and considerable increase in culture volume, but the volumeof the workable supernatant (approximately 7 L afterbiomass removal) hardly changed during the fermentationprocess (Figure 3).Since a high percentage of the culture is biomass, theappropriate way to express angiostatin production is in mgper liter supernatant instead of mg per liter culture, theaverage production (based on five consecutive runs) was20 (+-5) mg Lsupernatant.Inducing the culture at higher celldensities resulted in significant problems with maintainingthe desired temperature and dissolved oxygen level becausethe high amounts of oxygen, needed for methanol oxidation,generate a large amount of heat during theexponential growth phase on methanol.When the culture density reached approximately 150OD at 600 nm (10% v/v), about 20 h after starting the fermentation,methanol addition was commenced and its concentrationin the culture was kept at 2 g L-1using thedescribed methanol sensor.