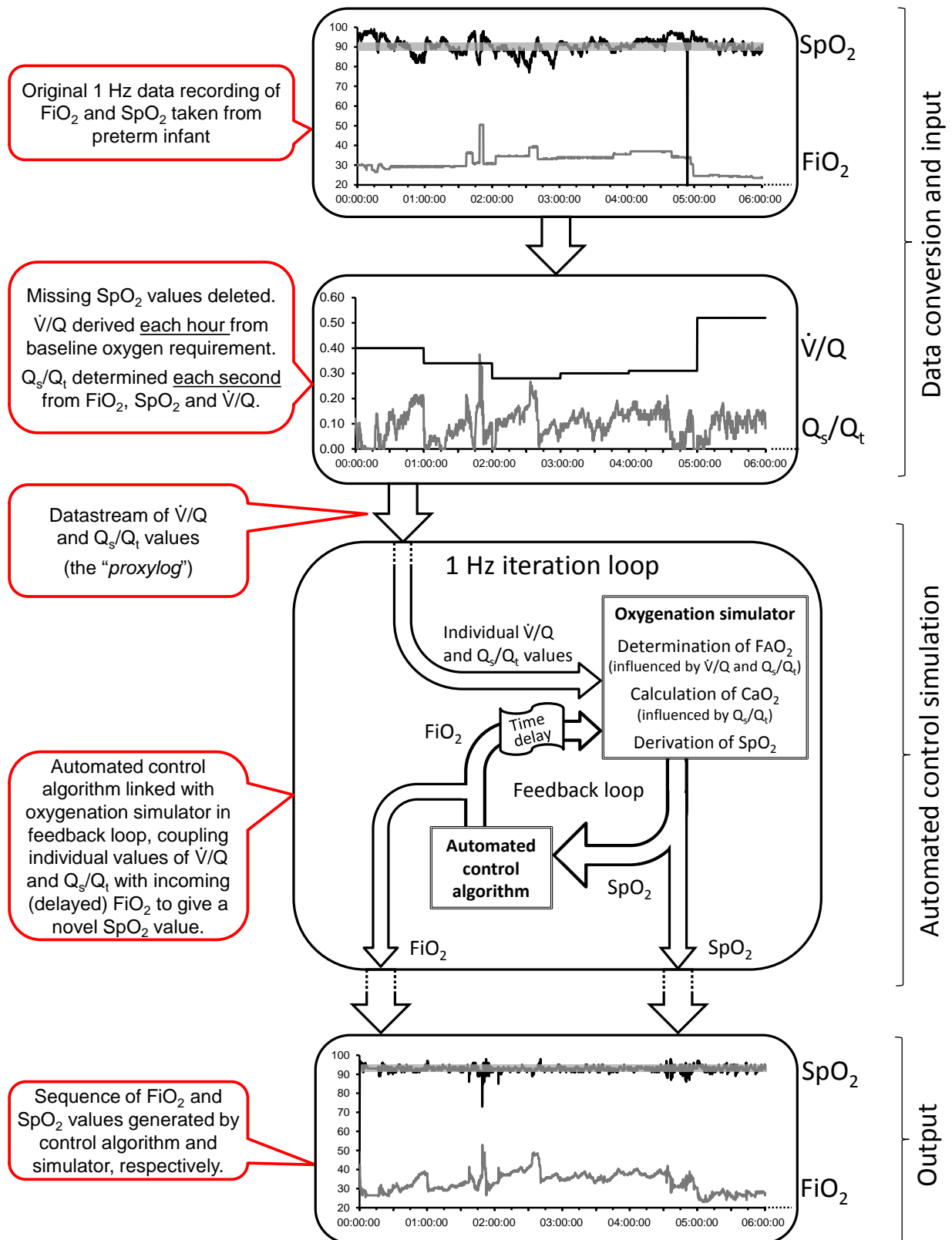


Development and pre-clinical testing of an adaptive algorithm for automated control of inspired oxygen in the preterm infant

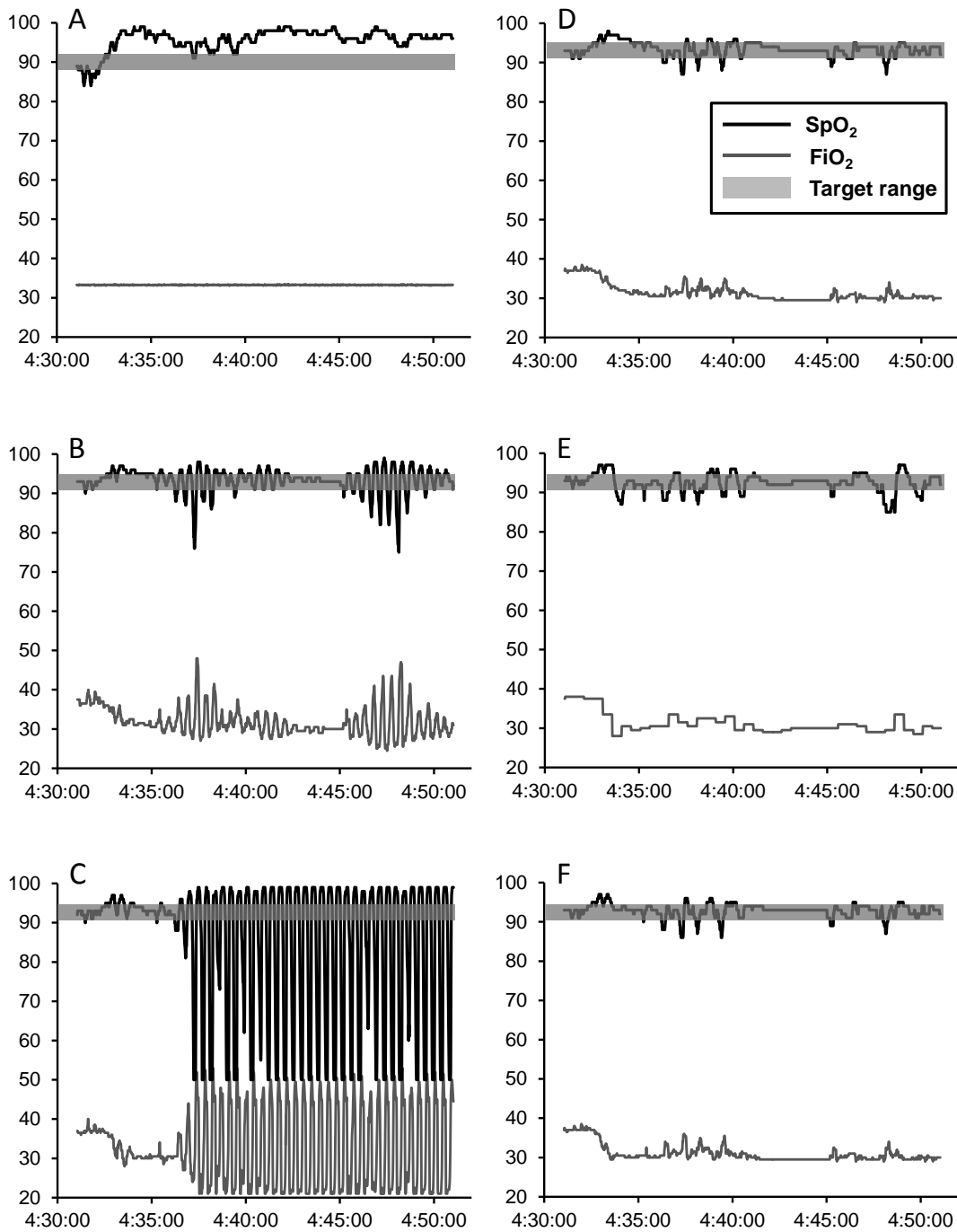
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ONLINE FIGURES



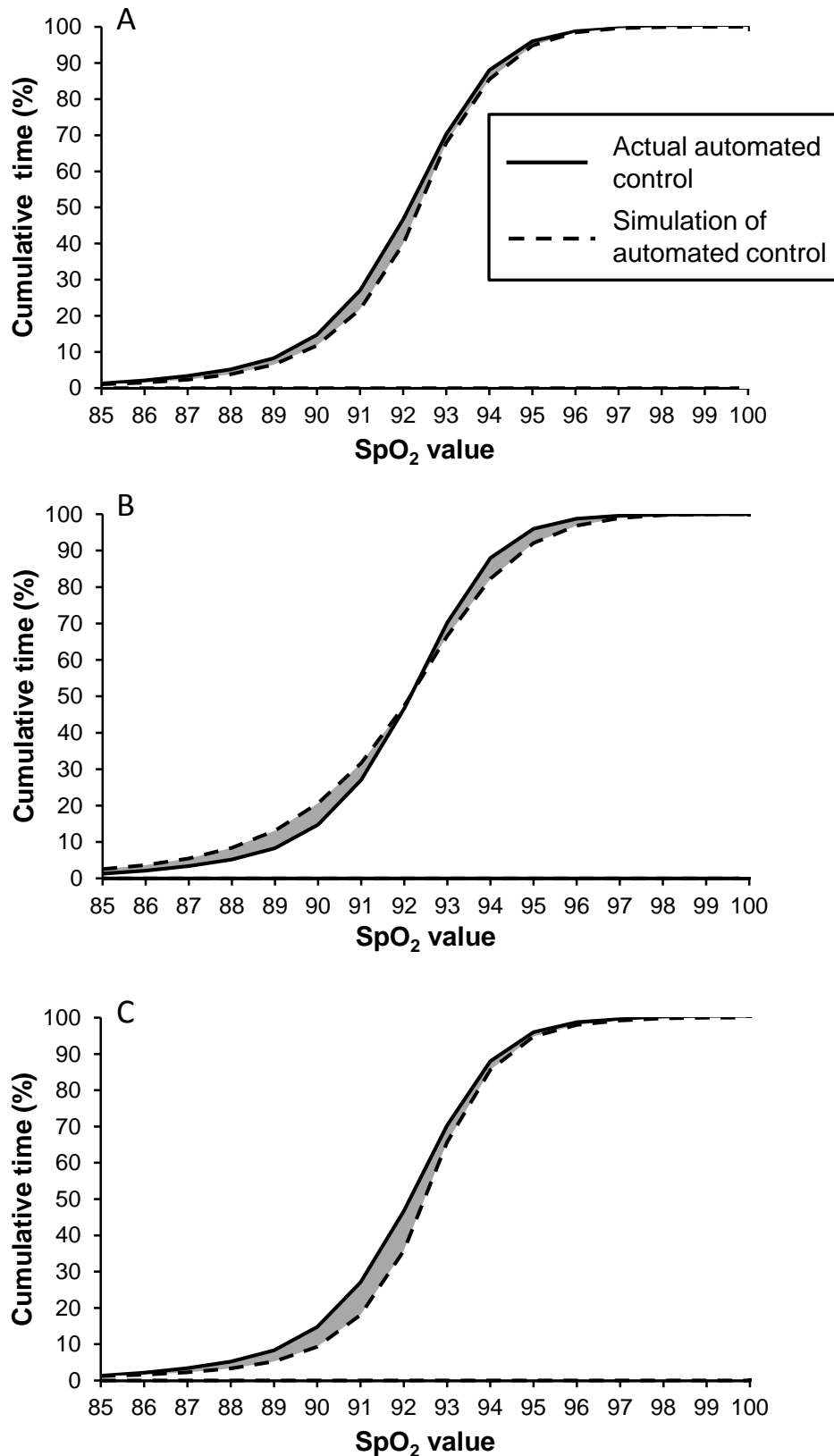
Online Figure 1. Algorithm evaluation using an oxygenation simulator

Diagrammatic representation of the approach to assessment of algorithm function. The original data recording (~24 h duration, 6 h depicted) is converted into a datastream of \dot{V}/Q and Q_s/Q_t values (the "proxylog"). The proxylog data in combination with an FiO_2 value from the control algorithm under test is then entered into the oxygenation simulation second by second. Calculations based on the alveolar gas equation lead to the generation of a novel value for SpO_2 each second, which is logged, and entered back into the algorithm thus closing the feedback loop. The new SpO_2 sequence, along with FiO_2 values from the algorithm, can then be analysed to evaluate the effectiveness of SpO_2 targeting.



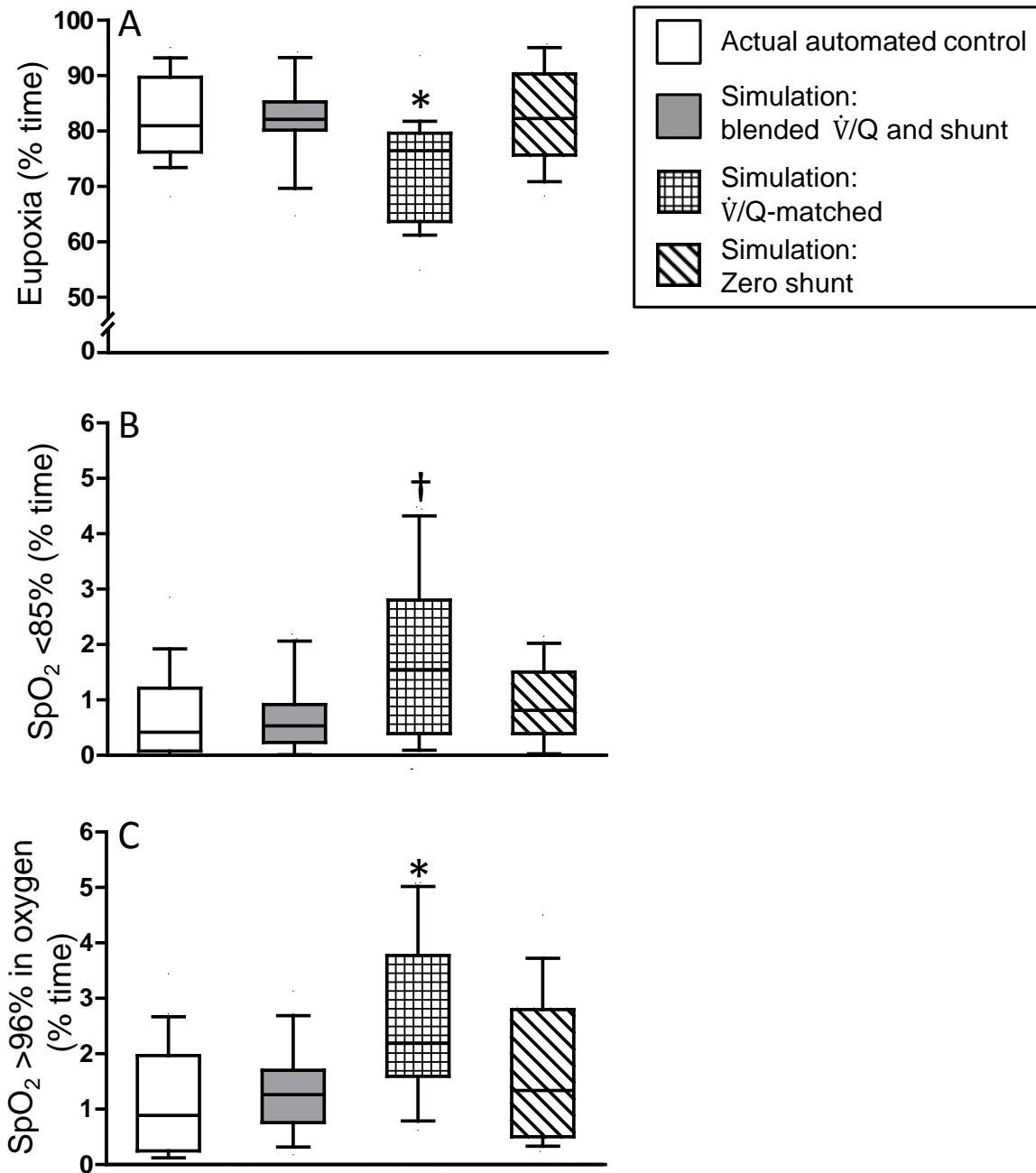
Online Figure 2. Examples of algorithm function

Sample 20 min recordings of SpO₂ (black line, Y-axis: % saturation) and FiO₂ (gray line, Y-axis: % oxygen). Gray band = SpO₂ target range. Panel A: original recording from an infant born at 24 weeks gestation, day 29, on high flow nasal cannula, SpO₂ target range 88-92%. No FiO₂ adjustment made, SpO₂ initially in hypoxaemic range, then fluctuating above target range. Panels B-F: simulation of automated oxygen control with different algorithms. B: Core PID algorithm without enhancing features. Eupoxia time 69%. Instability causing oscillation in SpO₂ with ~15 second periodicity noted at several points, induced by immoderate FiO₂ adjustments. C: Enhanced algorithm without K_p adaptation. Eupoxia time 32%. Substantial instability in SpO₂ control noted during the recording. D: Enhanced algorithm without Severinghaus compensation (and thus less rapid reduction in FiO₂ in response to high SpO₂ values). Eupoxia time 84%. An episode of prolonged hyperoxaemia (SpO₂ >96% for 41 seconds) is noted from 4:33:14. E: Enhanced algorithm with 30 second lockout after each FiO₂ adjustment. Eupoxia time 75%. F: Enhanced algorithm. Eupoxia time 90%.



Online Figure 3. Comparison of simulated and actual automated control – SpO₂ histograms

Cumulative SpO₂ histograms of pooled data from 20 preterm infants [Plottier et al, companion paper], with in each panel a comparison of the histogram derived from simulation of automated control with that of actual automated control using the same enhanced PID algorithm. See online supplemental text for further details. Panel A: Simulation using a blended \dot{V}/Q and shunt assumption in generating the proxylog file; panel B: simulation using a \dot{V}/Q -matched assumption; panel C: simulation using a zero shunt assumption. Shaded grey area: discrepancy between simulated and actual histograms. Values for this discrepancy in the group of 20 infants were greater for the zero shunt assumption than for the blended \dot{V}/Q and shunt assumption ($P < 0.05$, Friedman ANOVA with Dunn's *post hoc* test).



Online Figure 4. Simulated and actual automated control – SpO_2 targeting indices

Eupoxia time (panel A), time with $SpO_2 < 85\%$ (panel B) and time with $SpO_2 > 96\%$ in oxygen (panel C) compared between different simulations of automated oxygen control and also compared with actual values during automated control in preterm infants ($n=20$) using the same enhanced PID algorithm. Box: median and 25th and 75th centiles. Whiskers: 10th and 90th centiles. * \dot{V}/Q -matched result differs from all other values, $P < 0.05$, Friedman ANOVA with Dunn's *post hoc* test. † \dot{V}/Q -matched result differs from actual automated control and blended \dot{V}/Q and shunt simulation, $P < 0.05$.