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## Claims

### Independent Method Claim

1. *A method for real-time control of a plasma-protein precipitation batch, the method comprising:*

1. **circulating** a slip-stream of a precipitation vessel through an at-line sensor loop;
2. **collecting signals** from at least one optical solids-proxy sensor and at least one non-optical solids-proxy sensor selected from the group consisting of: turbidity, ultrasonic attenuation, acoustic resonance frequency shift, dielectric spectroscopy, laser-diffraction particle-size analysis, and ultraviolet absorbance at approximately 280 nm;
3. **computing** a fused precipitation-percentage estimate  $\hat{P}\%$  by weighting the collected signals according to a confidence model;
4. **comparing**  $\hat{P}\%$  with a target set-point;
5. **adjusting** a dosing rate of a precipitating agent responsive to said comparison by modulating a flow or duty-cycle of a reagent pump according to a control algorithm; and
6. **verifying filtration readiness** by monitoring a trans-membrane-pressure slope of a filtration unit that receives liquor from the precipitation vessel, and selectively **recycling** the liquor to the precipitation vessel when the slope exceeds a predetermined threshold.

### Dependent Claims

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Limitation (maps to embodiment)

2. The method of claim 1, wherein the optical solids-proxy sensor further comprises an ultraviolet absorbance detector measuring protein concentration in a clarified side stream obtained through a micro-filter of nominal pore size not greater than 0.45  $\mu\text{m}$ . (E-2)
3. The method of claim 1, wherein the non-optical solids-proxy sensor comprises an ultrasonic time-of-flight attenuation meter operating between 2 MHz and 10 MHz. (E-1)

4. The method of claim 1, wherein the non-optical solids-proxy sensor comprises an in-tank acoustic resonance probe having a fundamental frequency between 30 kHz and 45 kHz. (E-3)
5. The method of claim 1, wherein the fused precipitation-percentage estimate further incorporates a dielectric phase-angle measurement obtained from a disposable dielectric-spectroscopy cartridge positioned in the slip-stream. (E-4)
6. The method of claim 1, wherein the fused precipitation-percentage estimate further incorporates a particle-size distribution obtained from a laser-diffraction scattering cell positioned in the slip-stream. (E-5)
7. The method of claim 1, wherein the adjusting step is executed by a model-predictive controller that optimizes a multi-variable state-space model of the precipitation kinetics subject to reagent-concentration and temperature constraints. (E-6)
8. The method of claim 1, wherein the adjusting step is executed by a rule-based look-up table derived from a design-of-experiments process-qualification study. (E-7)
9. The method of claim 1, wherein the dosing rate is applied as a pulse-width-modulated flow having a carrier frequency of 5 Hz to 15 Hz and a minimum pulse width of 50 milliseconds. (E-10)
10. The method of claim 1, further comprising a dual-stage precipitation sequence in which a first stage adjusts pH to between 4.9 and 5.3 and a second stage meters polyethylene glycol at a concentration between 4 % and 10 % w/v. (E-11)
11. The method of claim 1, wherein the precipitation vessel jacket is temperature-ramped from below 0 °C to above 5 °C while dosing the precipitating agent, and the control algorithm compensates the fused precipitation-percentage estimate for temperature dependence. (E-12)

12. The method of claim 1, further comprising detecting sensor anomalies using a machine-learning classifier trained on historical batch data and, upon detecting an anomaly, switching the control algorithm to a predefined fallback dosing recipe. (E-8)
  13. The method of claim 1, wherein the verifying step further comprises calculating the slope of the trans-membrane pressure under constant-flux filtration and permitting advancement only when the slope is less than or equal to 5 kPa min<sup>-1</sup>. (E-9)
  14. The method of claim 1, wherein at least one solids-proxy sensor performs an automated self-calibration by routing a zero-calibration fluid through the sensor path at intervals not greater than 30 minutes. (E-14)
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### **Claim 15 – Independent Apparatus (System) Claim**

15. *An apparatus for real-time control of a plasma-protein precipitation batch, the apparatus comprising:*

1. **a precipitation vessel** (T-101) configured to receive a plasma-protein solution and equipped with an agitator and a temperature-controlled jacket;
2. **a slip-stream loop** comprising an isolation valve (XV-301), a sanitary circulation pump (P-201), and a flow cell (FC-301);
3. **at least one optical solids-proxy sensor** housed in the flow cell and selected from the group consisting of a turbidity sensor (NTU-301), a laser-diffraction scattering detector, and an ultraviolet absorbance detector (UV-401);
4. **at least one non-optical solids-proxy sensor** housed in the flow cell or precipitation vessel and selected from the group consisting of an ultrasonic attenuation sensor (US-302), an acoustic resonance probe (803-1), and a dielectric spectroscopy cartridge (804-1);
5. **a reagent-dosing subsystem** comprising a reagent reservoir, a metering pump (PD-202), and a controllable duty-cycle or flow-rate actuator;
6. **a filtration unit** downstream of the precipitation vessel and comprising pressure sensors (PT-501A, PT-501B) configured to measure a trans-membrane pressure; and

7. **a programmable controller** (FUS-900) operably coupled to the optical and non-optical sensors, the metering pump, and the pressure sensors, the programmable controller being configured to:
    1. compute a fused precipitation-percentage estimate  $\hat{P}\%$  from the sensor signals;
    2. compare  $\hat{P}\%$  with a target set-point and modulate the metering pump accordingly; and
    3. determine filtration readiness by evaluating a slope of the trans-membrane pressure and actuating a recycle valve (XV-403) when the slope exceeds a predetermined threshold.
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### **Claim 16 – Independent Computer-Readable-Medium (CRM) Claim**

**16.** *A non-transitory computer-readable medium storing instructions that, when executed by one or more processors, cause the processors to perform operations comprising:*

1. **receiving** a first solids-proxy signal from an optical sensor and a second solids-proxy signal from a non-optical sensor that monitor a plasma-protein precipitation batch;
2. **generating** a fused precipitation-percentage estimate  $\hat{P}\%$  by weighting the first and second signals according to a confidence model;
3. **determining** a control error by comparing the fused precipitation-percentage estimate to a target set-point;
4. **outputting** a control command that adjusts a dosing rate of a precipitating agent in response to the control error;
5. **receiving** pressure data from a filtration module and calculating a trans-membrane-pressure slope; and
6. **outputting** a recycle command to return batch liquor to the precipitation vessel when the trans-membrane-pressure slope exceeds a threshold.