bioconversion of methane. Traditional bioprocesses to produce PHA from methane thus maintain low methanotroph densities in the aqueous broth, which low densities in turn provide low PHA productivity per unit volume of bioreactor. Accordingly, commercially available PHA's have been significantly more expensive than conventional petroleum-based polymers and therefore have not met with widespread commercial acceptance.

[6] In general, the bioprocesses for making PHA-containing products from methane-containing gases comprise the steps of growing a population of methanotrophs ("balanced cell growth") and then subjecting the methanotrophs to environmental conditions that do not support growth of the population of the microorganisms but foster production of PHA by the methanotrophs ("unbalanced cell growth"). Where PHA is the sought product, the PHA is subsequently harvested from the microorganisms. Both methane-containing gas and oxygen-containing gas are supplied to the aqueous broth containing the methanotrophs for the growth of the population of methanotrophs and their production of PHA.

[7] Accordingly a need exists to produce PHA-containing products from methane-containing gases with higher productivities per unit volume of bioreactor. Advantageously, preferred processes would achieve higher productivities in an economically-attractive manner.

Summary

[8] By this disclosure bioprocesses are provided for making PHA-containing products from methane-containing gases with high productivities. In accordance with this disclosure, a high density of methanotrophs can be achieved per unit of bioreactor volume without undue cooling costs associated with the substantial exothermic nature of the bioconversion of methane. The processes of this disclosure facilitate desirable high mass transfer rates of methane from the gas phase to the aqueous broth or medium. These high mass transfer rates support high methanotroph densities. However, high mass transfer rates and high methanotroph densities result in greater generation of heat and greater production of carbon dioxide. The processes of this disclosure integrate the ability to achieve high methane transfer rates with heat removal to maintain the aqueous medium at suitable temperatures for the bioprocess.

[9] In the processes of this disclosure, a portion of aqueous medium containing carbon dioxide generated by the methanotrophs is withdrawn from the reaction zone and

contacted with a stripping gas to remove dissolved carbon dioxide from the withdrawn aqueous medium (resulting in "carbon dioxide-lean medium or broth"). At least a portion, and preferably essentially all, of the carbon dioxide-lean medium is passed to the reaction zone where it becomes part of the aqueous medium in the reaction zone. The removal of carbon dioxide from the aqueous medium results in increased rates of mass transfer of each of methane and oxygen to the aqueous medium in the reaction zone.

[10] Additionally, during the contact with the stripping gas, the evaporation of carbon dioxide and water from the withdrawn aqueous medium results in cooling the aqueous medium. As the population of methanotrophs increases, so does the generation of carbon dioxide. Accordingly, the heat removed through evaporative cooling due to carbon dioxide vaporization somewhat tracks the population growth of the methanotrophs. The extent of heat removal due to water vaporization will, of course, relate to the relative humidity of the stripping gas. Since water is also formed during the metabolic oxidation of methane to carbon dioxide, the vaporization of water can be beneficial from the standpoint of maintaining a constant volume of aqueous medium during the process.

[11] For purposes herein, the term "limiting substrate" means the one of methane or oxygen that is the more limiting parameter for adequate mass transfer for balanced cell growth and/or unbalanced cell growth at any given time in the process. It is to be understood that during an operation, it is possible for one substrate to be limiting for a period of time and then another substrate to be limiting. In most operations, the mass transfer rate of methane is limiting the balanced cell growth and unbalanced cell growth at high methanotroph densities. However, this disclosure contemplates modes of operations where oxygen mass transfer is the limiting parameter. For example, as will be discussed in more detail later, one or more of methanol, formic acid or water soluble salt thereof can be added to the aqueous medium, in which case, oxygen mass transfer could become the limiting substrate.

[12] A broad example of this disclosure pertains to high productivity processes for bioconverting methane to product containing polyhydroxyalkanoate, e.g., PHA or protein containing modulated PHA content, comprising (a) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with an aqueous medium having a population of methanotrophs therein, said medium containing nutrients for the growth of the population of the methanotroph to provide a methanotroph-rich aqueous medium, said growth of the population of methanotrophs also

resulting in the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; (b) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with at least a portion of the methanotroph-rich aqueous medium, said medium having a limitation, e.g., a substantial absence to create nutrient limited conditions that inhibit the growth of the population of methanotrophs, of at least one nutrient required for the growth of the population of the methanotrophs, to cause production of polyhydroxyalkanoate by the methanotrophs and the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; and (c) separating the polyhydroxyalkanoate-containing methanotrophs from the aqueous medium of step (b), wherein for at least a portion of the duration of each of steps (a) and (b):

i. the rate of passing at least one limiting substrate gas to the reaction zone in each of steps (a) and (b) is (A) at substrate-diffusion conditions and, optionally and preferably, (B) is modulated to provide a substantially stable molar concentration of methane in the unreacted gases;

ii. in at least one of steps (a) and (b) a portion of the aqueous medium is continuously withdrawn from the reaction zone and contacted with a stripping gas to remove carbon dioxide and provide a carbon dioxide-lean aqueous medium; and

iii. recycling at least a portion of the carbon dioxide-lean aqueous medium to the reaction zone of at least one of steps (a) and (b).

Preferably substep (ii) is conducted at least during the time that the population of methanotrophs is at least about 8, preferably at least about 10, grams per liter (as measured by dry cell mass), and often at least during a period of time where the population of methanotrophs resides within the range of about 8 and 80, and preferably between about 10 and 60, grams per liter (as measured by dry cell mass).

[12a] In one aspect, there is provided, a high productivity process for bioconverting methane to product containing polyhydroxyalkanoate comprising (a) passing substrate gas comprising a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with an aqueous medium having a population of methanotrophs therein, said medium containing nutrients for the growth of the population of the methanotroph to provide a methanotroph-rich aqueous medium, said

growth of the population of methanotrophs also resulting in the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; (b) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with at least a portion of the methanotroph-rich aqueous medium, said medium having a limitation of at least one nutrient required for the growth of the population of the methanotrophs to create nutrient limited conditions that inhibit the growth of the population of methanotrophs and to cause production of polyhydroxyalkanoate – by the methanotrophs and the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; and (c) separating the polyhydroxyalkanoate-containing methanotrophs from the aqueous medium of step (b), wherein for at least a portion of the duration of each steps (a) and (b):

i. the rate of passing at least one substrate gas-containing gas to the reaction zone in each of steps (a) and (b) is at substrate-diffusion conditions;

ii. in at least one of steps (a) and (b) a portion of the aqueous medium is continuously withdrawn from the reaction zone and contacted with a stripping gas to remove carbon dioxide and provide a carbon dioxide-lean aqueous medium; and

iii. passing at least a portion of the carbon dioxide-lean aqueous medium to the reaction zone of at least one of steps (a) and (b).

[13] In another broad example of this disclosure, one or both of methanol and formic acid or water soluble salt thereof ("oxygenated C1 compound") is added to the aqueous broth during either or both of the growth of the methanotrophs or the production of PHA phases. The oxygenated C1 compound serves to provide additional carbon substrate to the methanotrophs and thus maintain population growth of the methanotrophs and production of PHA at a rate beyond that which can be supported by the mass transfer rate

of methane from the gas phase to the aqueous medium under a given set of conditions. Additionally, the metabolic conversion of the oxygenated C1 compound is less exothermic than that of methane per carbon atom. Thus, this example pertains to high productivity processes for bioconverting methane to product containing polyhydroxyalkanoate comprising (a) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with an aqueous medium having a population of methanotrophs therein, said medium containing nutrients for the growth of the population of the methanotrophs to provide a methanotroph-rich aqueous medium, said growth of the population of microorganisms also resulting in the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; (b) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with at least a portion of the methanotroph-rich aqueous medium, said medium containing an absence of at least one nutrient required for the growth of the population of the methanotrophs to cause production of polyhydroxyalkanoate and the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; and (c) separating the polyhydroxyalkanoate-containing methanotrophs from the aqueous medium of step (b), wherein an oxygenated C1 compound of at least one of methanol and formic acid or water soluble salt thereof is supplied to the aqueous medium in at least one of steps (a) and (b). Preferably the oxygenated C1 compound is supplied at least under methane diffusion limited conditions.

[13a] In yet another aspect, there is provided, a high productivity process for bioconverting methane to product containing polyhydroxyalkanoate comprising (a) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with an aqueous medium having a population of methanotrophs therein, said medium containing nutrients for the growth of the population of the methanotrophs to provide a methanotroph-rich aqueous medium, said growth of the population of methanotrophs also resulting in the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; (b) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with at least a portion of the methanotroph-rich aqueous medium, said medium having a substantial absence of at least one nutrient required for the growth of the population of the methanotroph, to cause production of polyhydroxyalkanoate and

the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; and (c) separating the polyhydroxyalkanoate-containing methanotrophs from the aqueous medium of step (b), wherein an oxygenated C1 compound of at least one of methanol and formic acid or water soluble salt thereof is supplied to the aqueous medium in at least one of steps (a) and (b).

[14] A yet further broad example of this disclosure pertains to high productivity processes for bioconverting methane to product containing polyhydroxyalkanoate comprising (a) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with an aqueous medium having a population of methanotrophs therein, said medium containing nutrients for the growth of the population of the methanotroph to provide a methanotroph-rich aqueous medium, said growth of the population of methanotrophs also resulting in the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; (b) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with at least a portion of the methanotroph-rich aqueous medium, said medium containing an absence of at least one nutrient required for the growth of the population of the methanotrophs, to cause production of polyhydroxyalkanoate and the

co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; and (c) separating the polyhydroxyalkanoate-containing methanotrophs from the aqueous medium of step (b), wherein for at least a portion of the duration of each of steps (a) and (b):

i. the rate of passing at least one limiting substrate gas to the reaction zone in each of steps (a) and (b) is (A) at substrate-diffusion conditions and, optionally and preferably, (B) is modulated to provide a substantially stable molar concentration of methane in the unreacted gases;

ii. in at least one of steps (a) and (b) a portion of the aqueous medium is continuously withdrawn from the reaction zone and contacted with a semi-permeable membrane to remove carbon dioxide and provide a carbon dioxide-lean aqueous medium; and

iii. recycling at least a portion of the carbon dioxide-lean aqueous medium to the reaction zone of at least one of steps (a) and (b).

[14a] In yet another aspect, there is provided, a high productivity process for bioconverting methane to product containing polyhydroxyalkanoate comprising (a) passing substrate gas comprising a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with an aqueous medium having a population of methanotrophs therein, said medium containing nutrients for the growth of the population of the methanotroph to provide a methanotroph-rich aqueous medium, said growth of the population of methanotrophs also resulting in the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; (b) passing a methane-containing gas and an oxygen-containing gas to a reaction zone for contact under fermentation conditions with at least a portion of the methanotroph-rich aqueous medium, said medium having a substantial a absence of at least one nutrient required for the growth of the population of the methanotrophs, to cause production of polyhydroxyalkanoate and the co-production of carbon dioxide, water and heat, and withdrawing unreacted gas from said reaction zone; and (c) separating the polyhydroxyalkanoate-containing methanotrophs from the aqueous medium of step (b), wherein for at least a portion of the duration of each steps (a) and (b):

i. the rate of passing at least one substrate gas-containing gas to the reaction zone in each of steps (a) and (b) is at substrate-diffusion conditions;

ii. in at least one of steps (a) and (b) a portion of the aqueous medium is continuously withdrawn from the reaction zone and contacted with a semi-permeable membrane to remove carbon dioxide and provide a carbon dioxide-lean aqueous medium; and

iii. passing at least a portion of the carbon dioxide-lean aqueous medium to the reaction zone of at least one of steps (a) and (b).

[15] The semi-permeable membrane used to remove carbon dioxide from the aqueous medium for at least one of steps (a) and (b) is preferably a degassing, or pervaporation, membrane permeable to carbon dioxide, and more preferably, the membrane also is permeable to water. The membrane, which may be organic or inorganic, serves as a barrier between the liquid phase and a vapor phase permeate. The driving force for the permeation of carbon dioxide and water is generally characterized as the differential in partial pressure. The partial pressure differential can be at least in part maintained by an absolute pressure differential across the membrane, e.g., the permeate side being under vacuum, and/or a sweep gas on the permeate side of the membrane. The sweep gas can be of the same type as used for stripping. The evaporation of the permeate, which is carbon dioxide and usually water, occurs on the permeate side of the membrane and provides cooling by the latent heat of vaporization.

Brief Description of the Drawing

[16] Figure 1 is a schematic depiction of an apparatus useful in processes of this invention.

Detailed Discussion

[17] All patents, published patent applications and articles referenced in this detailed description are hereby incorporated by reference in their entireties.