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Modeling and simulation of continuous production of L (+) glutamic acid in a membrane-integrated bioreactor

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ABSTRACT

Modelling and simulation of direct and continuous production of L (+) glutamic acid under non-neutralizing conditions in a membrane-integrated bioreactor was done. The model describes a green and continuous process using sugarcane juice as a cheap and renewable carbon source for its microbial conversion to glutamic acid. Provisions of continuous withdrawal of product and downstream separation and recycle of microbial cells and unconverted carbon source allowed sustained production without pH adjustment. Appropriate microfiltration and nano-filtration membrane modules did the separation job efficiently. The model developed with extended Nernst-Planck approach captured the relevant transport phenomena along with fermentation kinetics under substrate-product inhibitions. Performance of the model is well reflected in low relative error (<0.05), high Willmott index ($d > 0.97$) and high overall correlation coefficient ($R^2 > 0.98$). The modelled system produced glutamic acid with a productivity of 8.2 g/(L h) and yield of 0.95 g/g at a reasonably high flux of 75 L/(m^2 h) under a transmembrane pressure of only 14–15 bar. The final product was obtained at a concentration of 55 g/L and could easily be concentrated further by an additional nanofiltration step.

1. Introduction

Amino acids like L-glutamic acid (GA) are widely used for human and animal nutrition, as ingredients of pharmaceutical products, cosmetics, agrochemicals and several other industrial derivatives. The demand for amino acids in the world market is in the magnitude of 10^6 tons/year [1]. Conventionally amino acids have been produced by protein hydrolysis, microbiological fermentation, chemical synthesis, and enzymatic process. Efforts towards development of fermentative process for production of GA through isolation of L-glutamic acid-producing bacteria [2–4] have been quite significant in the recent years. Immobilization method of whole microbial cells has also been tried in calcium alginate or agar for continuous production of GA, but the product concentration remains low due to leakage of cells, inefficient mass transfer and lack of general matrix for immobilizing different cells [5]. Reported investigations of GA production mostly concentrate on using finished raw materials rather than a renewable or low cost waste material as carbon source [6]. In the back drop of prevailing low price of sugar cane in the major sugar cane growing countries (India, Brazil), large scale use of sugar cane juice as a clean, renewable carbon source for fermentative production of organic and amino acids holds the great promise of economic uplift of the millions of distressed sugarcane growers [7]. Efficient separation of other impurities from the fermentation broth is essential during downstream purification to produce monomer grade GA. Conventional purification schemes involve a number of downstream treatment steps like precipitation, filtration, acidification, neutralization, carbon adsorption and crystallization [2]. However conventional batch fermentation suffers from high labour cost due to frequent shutdown and start-up of batch process, low volumetric productivity and product-substrate inhibition. Moreover, such production processes are not eco-friendly and product purity and productivity are often compromised. Instead of direct production of acid, most of the investigated production schemes produce salt of the acid in pH-controlled regime necessitating further treatments with acids and alkalis to regenerate acid.

GA is produced through aerobic process of fermentation using *Corynebacterium* or *Brevibacterium* strains collectively known as *Corynebacterium glutamicum* [8]. Batch or fed-batch fermentation process is normally used for the commercial production of GA or

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Nomenclatures

Microbial kinetics and continuous fermentation

K_d	cell death rate constant (h^{-1})
$K_{d,glu}$	cell death rate constant while using glucose substrate (h^{-1})
$K_{d,fru}$	cell death rate constant while using fructose substrate (h^{-1})
$K_{si,GA}$	substrate inhibition constant for glutamic acid production (g/L)
$K_{si,s}$	substrate inhibition constant for sugar consumption (g/L)
$K_{pi,GA}$	product inhibition constant for glutamic acid production (g/L)
$K_{pi,s}$	product inhibition constant for sugar consumption (g/L)
$K_{pi,X}$	product inhibition constant for growth of biomass (g/L)
$K_{sl,GA}$	substrate limitation constant for glutamic acid production (g/L)
$K_{sl,s}$	substrate limitation constant for sugar consumption (g/L)
$K_{sl,X}$	substrate limitation constant for growth of biomass (g/L)
$K_{glu,X}$	glucose limitation constant for growth of biomass (g/L)
$K_{fru,X}$	fructose limitation constant for growth of biomass (g/L)
K_{si}	substrate inhibition constant (g/L)
S_{glu}, S_{fru}	concentration of glucose and fructose (g/L)
P	glutamic acid concentration (g/L)
C_{bleed}	cell bleeding ratio
V_f	working volume of the fermenter (cm^3)
$q_{GA,max}$	maximum specific glutamic acid production rate (g/g h)
$q_{GA,net}$	maximum specific glutamic acid production rate in continuous process (g/g h)
$q_{s,max}$	maximum specific sugar utilization rate (g/g h)
R^2	correlation coefficient
S_0/S	concentration of the sugars (g/L)
t	fermentation time (h)
X	biomass concentration (g/L)
X_{glu}/X_{fru}	biomass concentration generated when glucose or fructose used as substrate (g/L)
X_t	biomass concentration in fermenter after starting of membrane cell recycles (g/L)
S	substrate concentration (g/L)
S_0	initial substrate concentration (g/L)
$S_{fer,ct}$	substrate concentration in fermenter after continuous process (g/L)
S_{rec}	substrate concentration in membrane cell recycle stream during continuous process (g/L) (negligible)
$P_{GA,fer,ct}$	product concentration in fermenter after starting continuous process (g/L)
P	product concentration in recycle stream of microfiltrate (g/L)
Y_{XS}	biomass yield on sugar consumption
Y_{SGA}	glutamic acid yield on sugar consumption
J_{MF}	the solvent flux in permeate stream of microfiltration ($L/(m^2h)$)
ΔP	transmembrane pressure (kg/cm^2)
R_m	membrane resistance (m^{-1})
R_f	membrane fouling resistance (m^{-1})
R_c	cake resistance (m^{-1})
J_s	uncharged solute flux (pore area basis) (mol/m^2s)
J_v	volumetric flux of uncharged solute ($L/(m^2h)$)

Greek symbols

α	growth-associated constant in Luedeking–Piret model (g/g)
β	net-specific growth rate (h^{-1})
μ, μ_{net}	specific growth rate (h^{-1})
μ	maximum specific growth rate (h^{-1})
μ_{glu}	specific growth rate for only glucose (h^{-1})
μ_{fru}	specific growth rate for only fructose (h^{-1})
μ_s	specific growth rate for only sucrose (h^{-1})

Microfiltration and nanofiltration

$c_{w,i}$	concentration of ion i (mol/m^3) on membrane wall
$c_{w,i,av}$	average concentration of ion i (mol/m^3) on membrane wall
$C_{p,i}$	concentration of ion i (mol/m^3) in permeate solution
$C_{B,GA}$	bulk concentration of glutamate (mol/m^3)
c	average concentration of uncharged solute concentration within pore (mol/m^3)
$D_{p,uc}$	uncharged solute pore diffusion coefficient (m^2/h)
D_i	hindered diffusivity of ion i (m^2/s)
$D_{b,i}$	bulk diffusivity of ion i (m^2/s)
F	Faraday constant