Particle Dynamics in a Rotating Wall Vessel Bioreactor

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Rotating bioreactors such as the High Aspect Ratio Vessel (HARV) provide a low shear and gentle mixing environment, ideal for mammalian cell culture in 3D. The HARV is a cylindrical "disc-shaped" batch culture vessel with no internal moving parts, that rotates about a single axis. Oxygenation is provided by a permeable silicon rubber membrane, allowing the diffusion of gases to and from the medium [1]. Cell culture in this bioreactor may be carried out using microcarriers and/or encapsulating cells within hydrogel particles. In our lab, tissue engineering from Embryonic Stem cells is of interest, and this has been implemented by inoculating the vessel with cells that have been previously encapsulated within Calcium alginate particles (Figure 1).

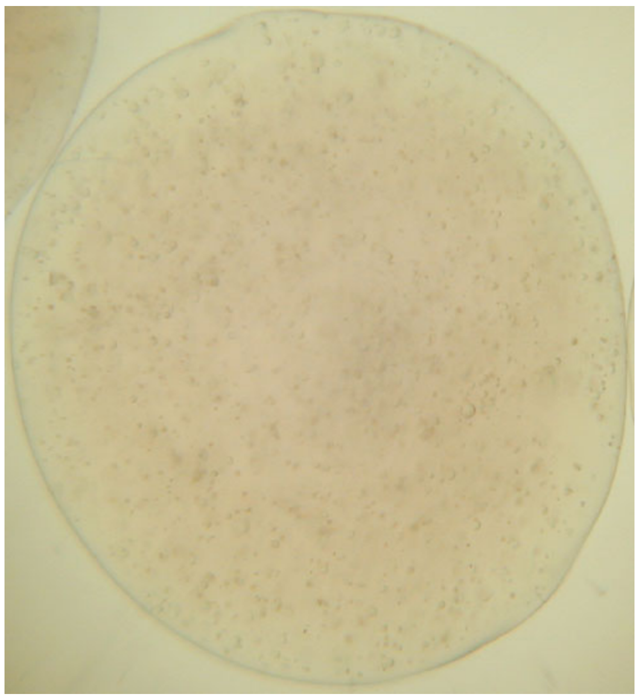

Figure 1. Murine Embryonic Stem cells encapsulated within a Calcium alginate bead.

For a single spherical particle suspended in the HARV, it has been shown that particle motion may be affected by: density difference between fluid and particle, vessel rotation rate, fluid viscosity and particle radius. Particles denser than the fluid medium (heavy) migrate to the wall, whereas particles that are less dense (light) migrate towards the vessel's centre [2]. In this study, a mathematical model describing the motion of a single particle has been developed. The model is 2-dimensional, and takes into account weight, buoyancy, drag, and centrifugal forces, and is derived in a rotating frame of reference (Figure 2).

<u>Model Development and Results</u>

Consider a 2D model of the HARV in the rotating frame of reference, where the fixed coordinate system is denoted by (X, Y), and the rotating coordinate system is denoted by (x, y). (x, y) rotates with angular velocity ω about an axis perpendicular to x and y, that passes through the origin O (Figure 2). The vessel is completely filled with liquid, and a solid spherical particle is suspended within the fluid-filled vessel [3].

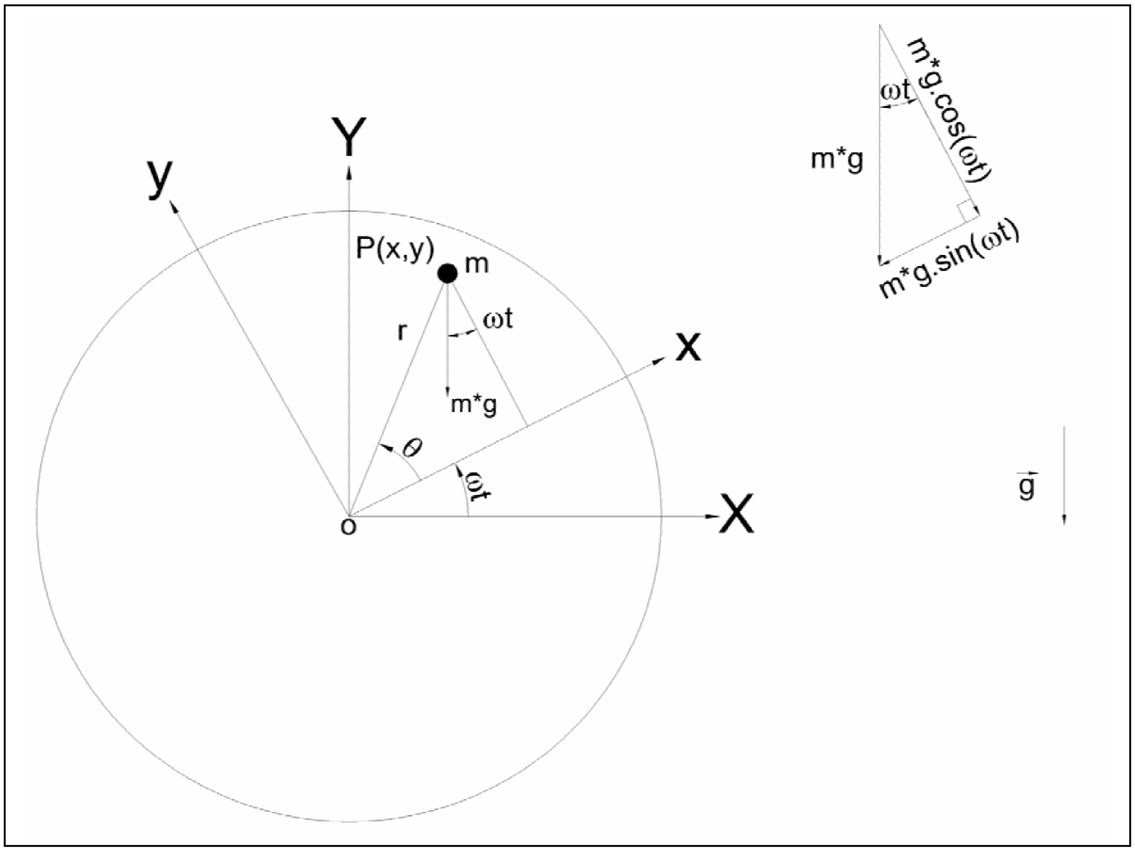

Figure 2. A 2D model of a solid spherical particle suspended in a rigidly rotating fluid [3].

The following assumptions are made:

- Fluid rotates as a rigid body with an angular velocity ω throughout the domain
- Any effect on the flow field caused by particle motion through the fluid is negligible
- Stokes flow is assumed
- The fluid is isothermal and Newtonian, with viscosity μ and density ρ_f
- The particle, P, is solid and spherical, with density ρ_p and radius a

The forces acting on the particle are summarised in Table 1.

Table 1. Forces acting on the particle

Force	Expression	Details
Buoyancy corrected weight	$m^* g$	m^* is the buoyancy corrected mass given by: $\rho^* V$, where V is particle volume, and $\rho^* = \rho_p - \rho_f$
Drag	fv	v is particle's velocity and f is Stokes drag coefficient given by: $6\pi\mu a$, where a is particle radius
Centrifugal	$m^* \omega^2 r$	r is the particle's radial position from the vessel's centre

The particle's equations of motion in each coordinate direction are given by:

$$\ddot{x}+B\dot{x}+Cx=D\sin(\omega t) \tag{1.1}$$

$$\ddot{y}+B\dot{y}+Cy=D\cos(\omega t) \tag{1.2}$$

Where $B=f/m_p$, $C=-m^*\omega^2/m_p$, and $D=-m^*g/m_p$

Their solution is given by:

$$x=x_1\exp(\lambda_1 t)+x_2\exp(\lambda_2 t)+\gamma\cos(\omega t-\varphi_1) \tag{1.3}$$

and

$$y=y_1\exp(\lambda_1 t)+y_2\exp(\lambda_2 t)+\gamma\cos(\omega t+\varphi_2) \tag{1.4}$$

Where $\gamma=\sqrt{\alpha_1^2+\alpha_2^2}$, $\varphi_1=a\tan(\alpha_2/\alpha_1)$, and $\varphi_2=(\alpha_1/\alpha_2)$. The roots of the auxiliary equation are $\lambda_1\approx-\frac{C}{B}$ and $\lambda_2\approx-B$. For a heavy particle, as $t\to\infty$, $\exp(\lambda_1 t)\to\infty$, $\therefore$ x and $y\to\infty$. However, if the product $\lambda_1 t$ is small such that $\exp(\lambda_1 t)\approx\gamma\cos(\omega t-\varphi_1)$, and $\exp(\lambda_1 t)\approx\gamma\cos(\omega t+\varphi_2)$, then $x\to x_1\exp(\lambda_1 t)+\gamma\cos(\omega t-\varphi_1)$, and $y\to y_1\exp(\lambda_1 t)+\gamma\sin(\omega t+\varphi_2)$. For a light particle, $\exp(\lambda_1 t)$ and $\exp(\lambda_2 t)\to 0$, $\therefore x\to\gamma\cos(\omega t-\varphi_1)$, and $y\to\gamma\sin(\omega t+\varphi_2)$.

For cases where the first exponential term doesn't dominate, the parametric equations give a spiral trajectory, where a single revolution of the vessel corresponds to a single ring of the spiral traced out by the particle (Figure 3). For a light particle, as time progresses, its trajectory migrates towards the vessel's centre until finally, it orbits the centre.

References:

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2. Gao H. Ayyaswamy PS. Ducheyne P. (1997). Dynamics of a microcarrier particle in the simulated microgravity environment of a rotating-wall vessel. Microgravity Science Technology, X/3, 154-165.

3. Kessler JO. (1992). The Internal Dynamics of Slowly Rotating Biological Systems. ASGSB Bulletin 5(2): 11-21.

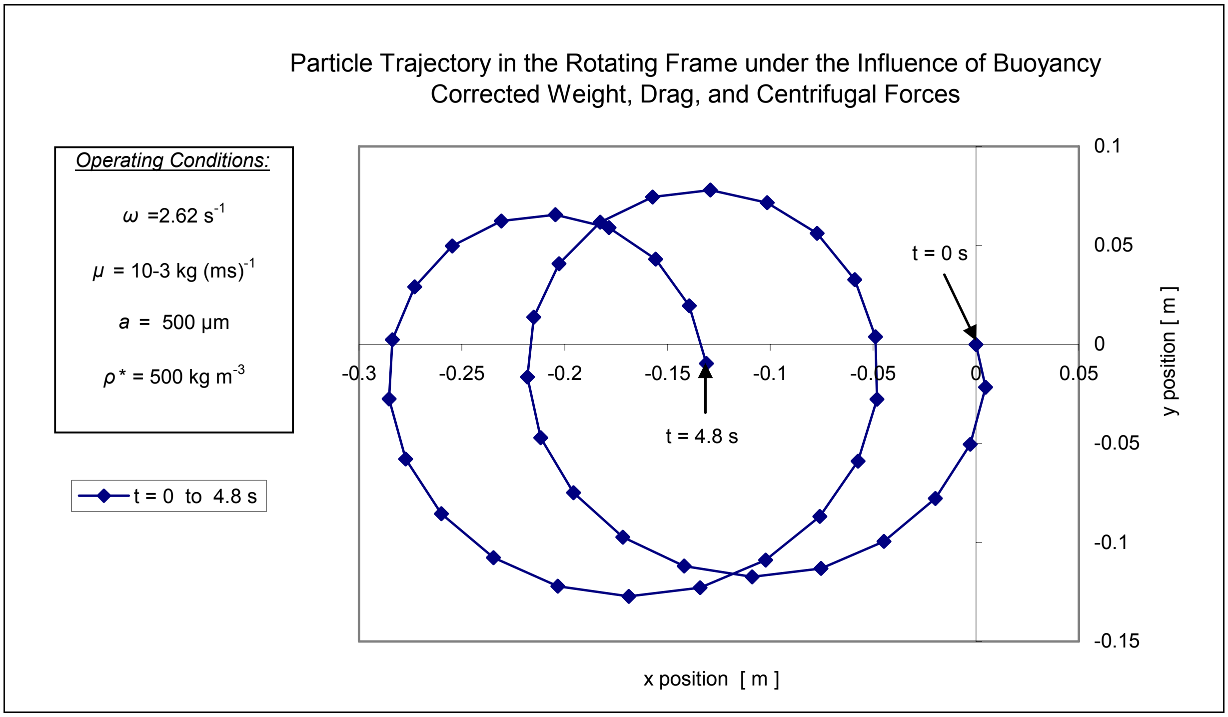

Figure 3. Particle trajectory. As the particle is heavy, it spirals radially outward towards the vessel wall.