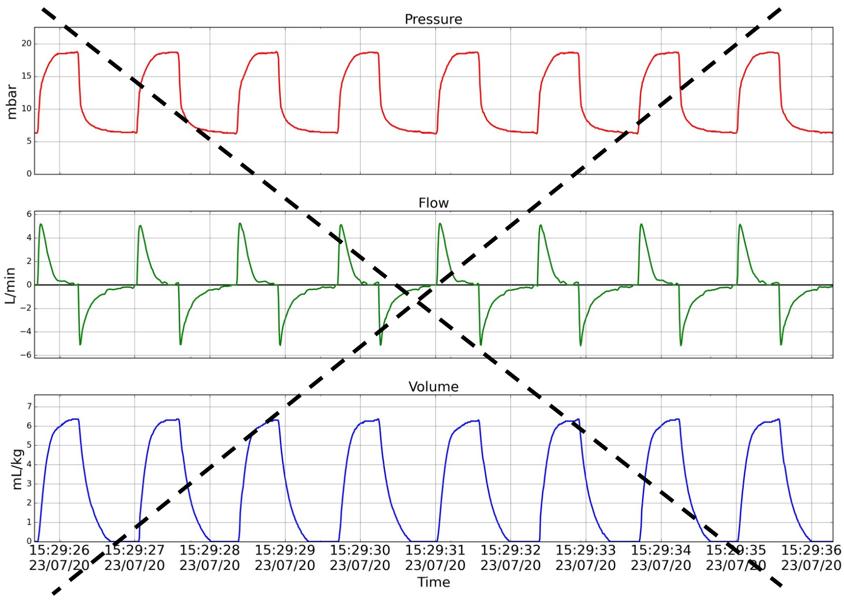
This is how we think about ventilator waveforms…

But they are not like unless the infant is muscle relaxed due to **patient-ventilator interactions**

Interactions can be:
GOOD
BAD
UGLY



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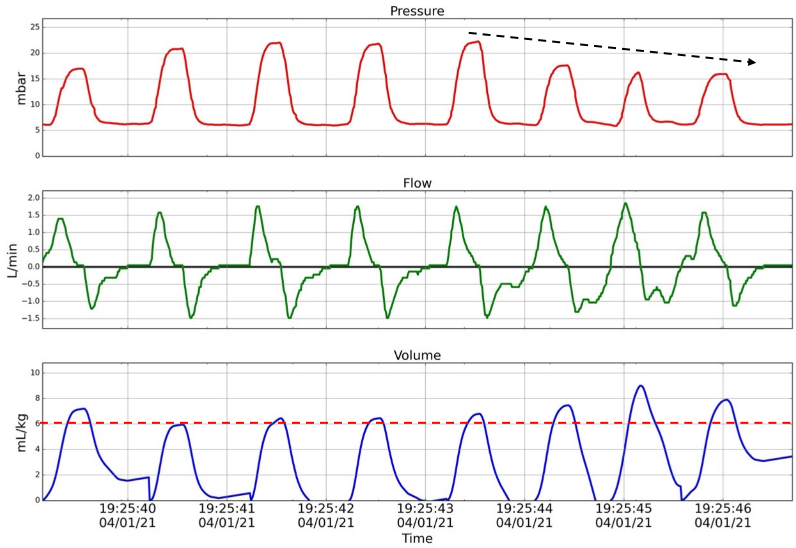
Patient-ventilator interactions – the good

Volume targeted ventilation

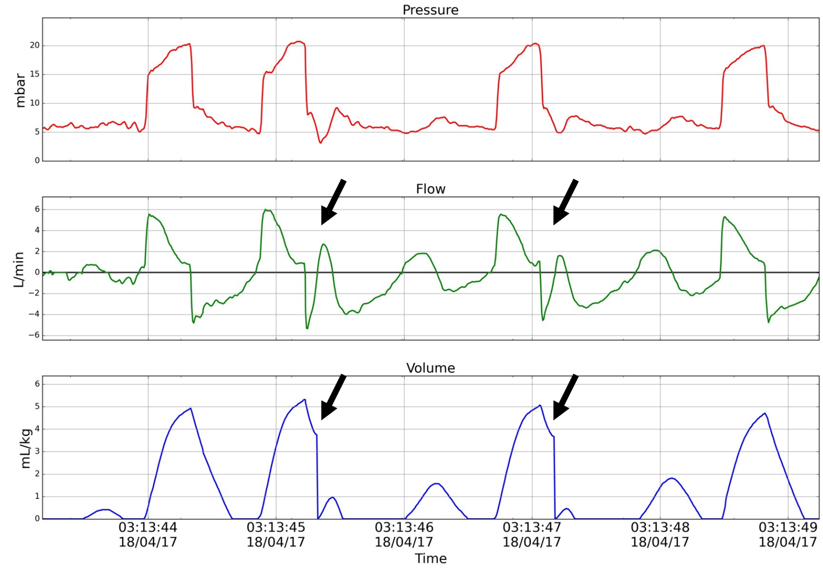


Patient-ventilator interactions – the bad

Interrupted expiration / Failed triggering

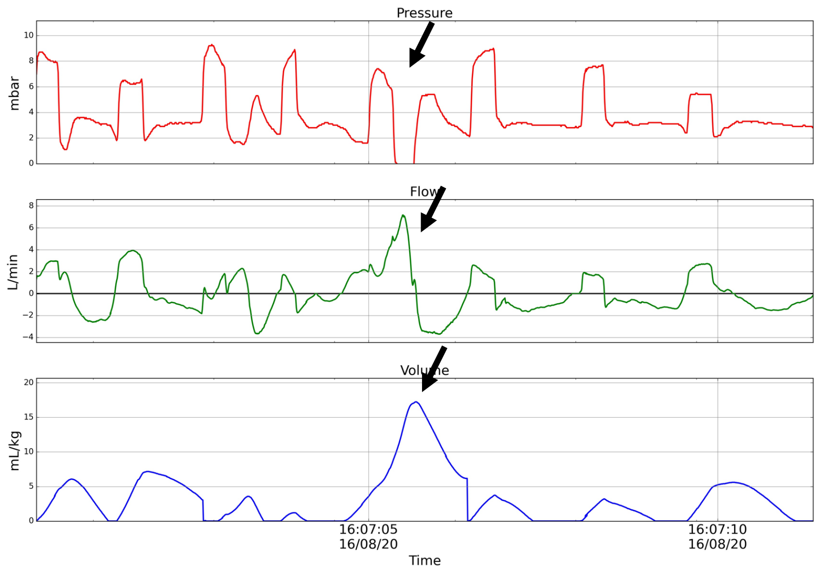
McCallion N *et al*, Arch Dis Child. 2005

- Manual review of ~6,000 breaths
- Occurred in 3%
- Interferes with VG ventilation



Patient-ventilator interactions – the ugly

Overall chaotic waveform with a sigh breath



Patient-ventilator interactions (PVIs) – asynchronies

- They can cause discomfort to the infant
- In adults they are associated with increased mortality
- Neonatal PVIs are different from adult asynchronies
- Their occurrence and significance in neonates is unknown

1. Neonatal clinicians do not have the time to watch ventilator screens for long periods
2. Neonatal ventilator data are not routinely stored or archived
3. There are no tools for automatically processing neonatal ventilator data and to identify patient-ventilator interactions

Downloading pressure, flow (volume) data with 100 – 125 Hz

- >2,000 days of ventilator data from 366 infants ventilated on NICU
- 88 days of ventilator data from 1,780 infants ventilated during transport
- ~150 million ventilator inflations/breaths
- ~20 billion data points
- ~600 Gigabyte data

		pressure	flow	volume
	Date_Time			
2793	2015-10-19 22:00:12.727	5.2713	0.0450	0.000
	2015-10-19 22:00:12.743	5.3713	0.1350	0.024
	2015-10-19 22:00:12.743	5.6214	0.4951	0.024
	2015-10-19 22:00:12.759	5.7714	0.7652	0.192
	2015-10-19 22:00:12.760	6.0215	1.0353	0.207

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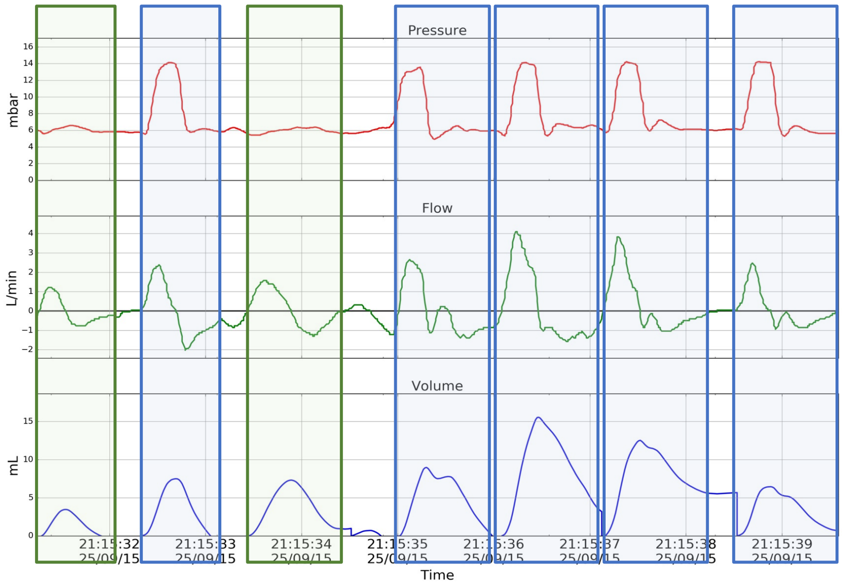
Automatic detection of respiratory cycles in ventilator data

Ventiliser

- Identifies ventilator inflations and spontaneous breaths in continuous ventilator data
- Characterises individual inflations and the subphases



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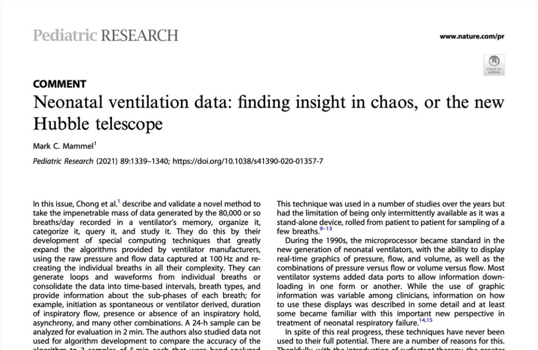
Chong D, Morley CJ, Belteki G. Computational analysis of neonatal ventilator waveforms and loops.
Pediatr Res. 2021;89(6):1432-1441.



Pediatric RESEARCH

www.nature.com/pr

COMMENT

Neonatal ventilation data: finding insight in chaos, or the new Hubble telescope

Mark C. Mammel[1]

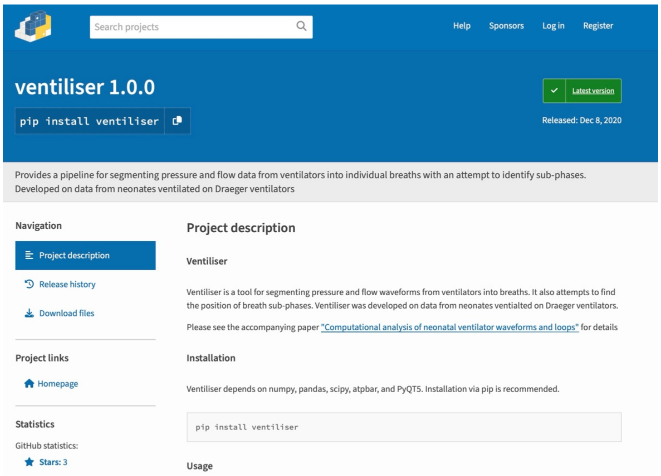
Pediatric Research (2021) 89:1339–1340; https://doi.org/10.1038/s41390-020-01357-7

In this issue, Chong et al.[1] describe and validate a novel method to take the impenetrable mass of data generated by the 80,000 or so breaths/day recorded in a ventilator's memory, organize it, categorize it, query it, and study it. They do this by their development of special computing techniques that greatly expand the algorithms provided by ventilator manufacturers, using the raw pressure and flow data captured at 100 Hz and re-creating the individual breaths in all their complexity. They can generate loops and waveforms from individual breaths or consolidate the data into time-based intervals, breath types, and provide information about the sub-phases of each breath; for example, initiation as spontaneous or ventilator derived, duration of inspiratory flow, presence or absence of an inspiratory hold, asynchrony, and many other combinations. A 24-h sample can be analyzed for evaluation in 2 min. The authors also studied data not used for algorithm development to compare the accuracy of the

This technique was used in a number of studies over the years but had the limitation of being only intermittently available as it was a stand-alone device, rolled from patient to patient for sampling of a few breaths.[9–13]

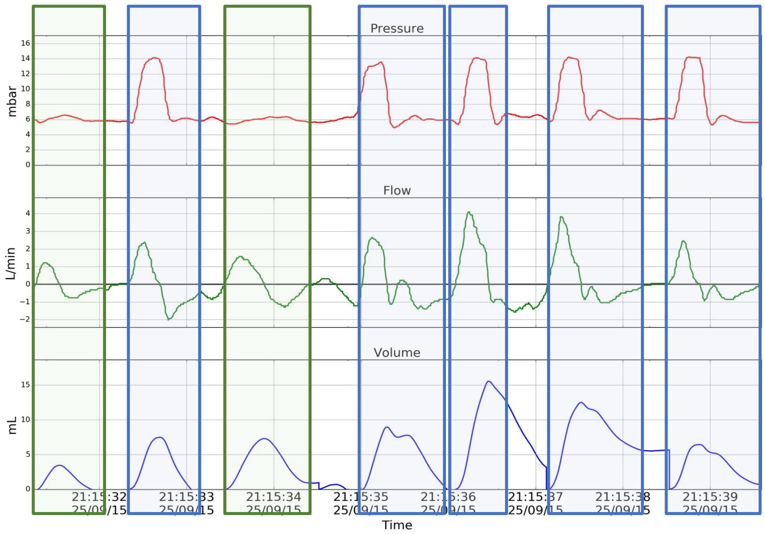
During the 1990s, the microprocessor became standard in the new generation of neonatal ventilators, with the ability to display real-time graphics of pressure, flow, and volume, as well as the combinations of pressure versus flow or volume versus flow. Most ventilator systems added data ports to allow information downloading in one form or another. While the use of graphic information was variable among clinicians, information on how to use these displays was described in some detail and at least some became familiar with this important new perspective in treatment of neonatal respiratory failure.[14,15]

In spite of this real progress, these techniques have never been used to their full potential. There are a number of reasons for this.



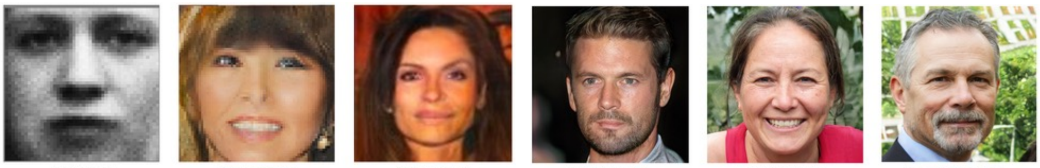
The next step is to identify specific patient-ventilator in the individual inflations automatically

How ?



Deep learning - neural networks

- Has revolutionised artificial intelligence over the last decade
- It drives image recognition, automatic translation, self-driving cars
- Can beat everyone on Earth in Chess, Go and computer games
- Deepfake images and videos are all based on it
- There is lots of hype around it…



GAN (2014) — *Original GAN concept ideated by Ian Goodfellow.*

DCGAN (2015) — *Uses transposed convolutions to upscale image resolution.*

CoGAN (2016) — *2 generators team up to fool 2 discriminators. Team members share some of the weights.*

ProGAN (2017) — *Avoid G&D undoing each other's learning by gradually increasing the resolution of the image.*

StyleGAN (2018) — *Better image control through adaptive instance normalization, a latent vector mapping network.*

StyleGAN 2 (2019) — *Best image quality by redesigning G's normalization, regularization and progressive growing.*

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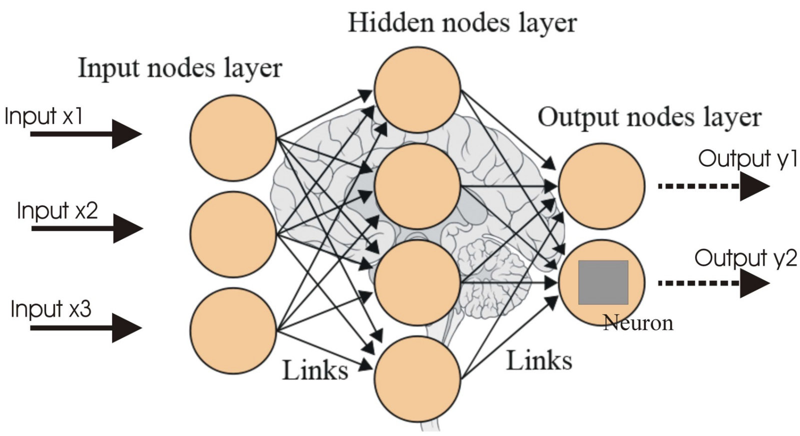
Neural networks – deep learning

Pressure	Flow
8.5	2.3
14	1.7
20	0.5



https://www.analyticsvidhya.com

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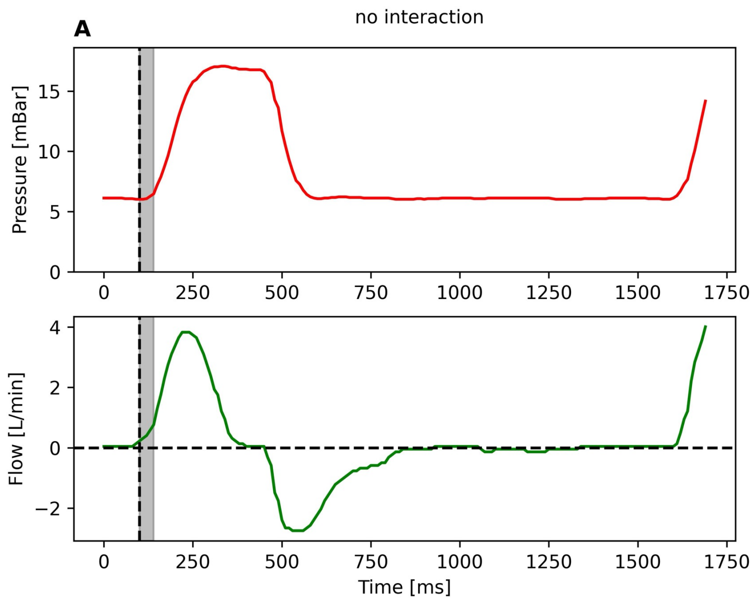
But - how to classify patient ventilator interactions ??

- No accepted neonatal classification
- Even in adults, one has been proposed only recently (Mireles-Cabodevila E, *et al*. Respir Care. 2022)
- Adapted it to neonatal ventilation

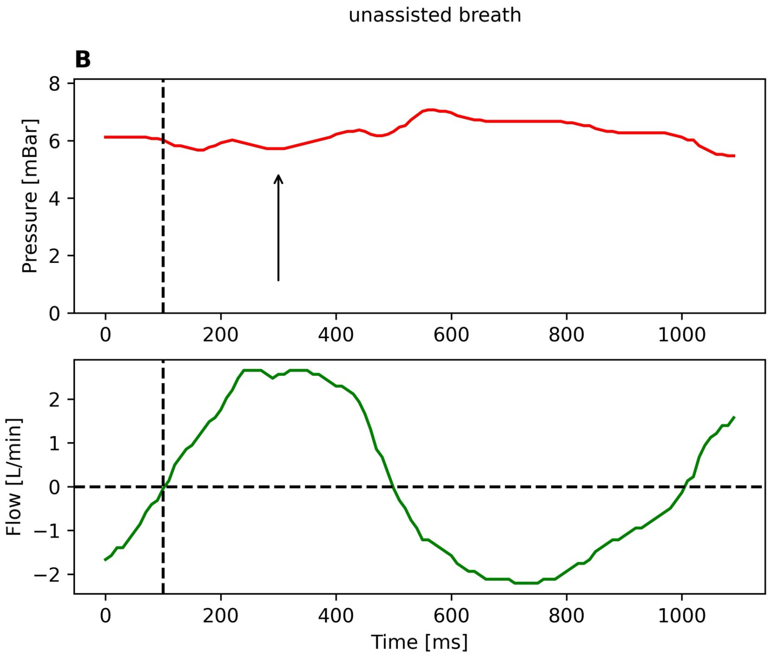
- Early triggering
- Late triggering
- Failed triggering
- Multiple triggering
- Work shifting
- Early cycling
- Late cycling
- Expiratory work

No interaction

Ventilator inflation started by either the infant or the ventilator with no other interaction



Unassisted breath



Spontaneous breath of the infant with no ventilator contribution

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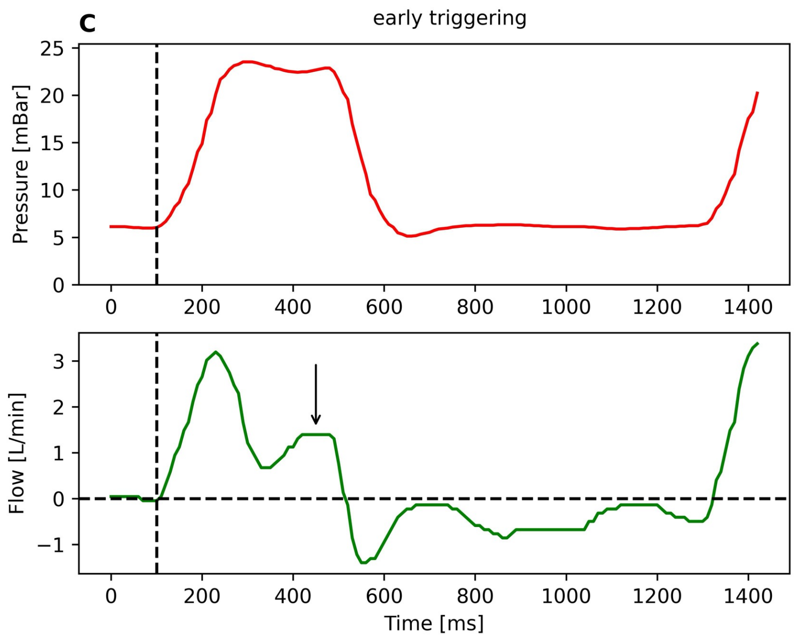
Early triggering



Baby’s inspiratory effort during the inspiratory phase of a ventilator inflation

- Reverse triggering
- Early inflation

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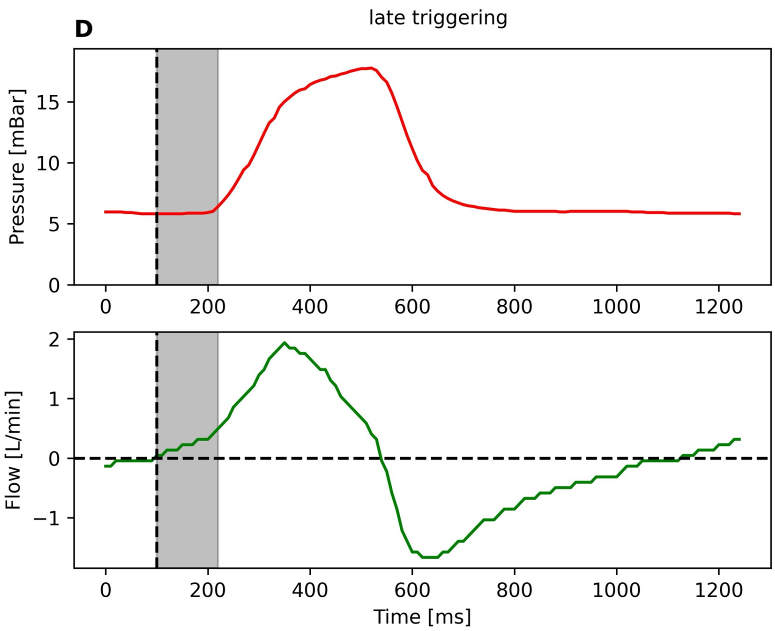
Late triggering

Pressure rise occurs >100 ms after beginning of infant's inspiratory effort.

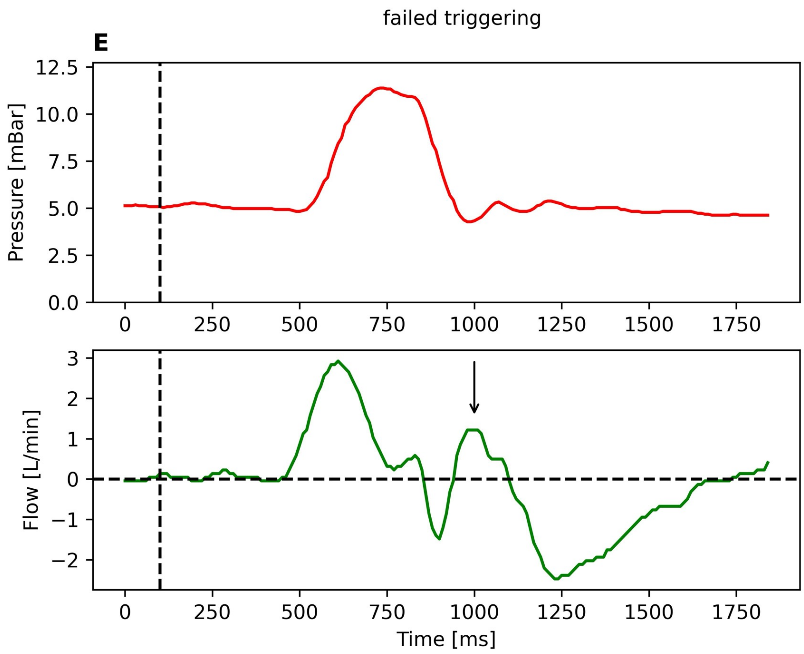
- Triggering delay
- Late inflation



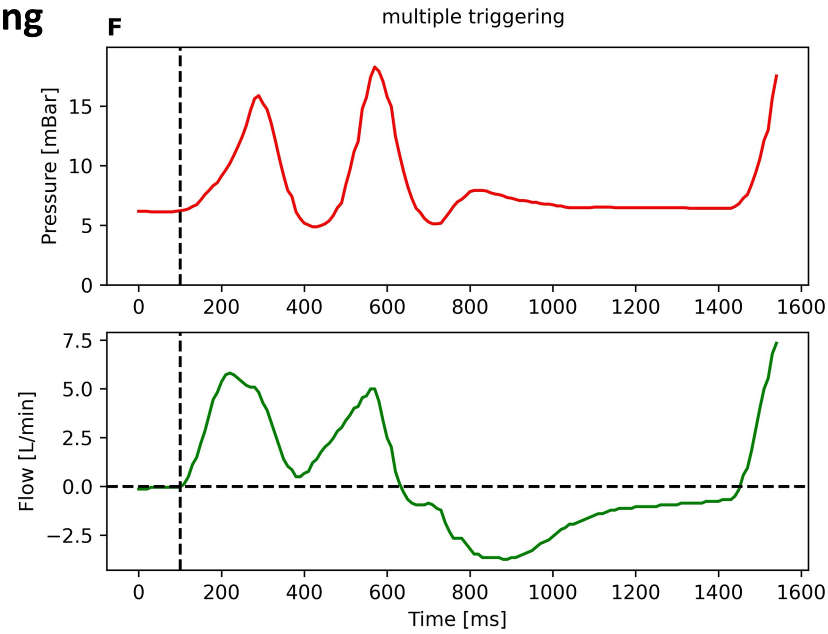
Failed triggering

Infant's inspiratory effort during the expiratory phase ventilator inflation

- Ineffective triggering
- Missed triggering
- Ineffective inspiratory effort during expiration
- Interrupted expiration



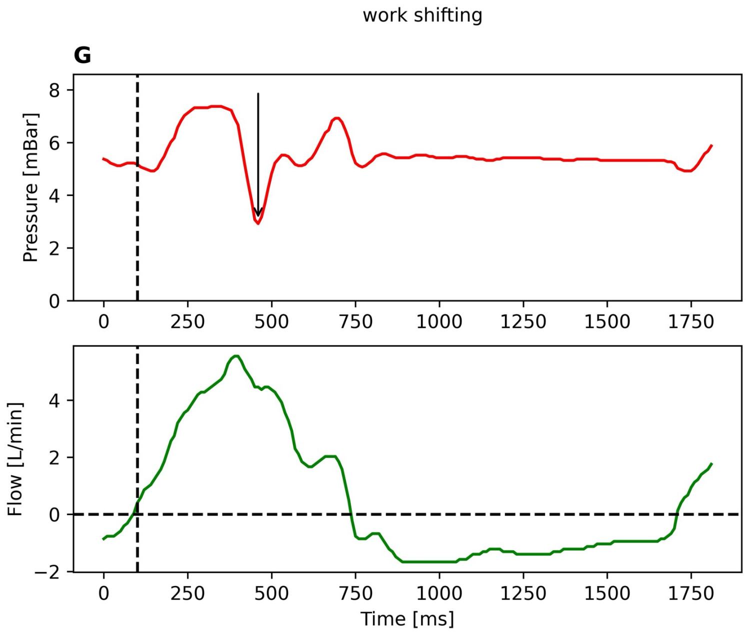
Multiple triggering



Two or more ventilator inflations with incomplete expiration between them

- Double triggering
- Double cycling
- Breath stacking

Work shifting



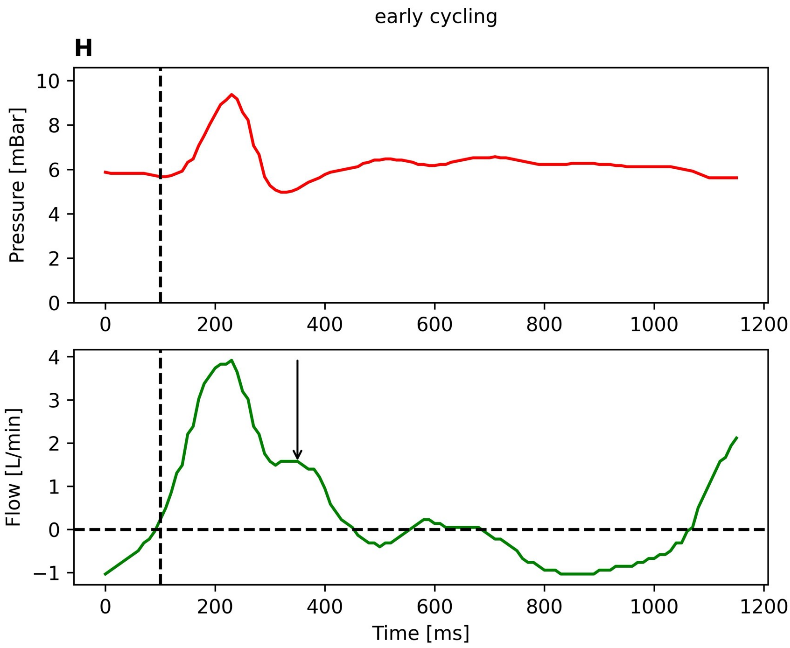
Pressure drops significantly with ongoing inspiratory flow

- Flow starvation
- Flow asynchrony

Early cycling

Infant's inspiratory effort after the return of pressure to PEEP level but before peak expiratory flow is reached

- Premature cycling



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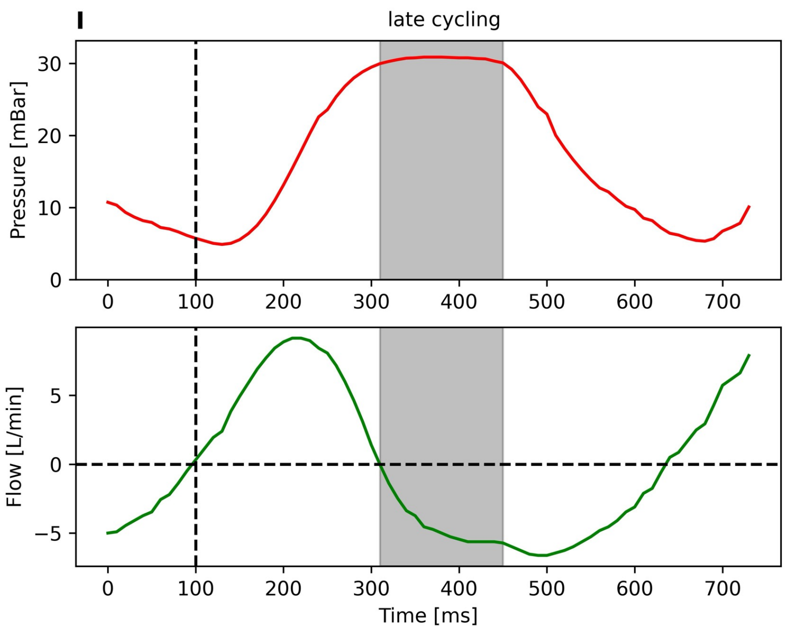
Late cycling

Infant's expiratory effort during the inspiratory phase of a ventilator inflation

- Delayed cycling



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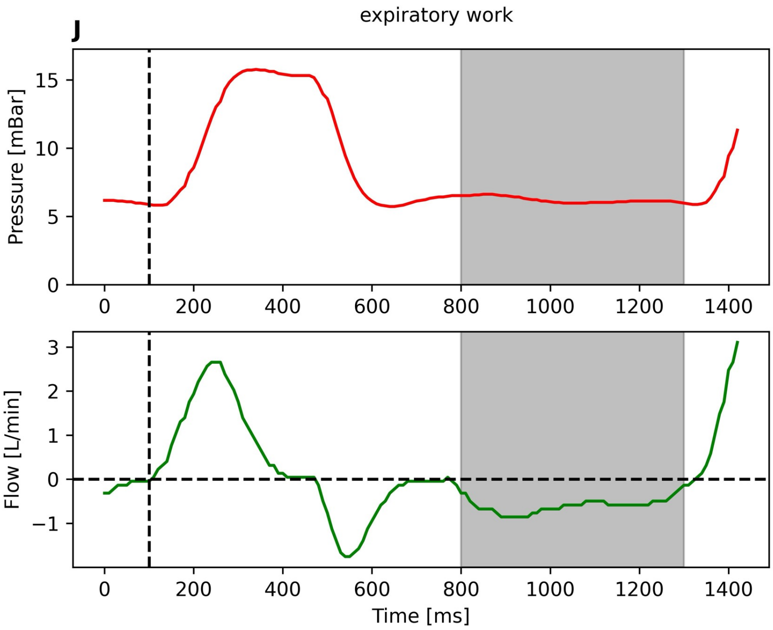
Expiratory work



Additional expiratory effort after an initial passive expiration

- Active expiration

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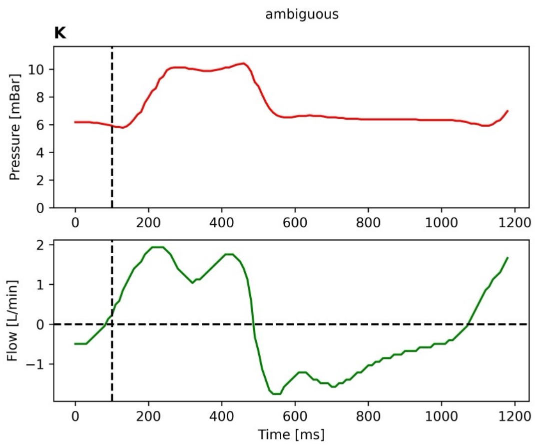
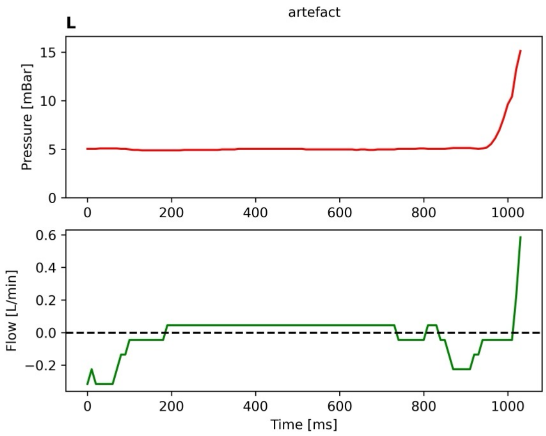
Ambiguous



Artifact



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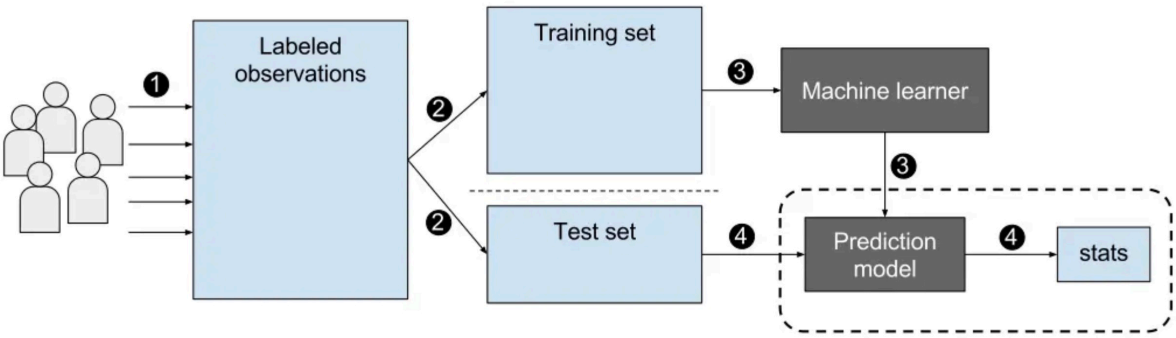
Supervised machine learning / deep learning

It requires manually annotated training and test sets – "ground truth"



Aurelien Geron: Hands-On Machine Learning with Scikit-Learn, Keras, and TensorFlow,

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Patients

Number of patients	23
Clinical details	Median (range)
Gestational age (weeks)	28.3 (24 – 41.6)
Postnatal age (days)	3 (0 – 52)
Current weight (grams)	1,845 (560 – 3,965)
Primary clinical problem	
Respiratory failure	12
Surgical	10
HIE	1
Ventilation mode	SIPPV-VG (n=19) SIMV-VG (n=3) PSV-VG (n=1)

Manual annotation of 500 breaths from each patient	Total: 23 * 500 = 11,500 breaths
Training set	9000 breaths (18 patients)
Test set	2500 breaths (3 patients)

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Frequency of asynchronies

Category	Combined dataset		Development dataset		Test dataset	
	Count	Percentage	Count	Percentage	Count	Percentage
No asynchrony	4,628	40.24%	3,461	38.5%	1,167	46.8%
Expiratory work	3,586	31.2%	2,666	29.7%	920	36.8%
Late cycling	1,142	9.9%	956	10.6%	186	7.4%
Late triggering	683	5.9%	563	6.3%	120	4.8%
Failed triggering	491	4.3%	363	4.0%	128	5.1%
Multiple triggering	151	1.3%	77	0.9%	74	3.0%
Early triggering	141	1.2%	88	1.0%	53	2.1%
Early cycling	114	1.0%	96	1.1%	18	0.7%
Work shifting	53	0.5%	53	0.6%	0	0.0%

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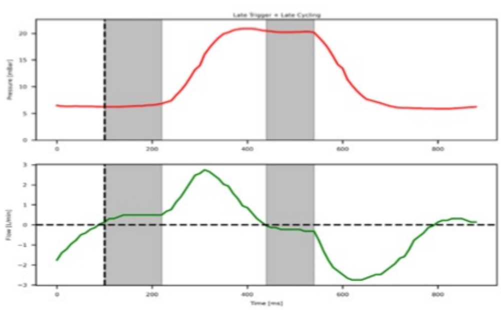
Some asynchronies occurred more or less frequently than expected

PVI pair	Odds ratio	P value
multiple triggering - early cycling	13.60	<0.000001*
multiple triggering - late cycling	9.00	<0.000001*
early triggering - failed triggering	6.97	<0.000001*
failed triggering - expiratory work	2.62	<0.000001*
late triggering - late cycling	2.23	<0.000001*
early cycling - expiratory work	2.15	0.00006*
multiple triggering - expiratory work	1.82	0.0004*
late cycling - expiratory work	0.66	<0.000001*
failed triggering - late cycling	0.54	0.0009*
early triggering - late cycling	0.40	0.02
early triggering - late triggering	0.00	0.0004*$



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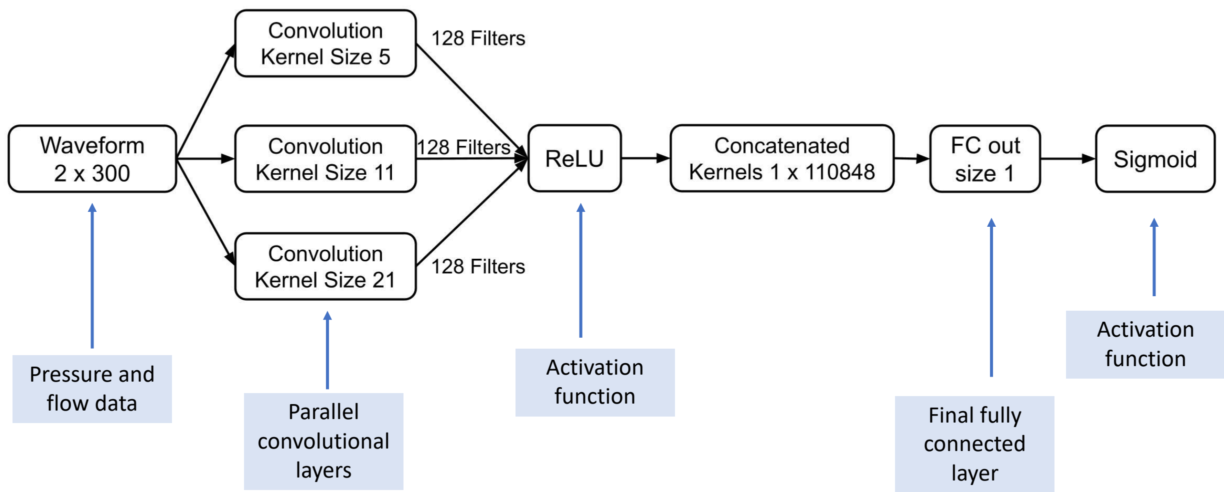
Our deep learning network



Deep learning classifier recognise patient-ventilator interaction with good sensitivity and specificity

Type of PVI	Test dataset			
	Sensitivity	Specificity	AUROC	F1 score
Early Triggering	0.857	0.996	0.968	0.809
Late Triggering	0.916	0.998	0.987	0.922
Failed Triggering	0.912	0.995	0.984	0.912
Multiple Triggering	0.917	0.999	0.997	0.917
Early Cycling	0.882	0.999	0.995	0.909
Late Cycling	0.969	0.966	0.99	0.9
Expiratory Work	0.961	0.957	0.987	0.934

AUROC = Area under the ROC curve

$$\text{F1 Score} = \frac{TP}{TP + \frac{1}{2}(FP + FN)}$$

Chong D, Belteki G. Detection and quantitative analysis of patient-ventilator interactions in ventilated infants by deep learning networks. *Pediatr Res*. 2024 Feb 5.

https://github.com/chongtwd/Detection-and-quantitative-analysis-of-patient-ventilator-interactions-in-ventilated-neonates

Summary

- Patient-ventilator interactions (PVIs) occur frequently in ventilated infants, affecting approximately half of ventilator inflations
- Different interactions are not independent from each other and they may affect the same respiratory cycle
- Deep learning classifiers can be developed to recognise PVIs with high sensitivity and specificity
- Automated identification of PVIs can facilitate clinical research as to their significance
- *I hope after this talk you will look at the ventilator screens more frequently…*

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Acknowledgements

- David Chong,
- Colin Morley
- Thomas Krüger, Kreske Brunckhorst (Dräger)
- Roland Hotz, Rainer Kühner (Acutronic, Vyaire)
- All doctors and nurses of NICU in Cambridge

www.github.com/belteki

https://www.researchgate.net/profile/Gusztav-Belteki

https://www.cambridgeperinatalgroup.org

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Thank you for your attention !

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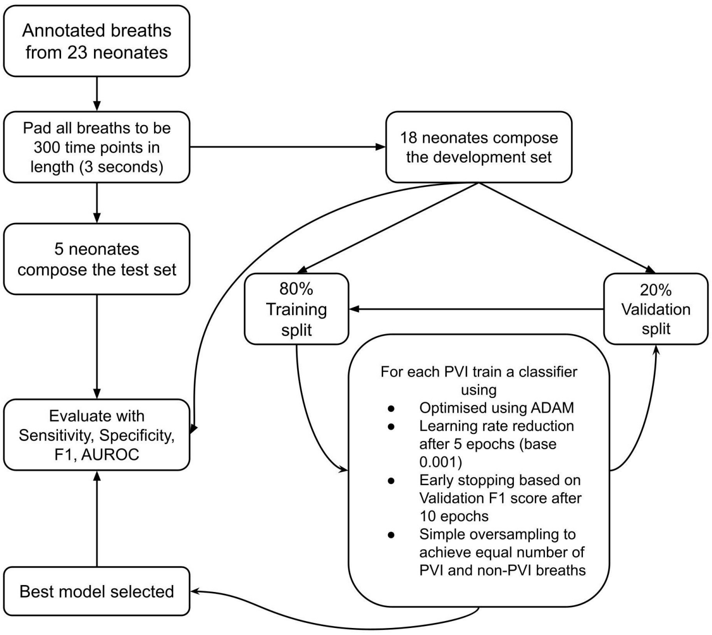

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