FIGURES:

The invention is further illustrated by the following figures, which are incorporated into the specification and support the enablement of the disclosed embodiments:

- **FIGURE 1:** Cytokine Dosing Logic Circuit
  A schematic illustrating the AI-guided cytokine modulation system, including sensor inputs, phenotype analysis pathways, and decision tree logic for IL-2, IL-7, IL-15, and IL-21 delivery.
- **FIGURE 2:** Bioreactor System Architecture
  A diagram showing the layout of the sterile closed-loop bioreactor, with cytokine infusion lines, sampling loops, inline filters, and tubing cassettes.
- **FIGURE 3:** Lysate Personalization and Antigen Timing Flow
  A process map for preparing, validating, and applying tumor lysates in immune education cycles, based on antigen profiling and immune response metrics.

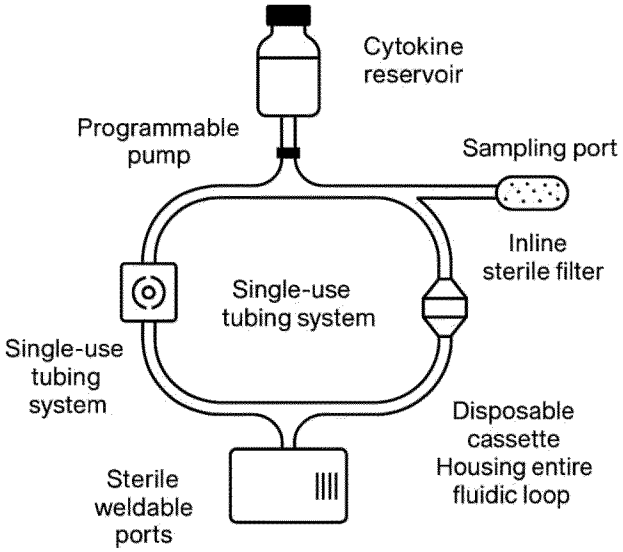

Figure 1
Tubing Layout Diagram

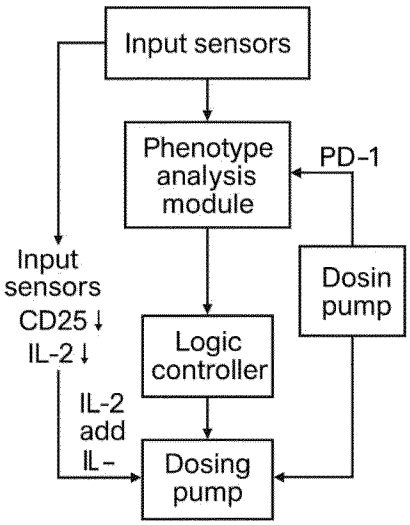

FIGURE 2
Batch execution and sensor feedback flowchart

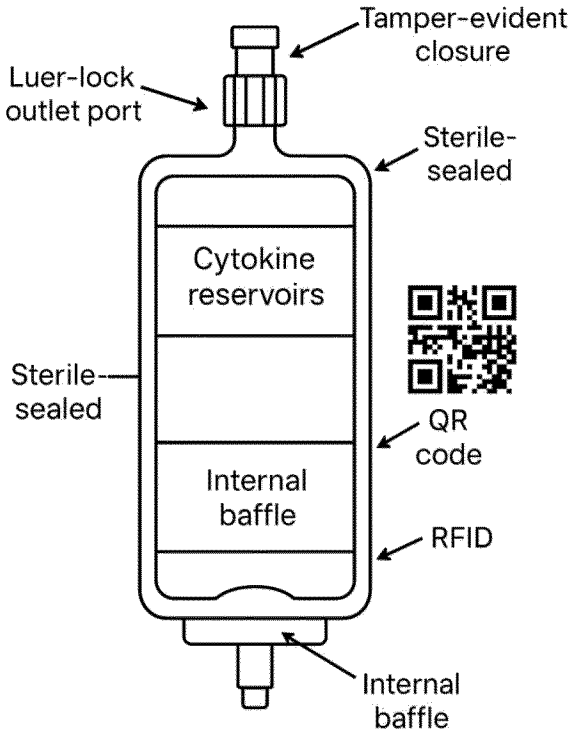

Figure 3
Cytokine Cartridge with QR/RFID and Baffle System

Input Signal	Interpretation	Cytokine / Intervention Recommendation	Titration Logic / Adjustment
CD8+ T cell low, CD4+ high	Effector cytotoxic response needs boosting	IL-2 (low), IL-15, IL-21	Monitor CD8+/CD4+ ratio increase; reduce IL-2 if CD25+ spikes
NK cells CD56dim low	Poor innate cytotoxicity	IL-15, IL-12	Increase IL-15 if IFN-γ stays low in culture
Tregs (CD25+FoxP3+) high	Immune suppression likely	Avoid IL-2; add IL-12, IFN-γ	Monitor Treg decline; IL-21 if rebound occurs
High PD-1+, TIM-3+ expression	Exhausted T cells	IL-21, low IL-2	Add IL-21 if granzyme B low; reduce IL-2 if CD107a absent
CD107a− / IFN-γ− low	Poor cytotoxic function	IL-21 or IL-12	Confirm granzyme B / perforin on Day 6
CD25+ rapidly rising (Day 2–4)	T cell overdrive or Treg surge	Reduce IL-2, maintain IL-15	Short IL-21 pulse or anti-CD25 mAb ex vivo
CD45RO+ memory phenotype lacking	Weak memory T cell formation	IL-7 + IL-21 (Day 4+)	Assess memory phenotype on Day 8
Strong IFN-γ gene signature	Inflamed tumor, checkpoint susceptibility	IL-15, IL-21 + PD-1 inhibitor	Focus CD8+ expansion; taper IL-2 if Tregs expand
Serum IL-6 / IL-10 elevated	Mixed inflammation / suppression	Avoid IL-2; add IFN-γ + GM-CSF	Titrate by IL-6 decay + CRP levels
Cold tumor (low MHC, low TILs)	APC induction needed	GM-CSF + IL-12	Monitor CD83/CD86 in culture
High TGF-β, VEGF, Gal-9	Immunosuppressive tumor microenv.	IFN-γ, IL-21; avoid IL-2	Consider HDACi or TGF-β inhibitor
Lactate ↑	Metabolic overactivation	Reduce cytokines globally	pH correction; IL-2 pause if acid persists
Glucose ↓	Energy stress / exhaustion risk	Add fresh nutrients, pause IL-2	Trigger nutrient feed if < 0.5 g/L
Ammonia ↑	Glutamine breakdown toxicity	Medium exchange or dilution	Pause cytokine feed; correct pH if needed
pH < 7.0	Culture acidosis	Hold cytokine dosing	Alert operator if uncorrected for >2 hours
DO < 40%	Hypoxic suppression	Boost IL-7 or switch to IL-21	Resume normal flow if DO stabilizes
High checkpoint ligands (PD-L1, Gal-9)	Tumor-induced exhaustion	IL-21 + IFN-γ; reduce IL-2	Trigger checkpoint logic only if CD8+ low
Extracellular vesicle (EV) spike	Hidden exhaustion / overactivation	Add IL-12 pulse or antigen delay	Reduce lysate dose if EVs + exhaustion markers
Low CD69/CD25 after lysate	Poor antigen education	Boost lysate or add APC co-culture	Resume IL-2 after rest period

EXTENSION: APPLICATION TO PLASMA FRACTIONATION

Adaptive Logic for Fractionation Skid Control

This invention further extends to the domain of plasma fractionation, wherein feedback-controlled process parameters are dynamically adjusted in real time during manufacturing of plasma-derived therapeutic proteins, including but not limited to IVIG, albumin, clotting factors, antithrombin, and immunomodulators.

Fractionation Control Inputs and Logic

The system includes sensors and logic modules that detect:

- Protein precipitation yield (e.g., for IgG or albumin)
- Ethanol concentration
- Temperature and pH stability
- Turbidity and viscosity during centrifugation or depth filtration
- Osmolality of buffers and product streams
- Viral inactivation completion markers

Adaptive Fractionation Logic Table

Input Signal	Interpretation	Adjustment	Trigger Logic
Protein yield < expected	Incomplete precipitation	Adjust ethanol %, temp, or mix time	Loop/recycle stage until yield $\geq$ threshold
IgG purity < 90%	Co-elution with albumin	Shift pH or chromatographic gradient	Select alternative resin or cut step
Osmolality high	Excess salt or solvent	Trigger diafiltration or dilution	Hold transfer until resolved
pH drift > ±0.3	Buffer degradation	Auto-titrate	Stop pump if unresolved after 5 min
Turbidity ↑	Aggregates or particulates	Add buffer or trigger filter switch	Clean loop if unresolved in 2 attempts
Viral inactivation check failed	Conditions insufficient	Repeat hold step	Lockout batch until completed