

## **Supporting Information**

### **A step toward balance: thrombin generation improvement via procoagulant factor and antithrombin supplementation**

by Alexander Y. Mitrophanov, Fania Szlam, Roman M. Sniecinski, Jerrold H. Levy,  
and Jaques Reifman

**Table S1. Coagulation factor concentrations in the stock solutions.**

**A. Supplemental information about Factors II, FVII, FIX, FX and antithrombin.**

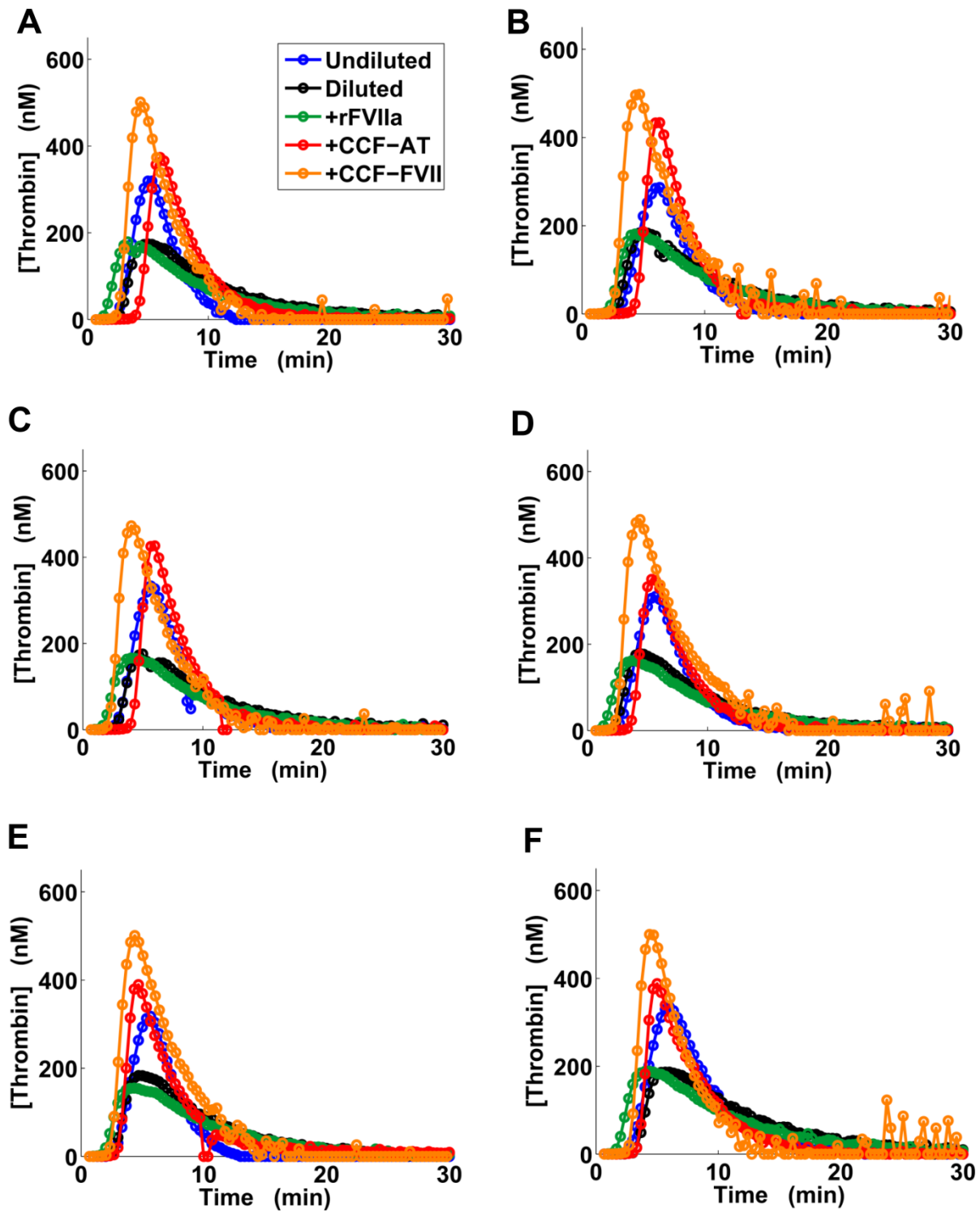
Protein (Human)	Concentration of stock solution (mg/mL)	Activity of stock solution (Units/mL)*	Average Baseline activity (%) of subject plasma	Average activity after 3-fold dilution (%)	Average activity of diluted plasma after treatment (%)	Corresponding clinical dose (Units/kg)&
Factor II	8.5	60.4	100.9	38.9	102.0	24.2
Factor VII	1.2	2584.8	117.4	43.7	115.4	28.7
Factor IX	5.3	945.0	114.9	36.0	119.0	30.8
Factor X	5.0	660.0	112.4	40.4	104.4	28.1
Antithrombin	8.4	60.5	111.4	37.5	104.4	28.8

\*One Unit activity = protein activity in one milliliter of normal plasma = 100% activity.

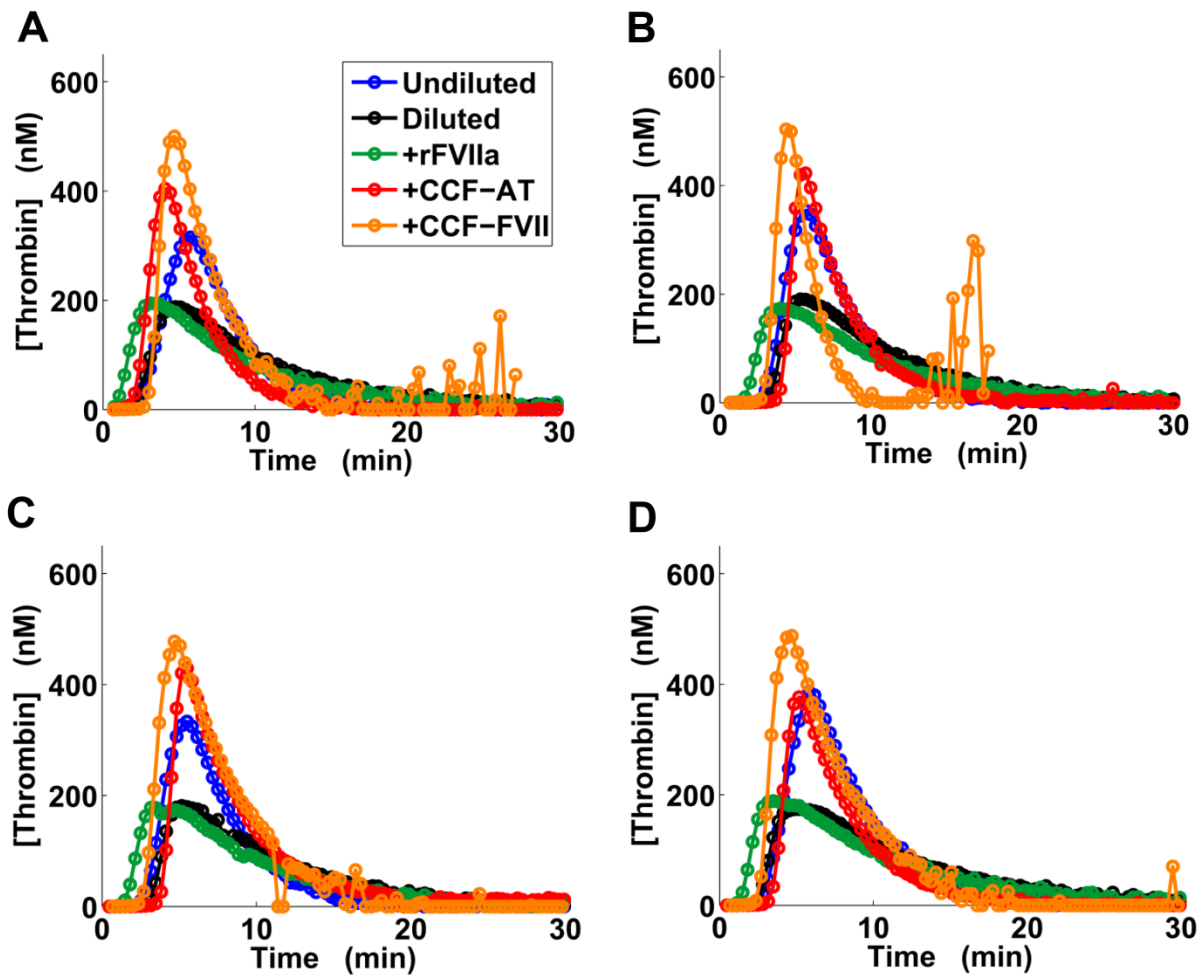
&Based on approximate plasma volume in normal subjects = 39 mL/kg.

**B. Supplemental information about rFVIIa.**

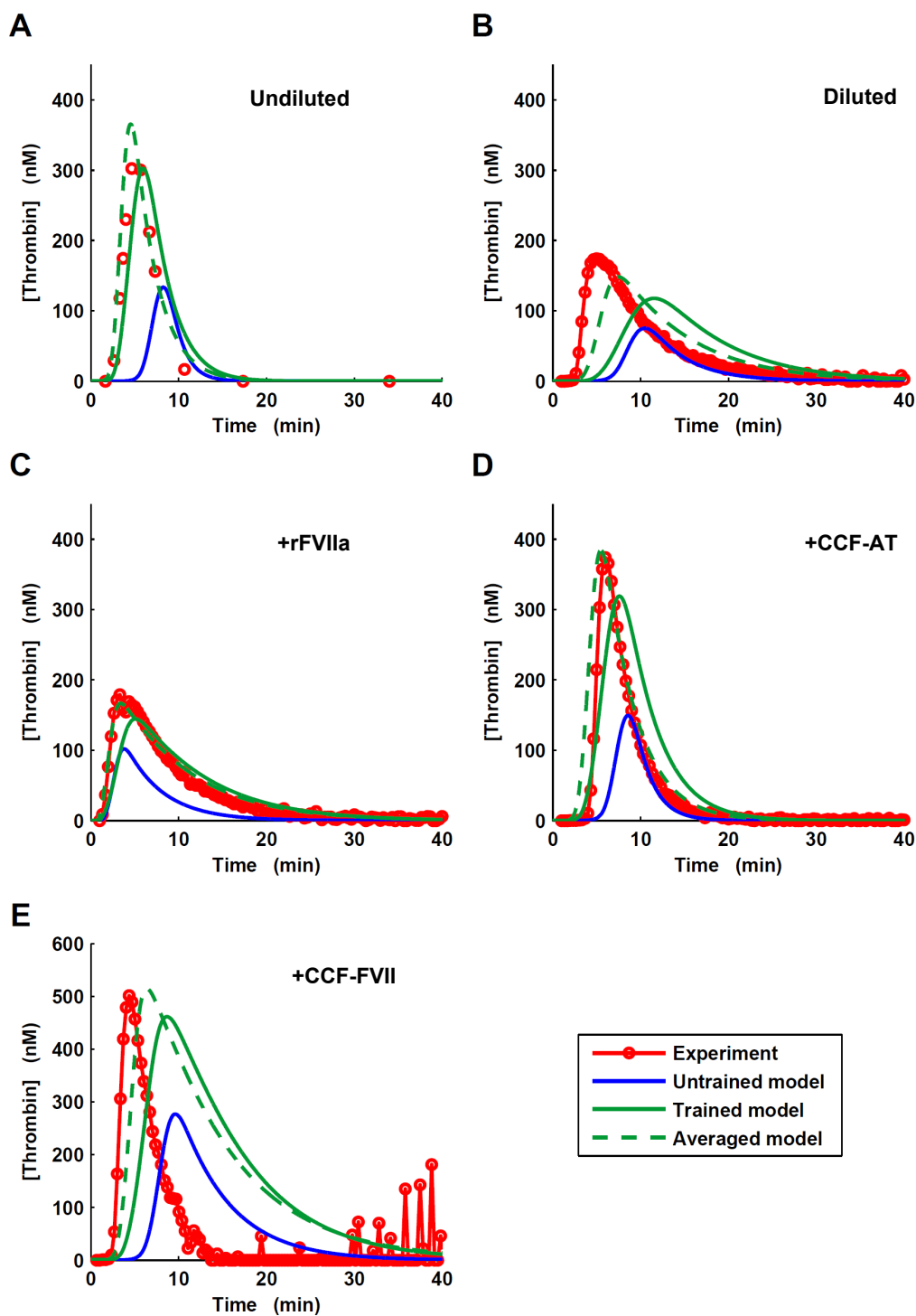
Protein	Concentration of stock solution mg/mL	Desired plasma Concentration (nM)	Corresponding Clinical dose µg/kg
rFVIIa	1.0	40.0	~90.0



**Fig. S1.** Thrombin generation trajectories for individual subjects. Shown are the raw Calibrated Automated Thrombogram trajectories for *subjects* #1-6 (A-F, respectively). The color of the trajectories represents the dilution/supplementation scenarios.

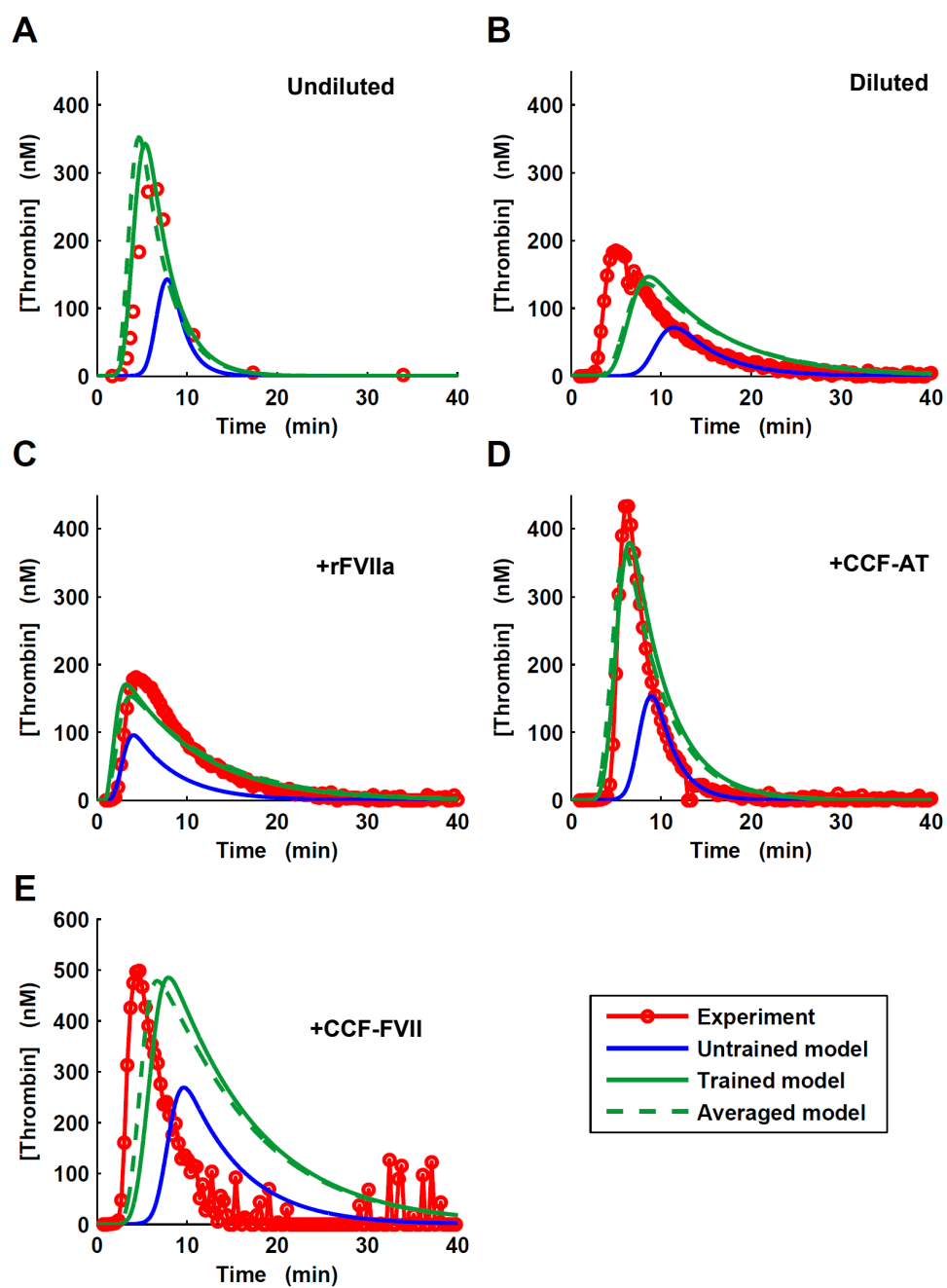


**Fig. S2.** Thrombin generation trajectories for individual subjects. Shown are the raw Calibrated Automated Thrombogram trajectories for *subjects* #7-10 (A-D, respectively). The color of the trajectories represents the dilution/supplementation scenarios.

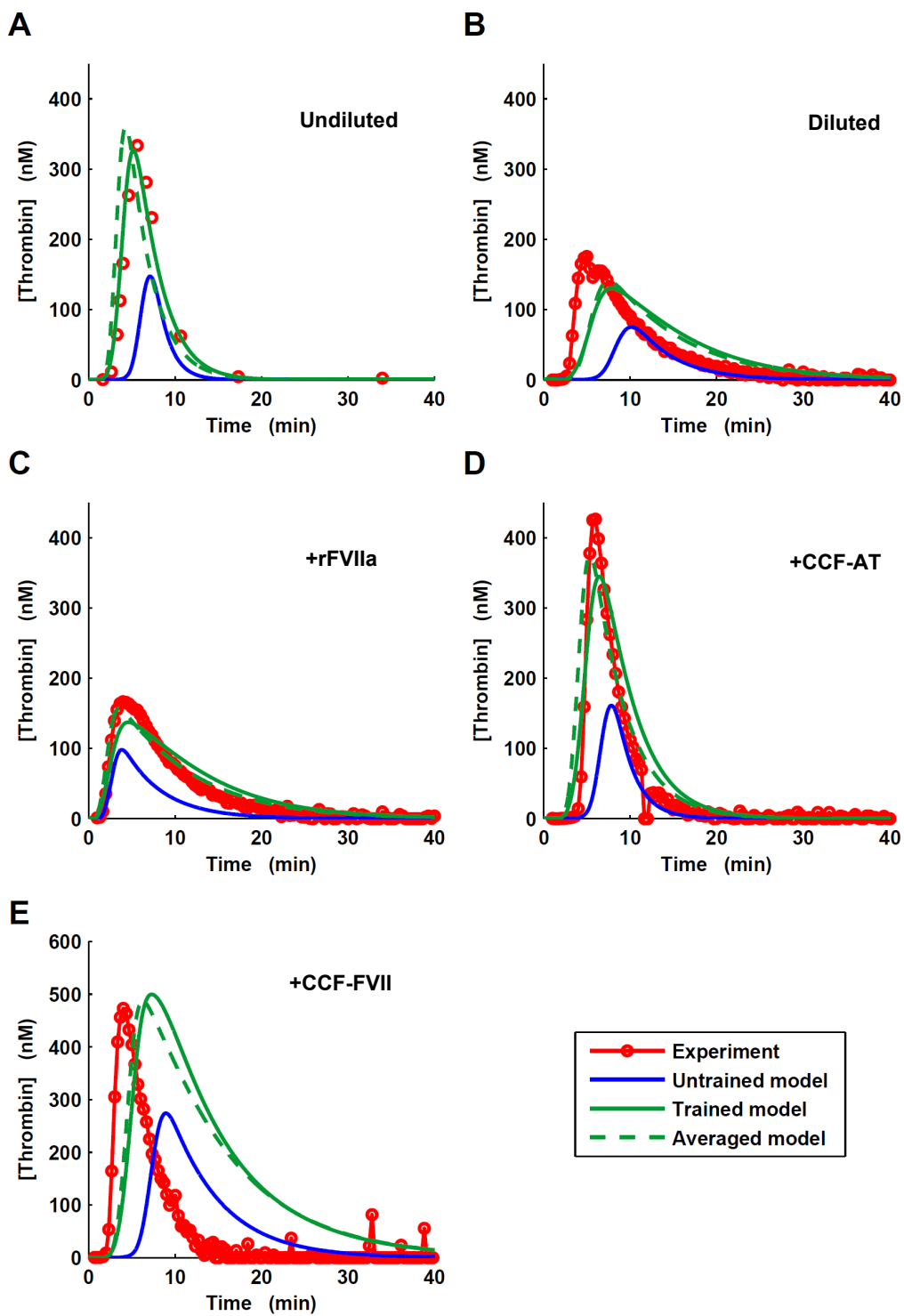


**Fig. S3.** Experimental data and modeling predictions for *subject #1*. Subplots *A-E* correspond to one of the following dilution/supplementation scenarios: undiluted plasma (*A*), diluted plasma (*B*), diluted plasma supplemented with rFVIIa (+rFVIIa, *C*), diluted plasma supplemented with CCF-AT (+CCF-AT, *D*), and diluted plasma supplemented with CCF-FVII (+CCF-FVII, *E*). The

experimental data (red circles and lines) are raw Calibrated Automated Thrombogram data for *subject #1* (Fig. S1A). For undiluted plasma (*A*), the red circles are not connected, which reflects the fact that these circles are selected data points forming a subset of all the measured points in the thrombin trajectory; this subset was used to train the model for other subjects. The blue lines (“untrained model”) show computational predictions obtained using the model before it was trained (i.e., the model with default kinetic parameter values). The green lines (“trained model”) show the predictions obtained using the model variant trained using the undiluted plasma thrombin generation data for *subjects #2-10* (Figs. S1-S2) as described in the Methods Section. The dashed green lines show the subject-specific predictions of the averaged-parameter model.

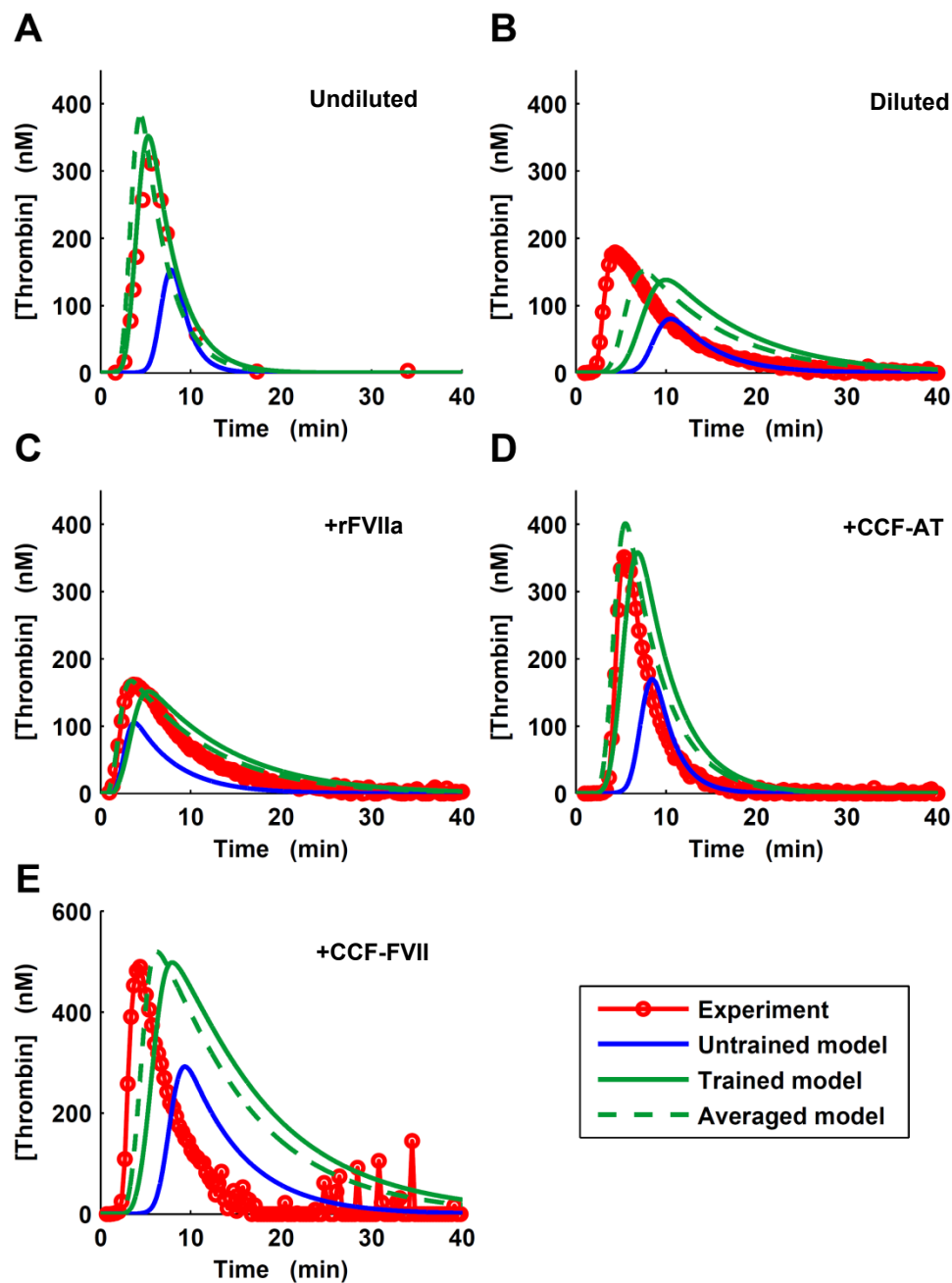


**Fig. S4.** Experimental data and modeling predictions for *subject #2*. The line designations are analogous to those in Fig. S3.

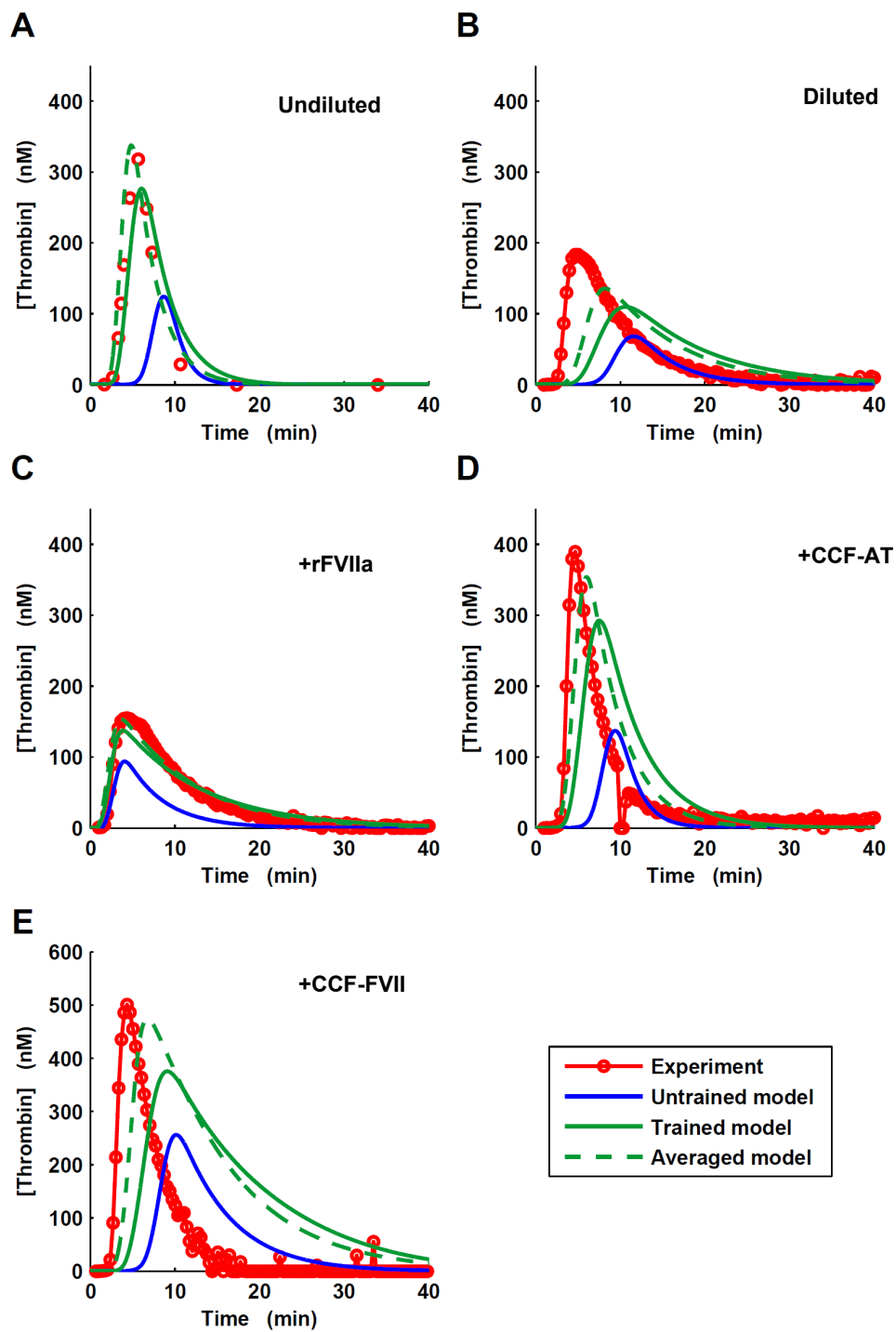


**Fig. S5.** Experimental data and modeling predictions for *subject #3*. The line designations are analogous to those in Fig. S3.

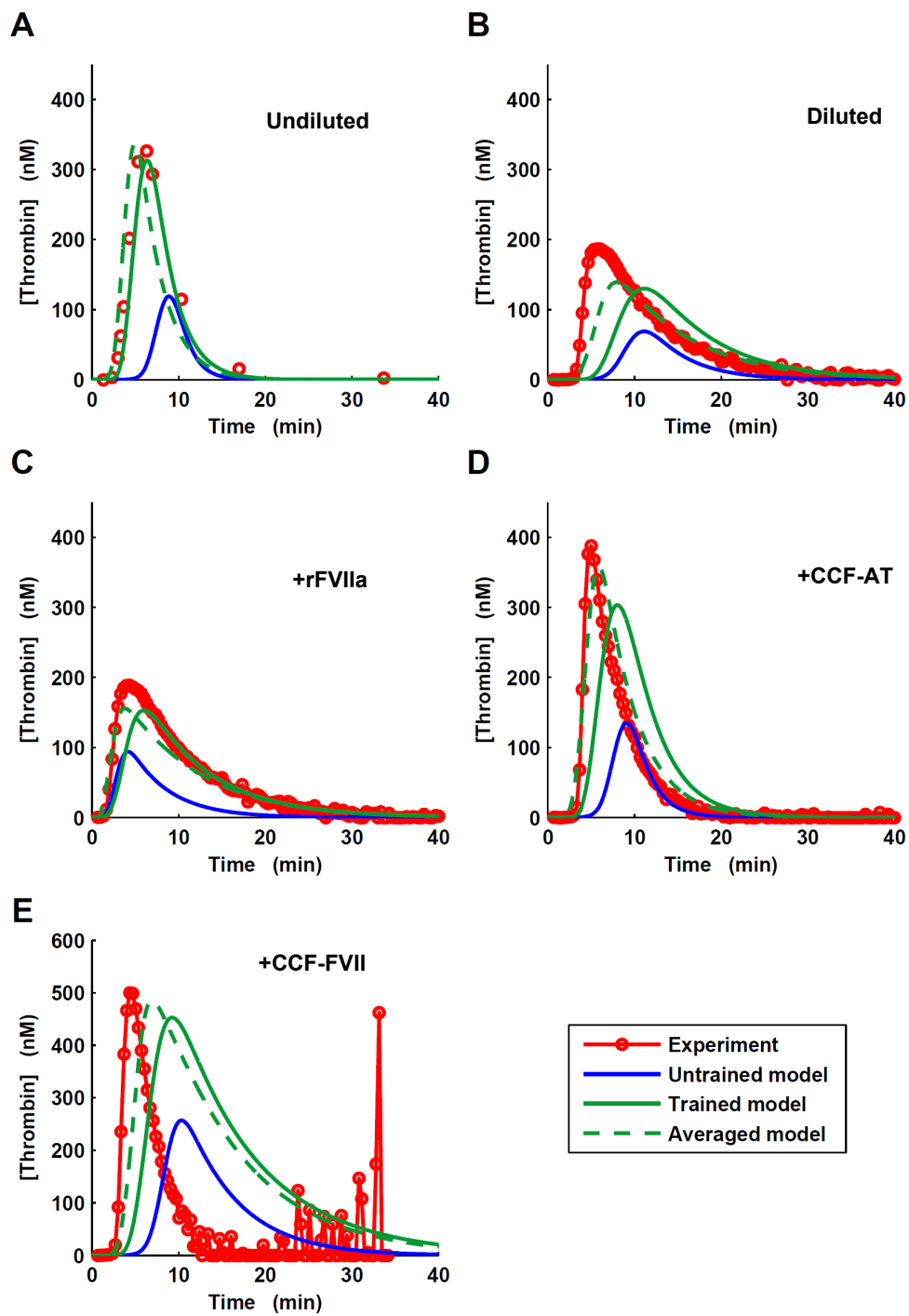




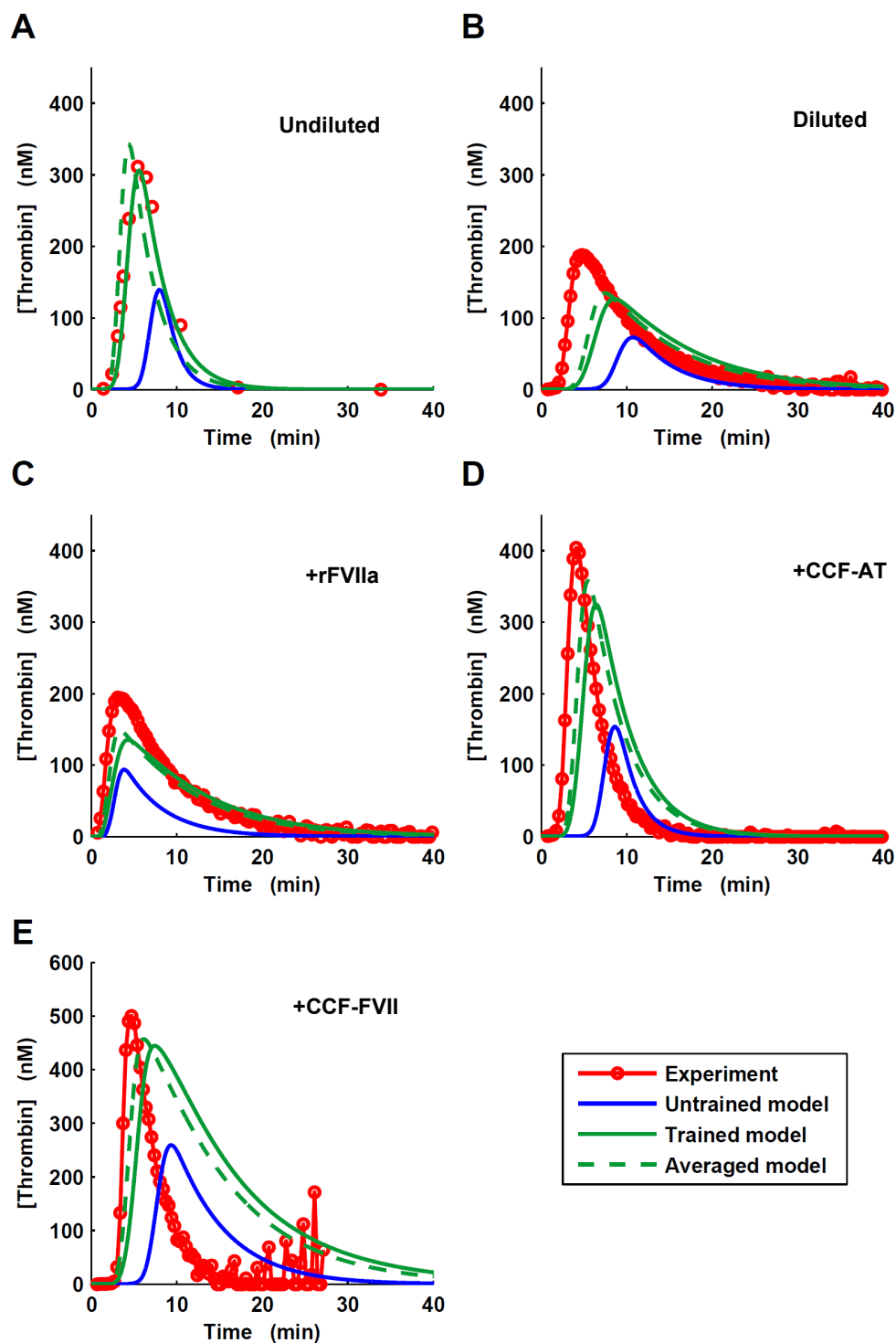
**Fig. S6.** Experimental data and modeling predictions for *subject #4*. The line designations are analogous to those in Fig. S3.



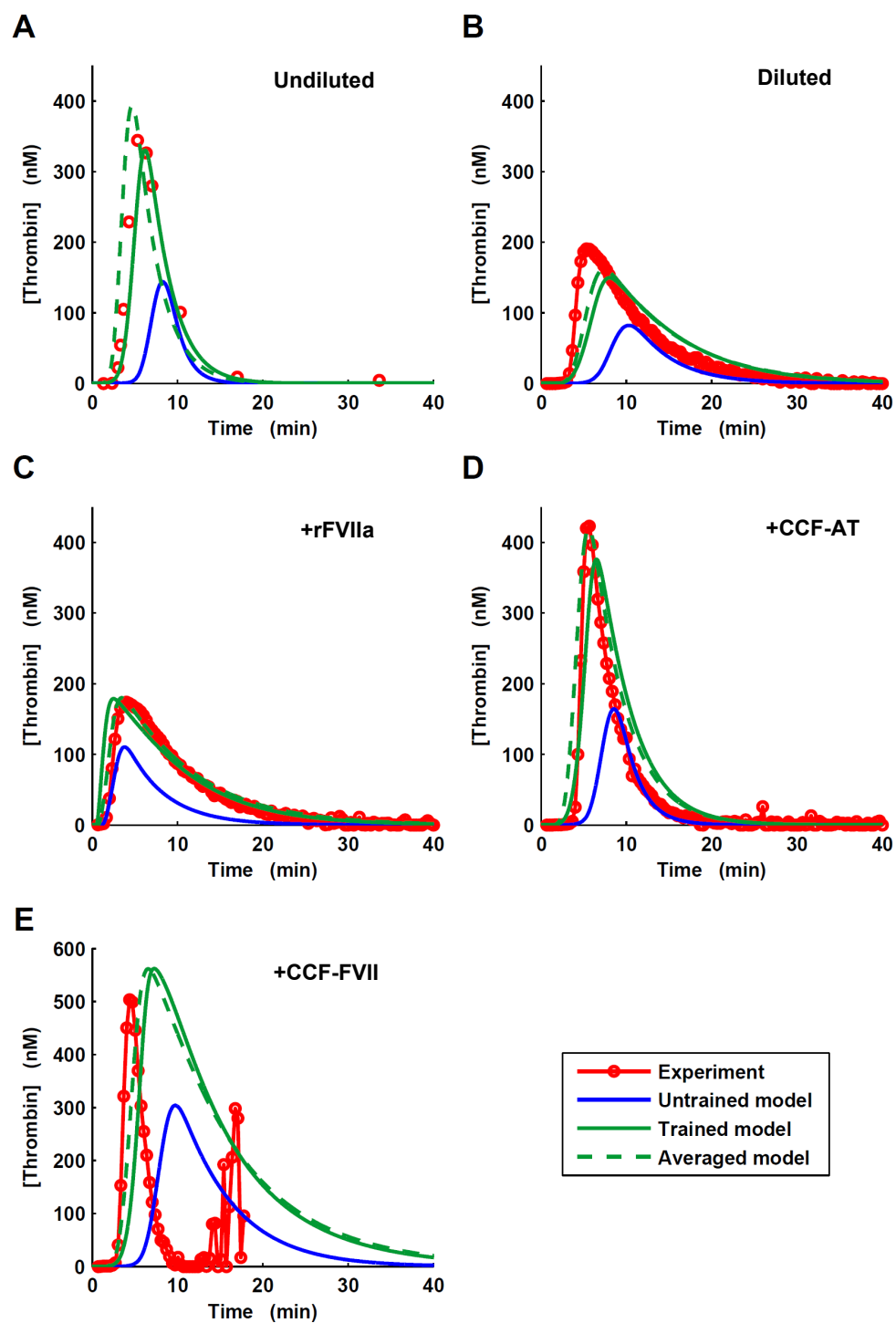
**Fig. S7.** Experimental data and modeling predictions for *subject #5*. The line designations are analogous to those in Fig. S3.



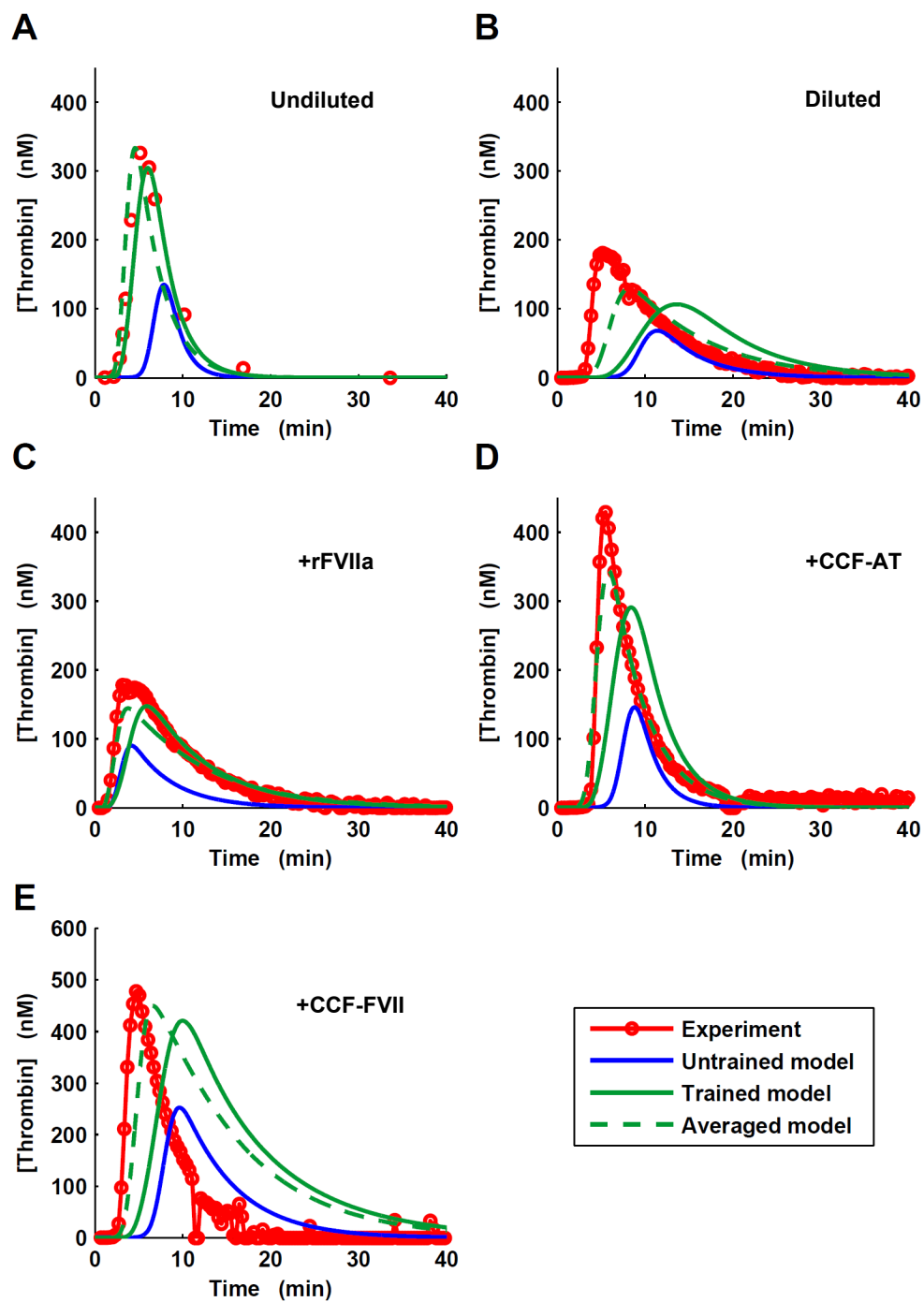
**Fig. S8.** Experimental data and modeling predictions for *subject #6*. The line designations are analogous to those in Fig. S3.



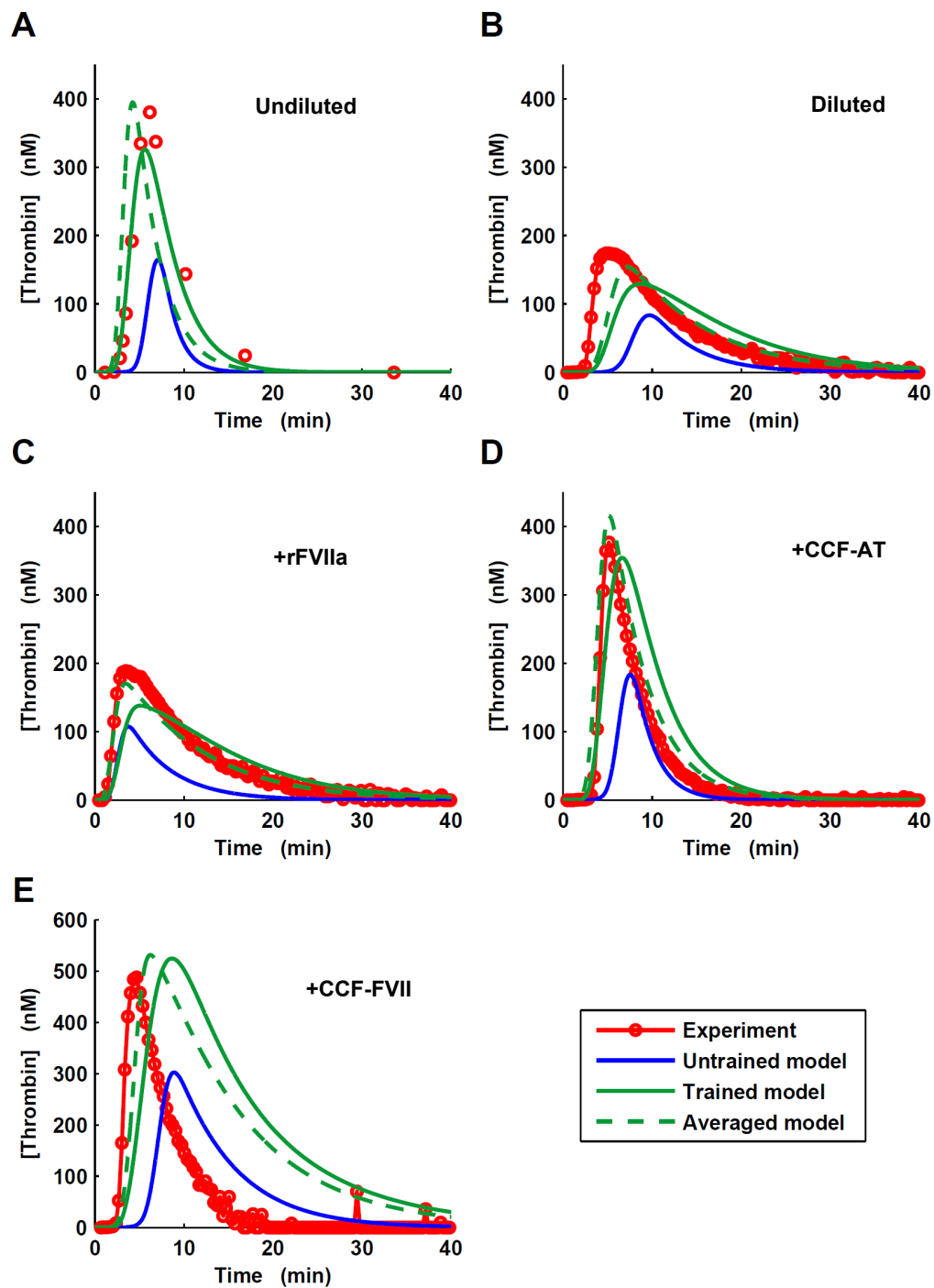
**Fig. S9.** Experimental data and modeling predictions for *subject* #7. The line designations are analogous to those in Fig. S3.



**Fig. S10.** Experimental data and modeling predictions for *subject #8*. The line designations are analogous to those in Fig. S3.



**Fig. S11.** Experimental data and modeling predictions for *subject #9*. The line designations are analogous to those in Fig. S3.



**Fig. S12.** Experimental data and modeling predictions for *subject #10*. The line designations are analogous to those in Fig. S3.