Supplementary Information

1. Lubrication Theory

In this section we show the derivation of Reynolds equation, which governs the fluid flow between two surfaces. The schematic is shown in the Fig 1.1, where the red and blue areas represent the surfaces which are in motion, and the vertical height between two points on the surface is $h(\mathrm{x}, \mathrm{z})$.

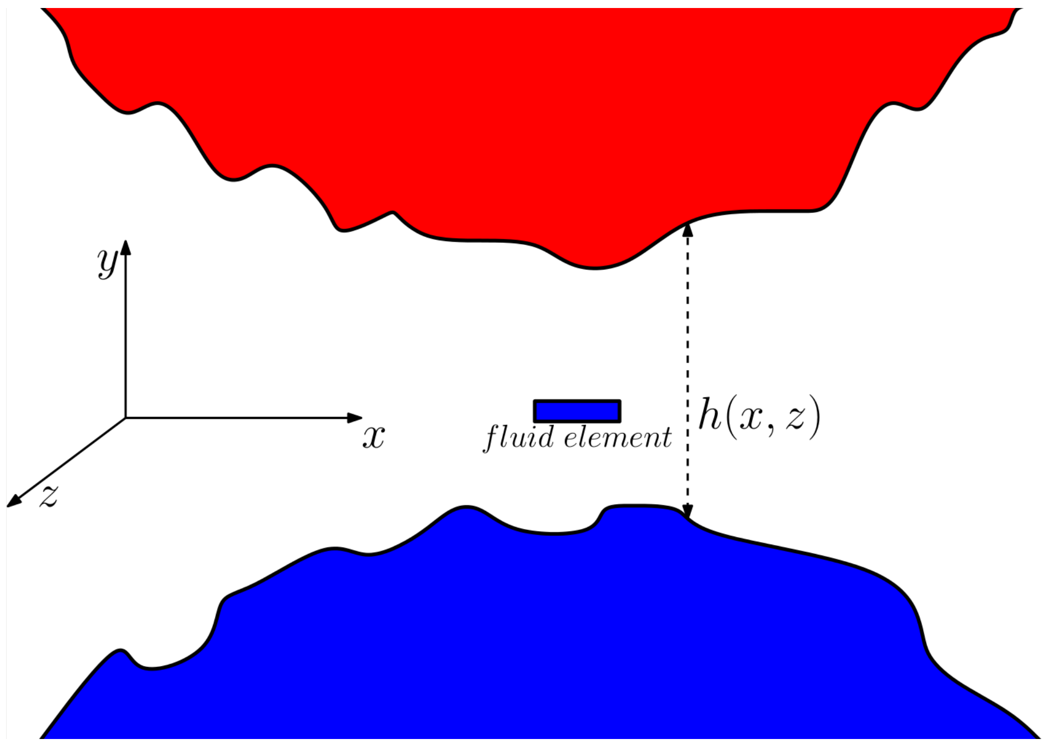


Fig 1.1 : Schematic

In the following derivation, we start with the Navier-Stokes equation, do a scaling analysis to keep the dominant components of the equation and finally getting to the Reynold's equation.

Navier Stokes equations

The most general form of Navier-Stokes equation is given as,

$$\rho\frac{\partial u}{\partial t}=\rho X-\frac{\partial p}{\partial x}+\frac{2}{3}\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial x}-\frac{\partial w}{\partial z}\right)\right]+\frac{2}{3}\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial x}-\frac{\partial v}{\partial y}\right)\right]+\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial u}{\partial y}+\frac{\partial v}{\partial x}\right)\right]+\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial x}+\frac{\partial u}{\partial z}\right)\right],$$

$$\rho\frac{\partial v}{\partial t}=\rho Y-\frac{\partial p}{\partial y}+\frac{2}{3}\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial v}{\partial y}-\frac{\partial w}{\partial z}\right)\right]+\frac{2}{3}\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial v}{\partial y}-\frac{\partial u}{\partial x}\right)\right]+\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial y}+\frac{\partial v}{\partial x}\right)\right]+\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial y}+\frac{\partial v}{\partial z}\right)\right], \quad 1.1$$

$$\rho\frac{\partial w}{\partial t}=\rho Z-\frac{\partial p}{\partial z}+\frac{2}{3}\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial z}-\frac{\partial v}{\partial y}\right)\right]+\frac{2}{3}\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial z}-\frac{\partial u}{\partial x}\right)\right]+\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial z}+\frac{\partial w}{\partial x}\right)\right]+\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial w}{\partial y}+\frac{\partial v}{\partial z}\right)\right],$$

where,
ρ is the density of the fluid,
u, v and w are the velocity components of fluid in x, y and z directions, respectively,
X, Y and Z are the body force components on fluid in x, y and z directions, respectively,
η is the fluid viscosity.

Assuming that, there is no body force on the fluid and also neglecting the inertial term, the Navier-Stokes equations can simplified to,

$$\begin{aligned}
\frac{\partial p}{\partial x} &= \frac{2}{3}\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial x}-\frac{\partial w}{\partial z}\right)\right]+\frac{2}{3}\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial x}-\frac{\partial v}{\partial y}\right)\right]+\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial u}{\partial y}+\frac{\partial v}{\partial x}\right)\right]+\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial x}+\frac{\partial u}{\partial z}\right)\right]\\
\frac{\partial p}{\partial y} &= \frac{2}{3}\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial v}{\partial y}-\frac{\partial w}{\partial z}\right)\right]+\frac{2}{3}\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial v}{\partial y}-\frac{\partial u}{\partial x}\right)\right]+\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial y}+\frac{\partial v}{\partial x}\right)\right]+\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial y}+\frac{\partial v}{\partial z}\right)\right],\\
\frac{\partial p}{\partial z} &= \frac{2}{3}\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial z}-\frac{\partial v}{\partial y}\right)\right]+\frac{2}{3}\frac{\partial}{\partial z}\left[\eta\left(\frac{\partial w}{\partial z}-\frac{\partial u}{\partial x}\right)\right]+\frac{\partial}{\partial x}\left[\eta\left(\frac{\partial u}{\partial z}+\frac{\partial w}{\partial x}\right)\right]+\frac{\partial}{\partial y}\left[\eta\left(\frac{\partial w}{\partial y}+\frac{\partial v}{\partial z}\right)\right]
\end{aligned} \qquad 1.2$$

We choose the following non-dimensionalizing scheme for the eqs. 1.2,

1) Time is non-dimensionalized by a characteristic time of the system, τ_0. Hence, $t = \tau_0 \bar{t}$.
2) Length dimensions associated in y-direction are normalized by local film thickness, h. Therefore, $y = h\bar{y}$ and $v = \frac{h}{\tau_0}\bar{v}$.
3) Length dimensions associated in x and z directions are normalized by characteristic length of the system, l, where, $\frac{h}{l} << 1$. Therefore, $x = h\bar{x}$, $z = h\bar{z}$, $u = \frac{l}{\tau_0}\bar{u}$ and $\mathrm{w} = \frac{l}{\tau_0}\bar{w}$.
4) Density is normalized by room temperature density, ρ_0, which results in, $\rho = \rho_0\bar{\rho}$.
5) Viscosity is normalized as, $\eta = \frac{\rho_0 l^2}{\tau_0}\bar{\eta}$.
6) Pressure is normalized as, $p = \frac{\rho_0 l^2}{\tau_0^2}\bar{p}$.

Applying this normalization scheme to the system of eqs. 1.2, to get,

$$\begin{aligned}
\frac{\partial \bar{p}}{\partial \bar{x}} &= \frac{2}{3}\frac{\partial}{\partial \bar{x}}\left[\bar{\eta}\left(\frac{\partial \bar{u}}{\partial \bar{x}}-\frac{\partial \bar{w}}{\partial \bar{z}}\right)\right]+\frac{2}{3}\frac{\partial}{\partial \bar{x}}\left[\bar{\eta}\left(\frac{\partial \bar{u}}{\partial \bar{x}}-\frac{\partial \bar{v}}{\partial \bar{y}}\right)\right]+\frac{\partial}{\partial \bar{y}}\left[\bar{\eta}\left(\frac{\partial \bar{u}}{\partial \bar{y}}\left(\frac{l}{h}\right)^2+\frac{\partial \bar{v}}{\partial \bar{x}}\right)\right]+\frac{\partial}{\partial \bar{z}}\left[\bar{\eta}\left(\frac{\partial \bar{w}}{\partial \bar{x}}+\frac{\partial \bar{u}}{\partial \bar{z}}\right)\right]\\
\frac{\partial \bar{p}}{\partial \bar{z}} &= \frac{2}{3}\frac{\partial}{\partial \bar{z}}\left[\bar{\eta}\left(\frac{\partial \bar{w}}{\partial \bar{z}}-\frac{\partial \bar{v}}{\partial \bar{y}}\right)\right]+\frac{2}{3}\frac{\partial}{\partial \bar{z}}\left[\bar{\eta}\left(\frac{\partial \bar{w}}{\partial \bar{z}}-\frac{\partial \bar{u}}{\partial \bar{x}}\right)\right]+\frac{\partial}{\partial \bar{x}}\left[\bar{\eta}\left(\frac{\partial \bar{u}}{\partial \bar{z}}+\frac{\partial \bar{w}}{\partial \bar{x}}\right)\right]+\frac{\partial}{\partial \bar{y}}\left[\bar{\eta}\left(\frac{\partial \bar{w}}{\partial \bar{y}}\left(\frac{l}{h}\right)^2+\frac{\partial \bar{v}}{\partial \bar{z}}\right)\right]
\end{aligned}, \qquad 1.3$$

Eq. 1.2b, the Navier-Stokes equation in y-direction is identically satisfied on both sides. The pressure gradient in y direction is negligible compared to the pressure gradients in x and z directions. On the right hand side, the quantities are also very small compared to the corresponding terms in eqs. 1.2a & c.

Looking at the eq. 1.3, the terms which are scaled by, $\left(\frac{l}{h}\right)^2 [>>1]$ are dominant and rest of the terms can be neglected on the right hand side. This gives,

$$\frac{\partial \overline{p}}{\partial \overline{x}} = \frac{\partial}{\partial \overline{y}}\left[\overline{\eta}\left(\frac{\partial \overline{u}}{\partial \overline{y}}\left(\frac{l}{h}\right)^2\right)\right] \quad \text{and} \quad \frac{\partial \overline{p}}{\partial \overline{z}} = \frac{\partial}{\partial \overline{y}}\left[\overline{\eta}\left(\frac{\partial \overline{w}}{\partial \overline{y}}\left(\frac{l}{h}\right)^2\right)\right]. \qquad 1.4$$

On plugging back the dimensional term into eqs. 1.4, one gets back the dimensional form as,

$$\frac{\partial p}{\partial x} = \frac{\partial}{\partial y}\left[\eta\left(\frac{\partial u}{\partial y}\right)\right] \quad \text{and} \quad \frac{\partial p}{\partial z} = \frac{\partial}{\partial y}\left[\eta\left(\frac{\partial w}{\partial y}\right)\right]. \qquad 1.5$$

For an iso-viscous system, the equations can be modified as,

$$\frac{\partial p}{\partial x} = \eta\frac{\partial^2 u}{\partial y^2} \quad \text{and} \quad \frac{\partial p}{\partial z} = \eta\frac{\partial^2 w}{\partial y^2}. \qquad 1.6$$

This same set of equations can also be obtained by a force balance on a fluid element shown in Figs. 1.1 and 1.2.

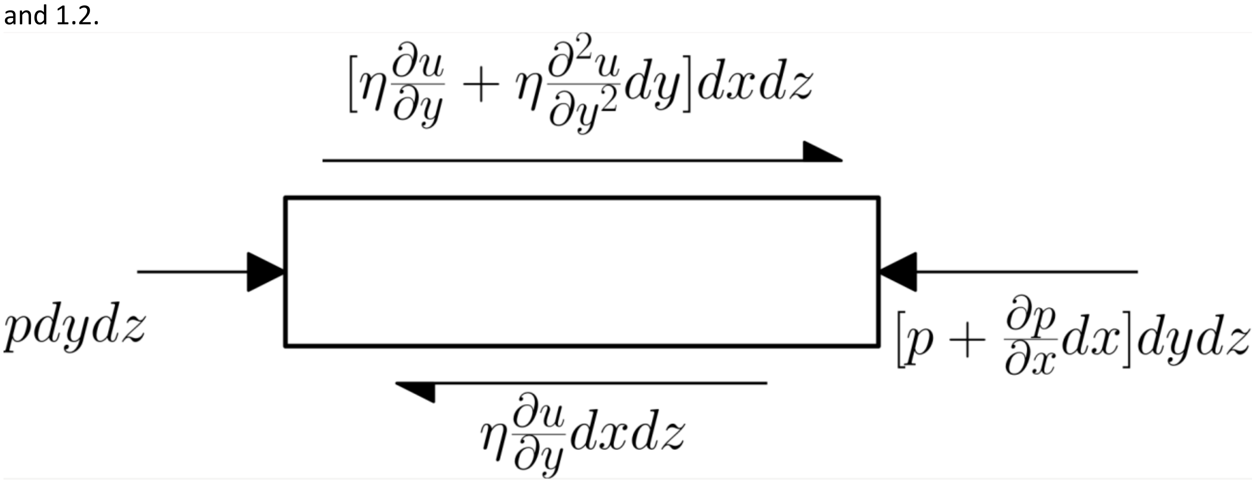


Fig A2 : Force balance on a fluid element

By doing a simple force balance in x-direction, on a fluid element between the two surfaces, as shown in Fig. 1.2, we can write the governing equations for fluid flow as,

$$\frac{\partial p}{\partial x} = \eta\frac{\partial^2 u}{\partial y^2}. \qquad 1.7$$

Similarly, a force balance in z direction will give us the equation,

$$\frac{\partial p}{\partial z} = \eta\frac{\partial^2 w}{\partial y^2}. \qquad 1.8$$

In the above expressions,

p is the pressure in the vertical fluid column and is assumed to be invariant along y axis,

η is the fluid viscosity.

Both eqs. 1.7 and 1.8 can be integrated twice each, to get the fluid velocities as,

$$u=\frac{1}{2\eta}\frac{\partial p}{\partial x}y^2+\frac{A}{\eta}y+B\ , \qquad 1.9$$

$$w=\frac{1}{2\eta}\frac{\partial p}{\partial z}y^2+\frac{C}{\eta}z+D\,. \qquad 1.10$$

Boundary conditions relevant to vesicle adhesion problem

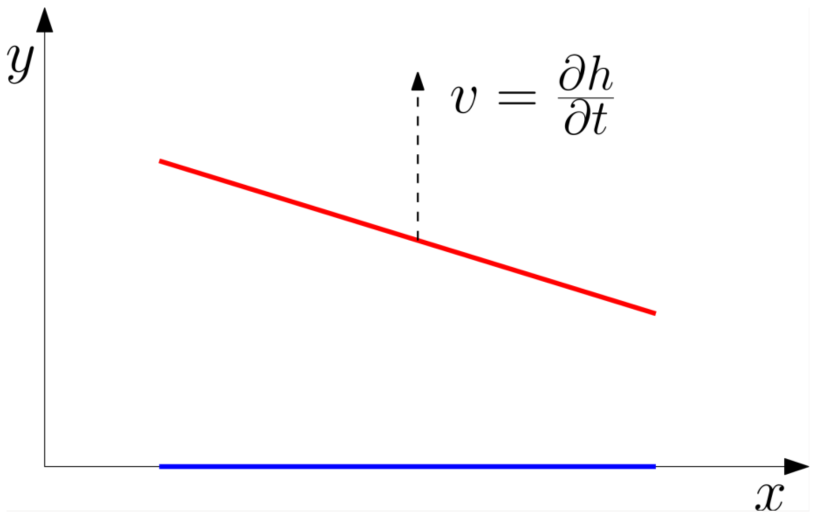


Fig 1.3 : Velocity boundary conditions

For the case of lipid membrane fusion and adhesion, the only velocity element is the one in vertical direction, $v=\frac{\partial h}{\partial t}$. Therefore, we have following boundary conditions for the velocity profiles obtained above in eqs. 1.9 and 1.10,

$$u=0, v=0 \text{ and } w=0, \text{ at } y=0\,, \qquad 1.11$$

$$u=0, v=\frac{\partial h}{\partial t} \text{ and } w=0, \text{ at } y=h\,. \qquad 1.12$$

Using these boundary conditions in eqs. 1.9 and 1.10, we get,

$$u=\frac{1}{2\eta}\frac{\partial p}{\partial x}\left(y^2-hy\right)\ , \qquad 1.13$$

$$w=\frac{1}{2\eta}\frac{\partial p}{\partial z}\left(y^2-hy\right). \qquad 1.14$$

Volume flow rates

The volume flow rate per unit length, in x and z direction can be defined as,

$$V_x=\int_0^h u\,dy=-\frac{h^3}{12\eta}\frac{\partial p}{\partial x}\ , \qquad 1.15$$

$$V_z=\int_0^h w\,dy=-\frac{h^3}{12\eta}\frac{\partial p}{\partial z}\ . \qquad 1.16$$

Continuity equation

The continuity equation for fluid is,

$$\frac{\partial \rho}{\partial t}+\frac{\partial(\rho u)}{\partial x}+\frac{\partial(\rho v)}{\partial y}+\frac{\partial(\rho w)}{\partial z}=0. \qquad 1.17$$

For a constant density system, the equation can be simplified to,

$$\frac{\partial u}{\partial x}+\frac{\partial v}{\partial y}+\frac{\partial w}{\partial z}=0. \qquad 1.18$$

On integrating this equation with respect to y, between the limits 0 and h, we get,

$$\int_0^h \frac{\partial u}{\partial x}dy+\int_0^h \frac{\partial v}{\partial y}dy+\int_0^h \frac{\partial w}{\partial z}dy=0.$$

Using Leibnitz rule of integration,

$$\frac{\partial}{\partial x}\int_0^h udy-\underbrace{u\big|_h}_{=0}\frac{\partial h}{\partial x}+v\big|_h-v\big|_0+\frac{\partial}{\partial z}\int_0^h wdy-\underbrace{w\big|_h}_{=0}\frac{\partial h}{\partial z}=0,$$

$$\Rightarrow \frac{\partial}{\partial x}\int_0^h udy+\frac{\partial h}{\partial t}+\frac{\partial}{\partial z}\int_0^h wdy=0,$$

$$\Rightarrow \frac{\partial V_x}{\partial x}+\frac{\partial V_z}{\partial z}+\frac{\partial h}{\partial t}=0.$$

Plugging in the expressions of V_x and V_y into the expression above to get,

$$\Rightarrow \frac{\partial}{\partial x}\left(h^3\frac{\partial p}{\partial x}\right)+\frac{\partial}{\partial z}\left(h^3\frac{\partial p}{\partial z}\right)=12\eta\frac{\partial h}{\partial t}. \qquad 1.19$$

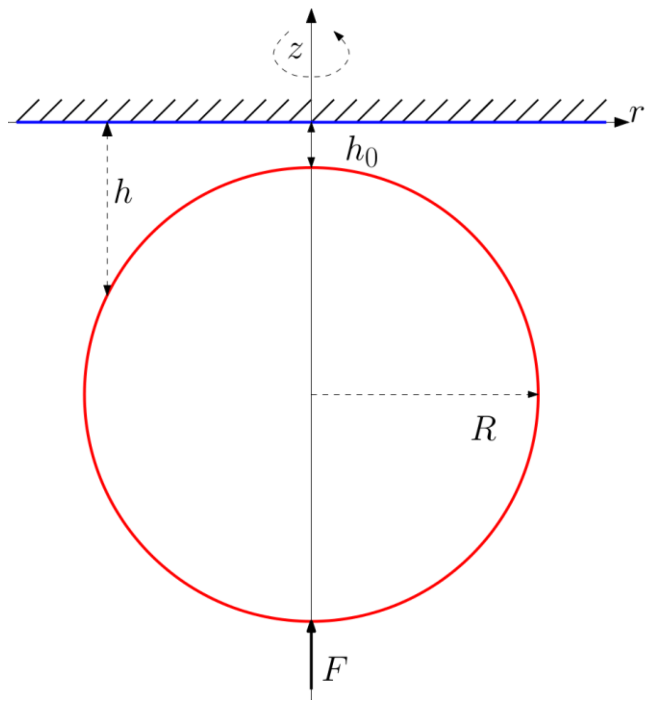
Eq. 1.19 above is referred to as Reynold's equation. In this case, it has been modified to account for the fluid squeezing between two surfaces, one held fixed and other approaching it along the vertical direction.

In more general form for any other geometry (spherical, cylindrical or Cartesian), it can written as,

$$\nabla\left(h^3\nabla p\right)=12\eta\frac{\partial h}{\partial t}. \qquad 1.20$$

2. Rigid sphere against a rigid substrate

Dimensional analysis



Starting with the Reynolds equation, which is the only governing equation for the case under consideration. The problem involves, pushing down a rigid sphere of radius R onto a flat rigid surface and in between the surfaces, there is fluid, which has to be squeezed away.

In the part of the geometry, where film thickness is small, following approximation for the fluid film thickness, can be made,

$$h(r,t) = h_0(t) + \frac{r^2}{2R}. \qquad 2.1$$

Next, consider the Reynolds equation,

$$\nabla\left(h^3 \nabla p\right) = 12\eta \frac{\partial h}{\partial t}, \qquad 2.2$$

and for the axis-symmetric case, it can written as,

$$\frac{\partial}{\partial r}\left(r h^3 \frac{\partial p}{\partial r}\right) = 12\eta r \frac{\partial h}{\partial t}. \qquad 2.3$$

Also, we have following constraint on the pressure distribution on the sphere, which has to be satisfied all times,

$$F = \int_0^\infty p(r,t)\, 2\pi r dr. \qquad 2.4$$

Non-dimensionalization

Following scheme has been chosen to non-dimensionalize eqs. 2.3 and 2.4.

$$\bar{r} = \frac{r}{R},\ \bar{h} = \frac{h}{R},\ \bar{p} = \frac{pR^2}{F}. \qquad 2.5$$

This when applied to eq. 2.3,

$$\frac{\partial}{\partial \bar{r}}\left(\bar{r}\left\{\bar{h}_0 + \frac{\bar{r}^2}{2}\right\}^3 \frac{\partial \bar{p}}{\partial \bar{r}}\right) = \frac{12\eta R^2}{F}\bar{r}\frac{\partial}{\partial t}\left(\bar{h}_0 + \frac{\bar{r}^2}{2}\right),$$

choosing, $\bar{t} = \frac{Ft}{12\eta R^2}$ to get,

$$\frac{\partial}{\partial \bar{r}}\left(\bar{r}\left\{\bar{h}_0 + \frac{\bar{r}^2}{2}\right\}^3 \frac{\partial \bar{p}}{\partial \bar{r}}\right) = \bar{r}\frac{\partial}{\partial \bar{t}}\left(\bar{h}_0 + \frac{\bar{r}^2}{2}\right). \qquad 2.6$$

Also, eq. 2.4 can written in non-dimensional form as,

$$\frac{1}{2\pi} = \int_0^\infty \bar{p}\left(\bar{r},\bar{t}\right)\bar{r}d\bar{r} \qquad 2.7$$

As seen from the non-dimensional analysis, the only quantity with the units of time is $\frac{\eta R^2}{F}$. So, the time of approach scales with $\frac{\eta R^2}{F}$ and is a function of initial and final separations between the surfaces, $\frac{h_{0,1}}{h_{0,2}}$. Therefore the time of approach of sphere against the rigid surface can be written as,

$$\Delta t = \frac{\eta R^2}{F} f\left(\frac{h_{0,1}}{h_{0,2}}\right). \qquad 2.8$$

This is also the nature of expression obtained from the analytical derivation appended in next section.

Analytical calculation

Consider a rigid sphere of radius R, being pushed onto a flat surface, while squeezing out fluid between the two surfaces. The separation between the lowermost point on the sphere and flat surface is referred to as h_0. The aim of this derivation is to get the time taken by the sphere to be brought down from initial bottommost separation of h_{0i} to final bottom most separation of h_{0f}, while a force F acts on the sphere in the downwards direction.

Thickness of lubrication film

The geometry of the problem has axis-symmetry, therefore r and z represents the coordinates. Henceforth, we have film thickness given as, $h = h(r,t)$. We can write an expression of h in terms of h_0 and r, as follows,

$$h = h_0 + \left[R - \left(R^2 - r^2 \right)^{1/2} \right],$$

$$\Rightarrow h = h_0 + R\left[1 - \left(1 - \frac{r^2}{R^2} \right)^{1/2} \right],$$

$$\Rightarrow h \approx h_0 + R\left[1 - \left(1 - \frac{1}{2}\frac{r^2}{R^2} - \frac{1}{8}\left(\frac{r^2}{R^2} \right)^2 - \frac{1}{16}\left(\frac{r^2}{R^2} \right)^4 - \dots \right) \right],$$

$$\Rightarrow h = h_0 + \frac{r^2}{2R}\left[1 + \frac{1}{4}\left(\frac{r^2}{R^2} \right) + \frac{1}{8}\left(\frac{r^2}{R^2} \right)^4 + \dots \right],$$

In the lubrication region, $r \ll R$, hence the above expression can be approximated as,

$$\Rightarrow h = h_0 + \frac{r^2}{2R} \qquad 2.9$$

Reynold's equation

The Reynolds equation for general coordinate system is given by,

$$\nabla\left[h^3 \nabla p \right] = 12\eta \frac{\partial h}{\partial t} \qquad 2.10$$

For an axis-symmetric case, the Reynold's equation is given as,

$$\frac{\partial}{\partial r}\left[r h^3 \frac{\partial p}{\partial r} \right] = 12\eta r \frac{\partial h}{\partial t} \qquad 2.11$$

where,

$p = p(r,t)$ is the fluid pressure in a vertical column of fluid film,

η is the fluid viscosity.

Solution

The Reynold's equation can be integrated to obtain an expression of pressure as a function of fluid film thickness.

Integrating once,

$$\frac{\partial}{\partial r}\left[rh^3\frac{\partial p}{\partial r}\right]=12\eta r\frac{\partial h}{\partial t},$$

$$\Rightarrow \frac{\partial p}{\partial r}=\frac{6\eta r}{h^3}\frac{\partial h}{\partial t}+\frac{A}{rh^3},$$

To avoid a singularity in pressure gradient at $r=0$, $A=0$. Hence, we get,

$$\Rightarrow \frac{\partial p}{\partial r}=\frac{6\eta r}{h^3}\frac{\partial h}{\partial t},$$

$$\Rightarrow \int dp=\left(6\eta\frac{\partial h}{\partial t}\right)\int\frac{r}{h^3}\,dr,$$

using, eq 1, we get, $Rdh=rdr$, pugging in above expression,

$$\Rightarrow \int dp=6\eta R\frac{\partial h}{\partial t}\int\frac{dh}{h^3},$$

$$\Rightarrow p=-\frac{3\eta R}{h^2}\frac{\partial h}{\partial t}+\mathrm{B},$$

For large h, the pressure goes to zero, for it to be satisfied, $B=0$. Hence,

$$p=-\frac{3\eta R}{h^2}\frac{\partial h}{\partial t}. \qquad 2.12$$

This pressure, at any point in time balances the net force applied onto the sphere,

$$\Rightarrow F=\int_0^\infty p(2\pi r dr),$$

$$\Rightarrow F=-\int_0^\infty \frac{3\eta R}{h^2}\frac{\partial h}{\partial t}(2\pi r dr),$$

$$\Rightarrow F=-\left(6\eta\pi R\frac{\partial h}{\partial t}\right)\int_0^\infty\frac{rdr}{h^2},$$

$$\Rightarrow F=-\left(6\eta\pi R^2\frac{\partial h}{\partial t}\right)\int_{h_0}^\infty\frac{dh}{h^2},$$

$$\Rightarrow F=-\frac{6\eta\pi R^2}{h_0}\frac{\partial h}{\partial t}. \qquad 2.13$$

Eq. 2.4 can be integrated to obtain the time of approach of the sphere from initial separation of h_{0i} to final separation of h_{0f} .

$$\frac{F}{6\eta\pi R^2}dt=-\frac{dh_0}{h_0}. \qquad 2.14$$

We will be integrating eq. 2.14 under different loading conditions, which describes the variation of force with the gap between the sphere and substrate.

1) Constant Force

Let the force on the sphere be given by the following function,

$F=nF_{1,max}$,

where,
n is the number of SNARE proteins working together,
$F_{1,max}$ is the maximum force exerted by a single SNARE protein.

Plugging in this expression of F into eq. 2.14 and integrating,

$$\frac{nF_{1,max}}{6\eta\pi R^2}\Delta t = -\int_{h_{0i}}^{h_{0f}} \frac{dh_0}{h_0} = \ln\frac{h_{0i}}{h_{0f}}$$

Hence,

$$\Delta t = \frac{6\eta\pi R^2}{nF_{1,max}}\ln\left(\frac{h_{0i}}{h_{0f}}\right). \qquad 2.15$$

2) Force changing with gap

Let the force on the sphere be given by the following function,

$$F = nF_{1,max}\left(\frac{h_0}{h^*}\right)^m, \qquad 2.16$$

where,
n is the number of SNARE proteins working together,
$F_{1,max}$ is the maximum force exerted by a single SNARE protein,
h_0 is the minimum gap between the rigid sphere and rigid substrate,
h^* is the characteristic length scale, chosen so that the force is $F_{1,max}$ at the maximum opening of SNARE.

The maximum opening for a single SNARE bundle is 13nm and measured force at that opening is 17pN. Hence, to F have desired functional properties, h^* must be 13nm.

Plugging in this expression of F into eq. 14 and integrating,

$$\frac{nF_{1,max}}{6\eta_0\pi R^2}\Delta t = -\int_{h_{0i}}^{h_{0f}} \frac{d\left(h_0/h^*\right)}{\left(h_0/h^*\right)^m} = \frac{1}{m}\left[\left(\frac{h^*}{h_{0f}}\right)^m - \left(\frac{h^*}{h_{0i}}\right)^m\right]$$

$$\Rightarrow \Delta t = \frac{6\eta\pi R^2}{mnF_{1,max}}\left[\left(\frac{h^*}{h_{0f}}\right)^m - \left(\frac{h^*}{h_{0i}}\right)^m\right]. \qquad 2.17$$

3. Rigid sphere against compliant substrate

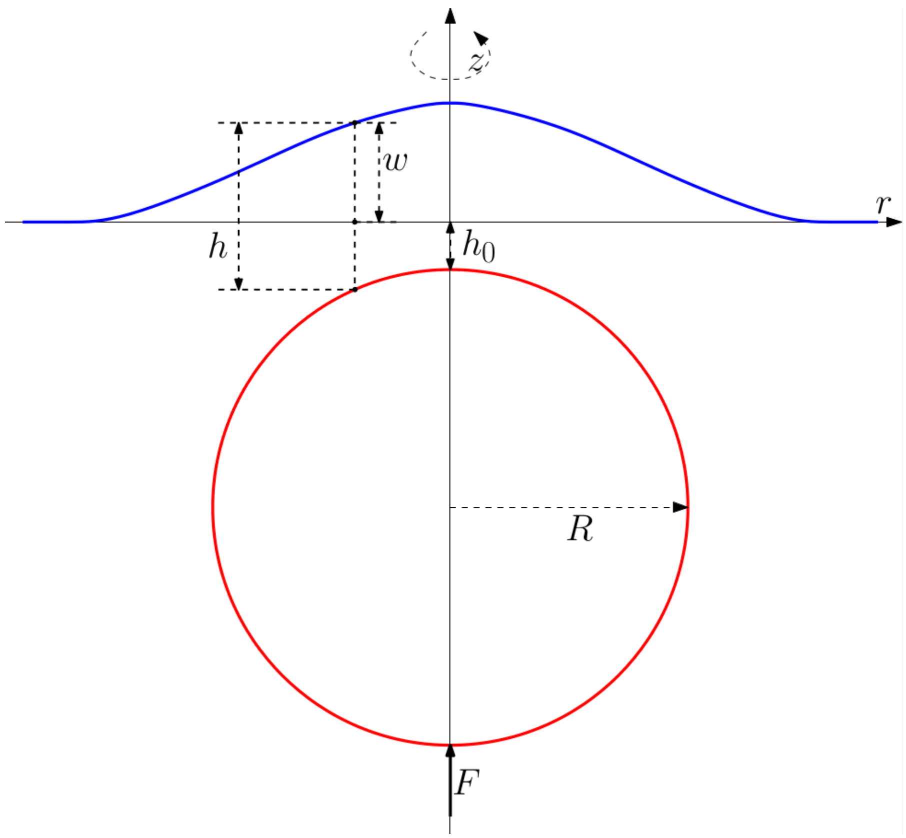


Fig 4: Rigid sphere traversing against a flat lipid membrane

Consider a rigid sphere of radius R , being pushed against a initially flat lipid membrane. During this process, the fluid between the two surfaces is squeezed out. The squeezing requires a radially outward pressure gradient for the fluid flow. This pressure field causes the membrane to deform and hence it is an interplay between the pressure field and membrane deformation.

The aim of this derivation is to get the governing equations for the motion of sphere, while a force F pushes it towards the flat lipid membrane.

Governing equations

This problem can be simplified a lot by exploiting the feature of axisymmetry. Under the assumption of axis-symmetry, mathematically this problem involves solving a partial differential equation (PDE) along with the system of ordinary differential equations (ODE's) which govern the deformation of the lipid membrane.

We begin with explaining the two sets of equations used in this analysis.

1) Hydrodynamics

The equation governing the hydrodynamics of the problem is called Reynolds equation. In its most general form, it can be written as,

$$\nabla\left[h^3\nabla p\right]=12\eta\frac{\partial h}{\partial t}. \quad 3.1$$

Under the axis-symmetric assumption, it can be written as,

$$\frac{\partial}{\partial r}\left[rh^3\frac{\partial p}{\partial r}\right]=12\eta r\frac{\partial h}{\partial t} \quad 3.2$$

along with,

$$h(r,t)=-h_0(t)+\frac{r^2}{2R}+w(r,t), \quad 3.3$$

where,

$h(r,t)$, is the film thickness at some time t and at some radial coordinate r,

$p(r,t)$, is the pressure in the fluid film,

η, is the fluid viscosity,

$h_0(t)$, is the separation between the lowermost point on the sphere and far field flat surface,

$w(r,t)$, is the vertical deformation of the surface.

Along with PDE in eq. 3.2, from force balance on the rigid sphere, following constraint equation can be obtained,

$$F=\int_0^\infty p(r,t)2\pi r dr, \quad 3.4$$

where, F is the applied force on the rigid sphere, pushing it towards the flat lipid membrane.

Since, the eq. 3.2 is a second order in space and first order in time, it comes along with two boundary conditions,

a) $\left.\frac{\partial p(r,t)}{\partial r}\right|_{r=0}=0$, due to the symmetry of geometry, 3.5(a-b)

b) $\left.p(r,t)\right|_{r\to\infty}\to 0$, in the far field the pressure in fluid film should go to zero,

and the following initial condition,

$p(r,t=0)=0$, initially there is no deformation in the system. 3.6

2) Lipid membrane deformation

The lipid membrane deformation is governed by a 4th order differential equation,

$$\frac{\kappa}{2}\nabla^4 w - T_0\nabla^2 w = -p(r) \ , \qquad 3.7$$

where,
κ , is the bending rigidity of the lipid membrane and has a value of $\sim 20k_B T$,
T_0 , is the far field pretension in the lipid membrane,
$w(r)$, is the deformation of the lipid membrane, and
$p(r)$, is the pressure acting on the lipid membrane at a given location.

Eq. 3.7 resembles a plate equation with a pretension in it.

Non-dimensionalization

Normalizing this system of equations in accordance to the following scheme,

$$\bar{r} = \frac{r}{R}, \quad \bar{z} = \frac{z}{R}, \quad \bar{H} = RH, \quad \bar{w} = \frac{w}{R}, \quad \bar{h}_0 = \frac{h_0}{R},$$
$$\bar{F} = \frac{FR}{\kappa},$$
$$\bar{T}_0 = \frac{T_0R^2}{\kappa}, \qquad 3.8(a\text{-}j)$$
$$\bar{p} = \frac{pR^3}{\kappa},$$
$$\bar{t} = \frac{\kappa t}{\eta R^3}.$$

Non-dimensionalizing the hydrodynamics equations to get,

$$\frac{\partial}{\partial \bar{r}}\left[\bar{r}\bar{h}^3\frac{\partial \bar{p}}{\partial \bar{r}}\right] = 12\bar{r}\frac{\partial \bar{h}}{\partial \bar{t}}, \qquad 3.9$$

along with,

$$\bar{h}(\bar{r},\bar{t}) = -\bar{h}_0(\bar{t}) + \frac{\bar{r}^2}{2} + \bar{w}(\bar{r},\bar{t}), \qquad 3.10$$

and following constraint equation,

$$\bar{F} = 2\pi\int_0^\infty \bar{p}(\bar{r},\bar{t})\bar{r}d\bar{r} \ . \qquad 3.11$$

The boundary conditions are normalized to,

a) $\left.\frac{\partial \bar{p}(\bar{r},\bar{t})}{\partial \bar{t}}\right|_{\bar{r}=0} = 0$, 3.12(a-b)

b) $\bar{p}(\bar{r},\bar{t})\big|_{\bar{r}\to\infty} \to 0$.

The initial condition becomes,
$$\bar{p}(\bar{r},\bar{t}=0)=0. \qquad 3.13$$

Non-dimensionalizing the lipid membrane deformation equation to get,
$$\nabla^4\bar{w}-2\bar{T}_0\nabla^2\bar{w}=-2\bar{p}\left(\bar{r}\right). \qquad 3.14$$

Equation 14 can be solved exactly analytically using Green's function to get,
$$\bar{w}\left(\bar{r}\right)=\frac{1}{\bar{T}_0}\left[K_0\left(\sqrt{2\bar{T}_0}\bar{r}\right)\int_0^{\bar{r}} I_0\left(\sqrt{2\bar{T}_0}\bar{\xi}\right)\bar{p}\left(\bar{\xi}\right)\bar{\xi}\,d\bar{\xi}+I_0\left(\sqrt{2\bar{T}_0}\bar{r}\right)\int_{\bar{r}}^{\infty} K_0\left(\sqrt{2\bar{T}_0}\bar{\xi}\right)\bar{p}\left(\bar{\xi}\right)\bar{\xi}\,d\bar{\xi}\right] \qquad 3.15$$

<u>Numerical solution</u>

This problem is solved in a displacment controlled manner, which means $\bar{h}_0$ is incremented in time according to a specified rate, $\frac{\partial\bar{h}_0}{\partial\bar{t}}$, then pressure is obtained numerically and subsequently the deformation of the lipid membrane.

The numerical solution of the problem has been broken down into two parts. The former involves the state when the lipid membrane is significantly deformed and in the later part the deformation of the lipid membrane is negligible compared to h_0. In the following section each stage is described along with its numerical implementation.

1) lipid membrane significantly deformed $\left(\bar{h}_0\approx\bar{w}|_{\bar{r}=0}\right)$

   The system of equations governing the fluid flow eqs 3.9-3.13 and 3.15 are solved using a numerical scheme, which is implicit, to obtain the pressure as a function of location along the radial direction while incrementing in time.

   The numerical implementation is described as follows,

   a) eq 3.9 can be expanded to get,
   $$\left[\bar{h}^3+3\bar{r}\bar{h}^2\frac{\partial\bar{h}}{\partial\bar{r}}\right]\frac{\partial\bar{p}}{\partial\bar{r}}+\bar{r}\bar{h}^3\frac{\partial^2\bar{p}}{\partial\bar{r}^2}=12\bar{r}\left(-\frac{\partial\bar{h}_0}{\partial\bar{t}}+\frac{\partial\bar{w}}{\partial\bar{t}}\right)$$

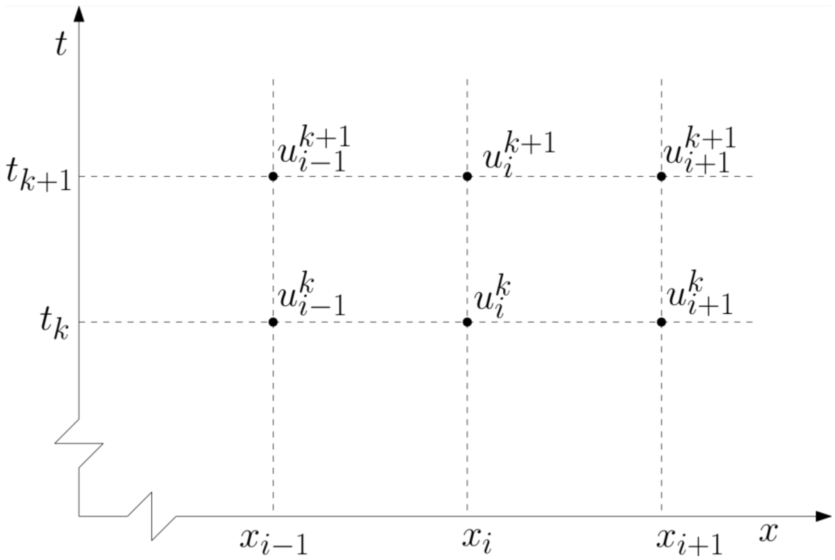


Fig 3.1 : Discretization scheme

b) to solve for pressure field at time $\bar{t}^{\,k+1}$, the above equation can discretized at a location $\bar{r}_i\ (i=1,2,3\ldots.N)$, while using the following definition of the derivatives,

$\left(\frac{\partial\bar{p}}{\partial\bar{r}}\right)_i^{k+1} = A_{i,i-1}\bar{p}_{i-1}^{k+1} + A_{i,i}\bar{p}_i^{k+1} + A_{i,i+1}\bar{p}_{i+1}^{k+1}$, and

$\left(\frac{\partial^2\bar{p}}{\partial\bar{r}^2}\right)_i^{k+1} = B_{i,i-1}\bar{p}_{i-1}^{k+1} + B_{i,i}\bar{p}_i^{k+1} + B_{i,i+1}\bar{p}_{i+1}^{k+1}$,

to obtain,

$$
\begin{aligned}
&\left[\left(\bar{h}^3 + 3\bar{r}\bar{h}^2\frac{\partial\bar{h}}{\partial\bar{r}}\right)_i^{k+1} A_{i,i-1} + \left(\bar{r}\bar{h}^3\right)_i^{k+1} B_{i,i-1}\right]\bar{p}_{i-1}^{k+1}\\
&+\left[\left(\bar{h}^3 + 3\bar{r}\bar{h}^2\frac{\partial\bar{h}}{\partial\bar{r}}\right)_i^{k+1} A_{i,i} + \left(\bar{r}\bar{h}^3\right)_i^{k+1} B_{i,i}\right]\bar{p}_{i}^{k+1}\\
&+\left[\left(\bar{h}^3 + 3\bar{r}\bar{h}^2\frac{\partial\bar{h}}{\partial\bar{r}}\right)_i^{k+1} A_{i,i+1} + \left(\bar{r}\bar{h}^3\right)_i^{k+1} B_{i,i+1}\right]\bar{p}_{i+1}^{k+1}\\
&=12\bar{r}_i\left[\left(\frac{\partial\bar{h}_0}{\partial t}\right)^{k+1} + \frac{\bar{w}_i^{k+1}-\bar{w}_i^{k}}{\Delta t}\right].
\end{aligned}
\qquad 3.16
$$

For these equations, $i=2,3,\ \ldots N-1$.

Also,

$\left(\frac{\partial\bar{h}}{\partial\bar{r}}\right)_i^{k+1} = A_{i,i-1}\bar{h}_{i-1}^{k+1} + A_{i,i}\bar{h}_i^{k+1} + A_{i,i+1}\bar{h}_{i+1}^{k+1}$,

along with,

$$\bar{h}_i^{k+1} = -\bar{h}_0^{k+1} + \frac{\bar{r}_i^2}{2} + \bar{w}_i^{k+1}.$$

c) Using the boundary condition eq 3.12b, $\bar{p}_N = 0$.

d) Using the boundary condition eq. 3.12a, to rewrite as,

$$\frac{\bar{r}_2}{\bar{r}_1}\frac{\bar{p}_1}{(\bar{r}_1 - \bar{r}_2)} + \frac{\bar{r}_1}{\bar{r}_2}\frac{\bar{p}_2}{(\bar{r}_2 - \bar{r}_1)} + \bar{p}_0\frac{\bar{r}_2 + \bar{r}_1}{\bar{r}_2\bar{r}_1}. \tag{3.17}$$

e) The rate of change of $\bar{h}_0$, $\frac{\partial \bar{h}_0}{\partial \bar{t}}$ is specified. For the present simulation it has been assumed to be,

$$\frac{\partial \bar{h}_0}{\partial \bar{t}} = -\frac{\bar{F}_{max}}{6\pi}\bar{h}_0\left(\frac{\bar{h}_0}{\bar{h}^*}\right)^m. \tag{3.18}$$

This is based on the result from the rigid substrate case when the SNARE forces decay in accordance with the $\bar{F} = \bar{F}_{max}\left(\frac{\bar{h}_0}{\bar{h}^*}\right)^m$. This dependence of $\frac{\partial \bar{h}_0}{\partial \bar{t}}$ on $\bar{h}_0$ can be tuned my changing the exponent m.

f) $\bar{h}_0$ is incremented at each time step, by the amount specified according to $\frac{\partial \bar{h}_0}{\partial \bar{t}}$,

$$\bar{h}_0^{k+1} = \bar{h}_0^k + \left(\frac{\partial \bar{h}_0}{\partial \bar{t}}\right)^k \Delta t.$$

g) For a specified $\bar{h}_0$, the equations 3.16 and 3.17 solved iteratively and a solution is obtained.

h) From the converged solution of pressure, Force on the sphere is numerically evaluated using the discretized form of equation 11,

$$\bar{F} = 2\pi\Delta r\sum_{i=1}^{N-1}\bar{p}_i\bar{r}_i. \tag{3.19}$$

This is simulated until the point that the deformation in the middle of the plasma membrane, $\bar{w}|_{\bar{r}=0}$ is negligible compared to $\bar{h}_0$.

Upto this point in the simulation force $\bar{F}$ and location of tip of the sphere $\bar{h}_0$, is measured at each time step. Using this data, a fitting of the form, $\bar{F} = \bar{F}_{max}\left(\frac{\bar{h}_0}{\bar{h}^*}\right)^x$ is done to obtain the exponent x.

2) lipid membrane deformation is negligible $\left(\bar{h}_0 \gg \bar{w}|_{\bar{r}=0}\right)$

In part 1 of the simulation scheme, the deformation at $\bar{r} = 0$ is compared with $\bar{h}_0$, and once it is below a threshold value, then it can be ignored. This assumption can simplify the expression of $\bar{h}$ as,

$$\bar{h}\left(\bar{r},\bar{t}\right)\approx-\bar{h}_0\left(\bar{t}\right)+\frac{\bar{r}^2}{2}.$$

This assumption makes the convergence in the iterative solver faster. The numerical scheme remains the same as described in part 1).

4. Small deformation of a flat lipid membrane

Consider a flat circular membrane, of radius l spanned in the polar coordinates of r and z. The governing equations for this membrane are given by,

$$\frac{\dot{Q}}{\dot{\xi}} = -\frac{Q}{r}\cos\varphi + 2H\left[d + \kappa H^2 + \kappa\left(2H + \frac{\sin\varphi}{r}\right)\frac{\sin\varphi}{r}\right] - p,$$
$$\frac{\dot{H}}{\dot{\xi}} = -\frac{Q}{\kappa},$$
$$\frac{\dot{\varphi}}{\dot{\xi}} = -2H - \frac{\sin\varphi}{r}, \qquad 4.1(a\text{-}e)$$
$$\frac{\dot{r}}{\dot{\xi}} = \cos\varphi,$$
$$\frac{\dot{z}}{\dot{\xi}} = \sin\varphi,$$

where, $\dot{\xi} = \frac{S}{r}$.

The boundary conditions associated with this membrane are,

1) at $S = 0$,
   $\varphi = 0$,
   $Q = 0$, 4.2(a-c)
   $r = 0$,
   these boundary conditions comply with the symmetry at the center of the geometry.
2) at $S = l$,
   $\varphi = 0$,
   $z = 0$, 4.2(d-f)
   $T = -d - \kappa H^2 - \kappa H\frac{\sin\varphi}{r} = T_0$,
   these boundary conditions mimic the far field boundary conditions of a flat lipid bilayer membrane in a finite sized geometry.

Non-dimensionalization

Normalizing this system of equations in accordance to the following scheme,

$$\bar{S} = \frac{S}{R}, \quad \bar{r} = \frac{r}{R}, \quad \bar{z} = \frac{z}{R}, \quad \bar{H} = RH, \quad \bar{\xi} = \frac{\xi}{R},$$
$$\bar{Q} = \frac{QR^2}{\kappa}, \ \bar{d} = \frac{dR^2}{\kappa}, \bar{T} = \frac{TR^2}{\kappa}, \qquad 4.3(a\text{-}i)$$
$$\bar{p} = \frac{pR^3}{\kappa}, \bar{t}^S = \frac{t^S R^3}{\kappa}.$$

In the above scheme, the quantity R is the radius of the synaptic vesicle and κ is the bending rigidity of the lipid bilayer membrane. On applying this non-dimensionalization scheme to the system of eqs. 4.1(a-e) and boundary conditions eqs. 4.2(a-f), we get,

$$\frac{\dot{\bar{Q}}}{\dot{\bar{\xi}}} = -\frac{\bar{Q}}{\bar{r}}\cos\varphi + 2\bar{H}\left[\bar{d} + \bar{H}^2 + \left(2\bar{H} + \frac{\sin\varphi}{\bar{r}}\right)\frac{\sin\varphi}{\bar{r}}\right] - \bar{p},$$
$$\frac{\dot{\bar{H}}}{\dot{\bar{\xi}}} = -\bar{Q},$$
$$\frac{\dot{\varphi}}{\dot{\bar{\xi}}} = -2\bar{H} - \frac{\sin\varphi}{\bar{r}}, \qquad \text{4.4(a-f)}$$
$$\frac{\dot{\bar{r}}}{\dot{\bar{\xi}}} = \cos\varphi,$$
$$\frac{\dot{\bar{z}}}{\dot{\bar{\xi}}} = \sin\varphi,$$

where, $\dot{\bar{\xi}} = \frac{\bar{S}}{\bar{r}}$.

The boundary conditions modify as follows,

1) at $\bar{S} = 0$,
   $\varphi = 0,$
   $\bar{Q} = 0,$ 4.5(a-c)
   $\bar{r} = 0,$
2) at $\bar{S} = \bar{l}$,
   $\varphi = 0,$
   $\bar{z} = 0,$ 4.5(d-f)
   $\bar{T} = -\bar{d} - \bar{H}^2 - \bar{H}\frac{\sin\varphi}{\bar{r}} = \bar{T}_0.$

<u>Udeformed membrane</u>

For an unperturbed membrane, in its undeformed configuration, the loading should be zero ($\bar{p} = 0$), and the system variables are given by,

$\bar{Q} = 0, \bar{H} = 0, \varphi = 0, \bar{r} = \bar{S}$ and $\bar{z} = 0,$ 4.6(a-f)

with $\bar{d} = -\bar{T}_0$.

<u>Perturbed solution</u>

Let's choose the following first order perturbation scheme about the undeformed configuration,

$\bar{Q} = 0 + \bar{Q}_1,$

$\bar{H} = 0 + \bar{H}_1,$ 4.7(a-f)
$\bar{\varphi} = 0 + \bar{\varphi}_1,$
$\bar{r} = \bar{S} + \bar{r}_1,$
$\bar{z} = 0 + \bar{z}_1,$
$\bar{d} = -\bar{T}_0 + \bar{d}_1.$

Now we can derive the boundary conditions in terms of the perturbed variables as follows,
The boundary conditions modify as follows,

1) at $\bar{S} = 0,$
   $\varphi = 0 \Rightarrow \varphi_1 = 0$
   $\bar{Q} = 0 \Rightarrow \bar{Q}_1 = 0$ 4.8(a-c)
   $\bar{r} = 0 \Rightarrow \bar{r}_1 = 0$
2) at $\bar{S} = \bar{l}$,
   $\varphi = 0 \Rightarrow \varphi_1 = 0$
   $\bar{z} = 0 \Rightarrow \bar{z}_1 = 0,$ 4.8(d-f)
   $-\bar{d} - \bar{H}^2 - \bar{H}\dfrac{\sin\varphi}{\bar{r}} = \bar{T}_0 \Rightarrow \bar{T}_0 - \bar{d}_1 - \bar{H}_1^2 - \bar{H}_1\dfrac{\varphi_1}{\bar{S} + \bar{r}} = \bar{T}_0 \Rightarrow \bar{d}_1 = 0.$

Hence, $\bar{d} = -\bar{T}_0.$

<u>Perturbing the governing equations</u>

We start with perturbing the equations one by one and get a linearized form of equations.

1) $$\frac{\dot{\bar{Q}}}{\dot{\bar{\xi}}} = -\frac{\bar{Q}}{\bar{r}}\cos\varphi + 2\bar{H}\left[\bar{d} + \bar{H}^2 + \left(2\bar{H} + \frac{\sin\varphi}{\bar{r}}\right)\frac{\sin\varphi}{\bar{r}}\right] - \bar{p}$$

$$\Rightarrow \dot{\bar{Q}} = -\dot{\bar{\xi}}\frac{\bar{Q}}{\bar{r}}\cos\varphi + 2\bar{H}\dot{\bar{\xi}}\left[\bar{d} + \bar{H}^2 + \left(2\bar{H} + \frac{\sin\varphi}{\bar{r}}\right)\frac{\sin\varphi}{\bar{r}}\right] - \bar{p}\dot{\bar{\xi}}$$

$$\Rightarrow \dot{\bar{Q}} = -\frac{\bar{Q}\bar{S}}{\bar{r}^2}\cos\varphi + 2\bar{H}\frac{\bar{S}}{\bar{r}}\left[\bar{d} + \bar{H}^2 + \left(2\bar{H} + \frac{\sin\varphi}{\bar{r}}\right)\frac{\sin\varphi}{\bar{r}}\right] - \bar{p}\frac{\bar{S}}{\bar{r}}$$

$$\Rightarrow \bar{r}^3\dot{\bar{Q}} = -\bar{Q}\bar{S}\bar{r}\cos\varphi + 2\bar{H}\bar{S}\left[\left(\bar{d} + \bar{H}^2\right)\bar{r}^2 + \left(2\bar{H}\bar{r} + \sin\varphi\right)\sin\varphi\right] - \bar{p}\bar{r}^2\bar{S}$$

plugging in the perturbed functions into the above expression and solving step by step,

$\left(\bar{d} + \bar{H}^2\right) = -\bar{T}_0 + \bar{H}_1^2 \approx -\bar{T}_0$,

$\bar{r}^2\left(\bar{d} + \bar{H}^2\right) = \left(\bar{S}^2 + 2\bar{r}_1\bar{S} + \bar{r}_1^2\right)\left(-\bar{T}_0\right) \approx -\left(\bar{S}^2 + 2\bar{r}_1\bar{S}\right)\bar{T}_0$,

$\left(2\bar{H}\bar{r} + \sin\varphi\right)\sin\varphi = \left[2\bar{H}_1\left(\bar{r}_1 + \bar{S}\right) + \varphi_1\right]\varphi_1 \approx 0$,

$\left[\bar{r}^2\left(\bar{d} + \bar{H}^2\right) + \left(2\bar{H}\bar{r} + \sin\varphi\right)\sin\varphi\right] = -\left(\bar{S}^2 + 2\bar{r}_1\bar{S}\right)\bar{T}_0$,

$2\bar{H}\bar{S}\left[\left(\bar{d} + \bar{H}^2\right)\bar{r}^2 + \left(2\bar{H}\bar{r} + \sin\varphi\right)\sin\varphi\right] = 2\bar{H}_1\bar{S}\left[-\left(\bar{S}^2 + 2\bar{r}_1\bar{S}\right)\bar{T}_0\right] \approx -2\bar{H}_1\bar{T}_0\bar{S}^3$,

$-\overline{p}\overline{r}^{2}\overline{S} \approx -p\left(\overline{S}^{2}+2\overline{r}_{1}\overline{S}\right)\overline{S}$,

$-\overline{Q}\overline{S}\overline{r}\cos\varphi = -\overline{Q}_{1}\overline{S}\left(\overline{r}_{1}+\overline{S}\right)\cos\varphi_{1} \approx -\overline{Q}_{1}\overline{S}^{2}$,

hence, the R.H.S. of equation simplifies to,

$-\overline{Q}\overline{S}\overline{r}\cos\varphi + 2\overline{H}\overline{S}\left[\left(\overline{d}+\overline{H}^{2}\right)\overline{r}^{2}+\left(2\overline{H}\overline{r}+\sin\varphi\right)\sin\varphi\right]-\overline{p}\overline{r}^{2}\overline{S} = -\overline{Q}_{1}\overline{S}^{2}-2\overline{H}_{1}\overline{T}_{0}\overline{S}^{3}-p\left(\overline{S}^{2}+2\overline{r}_{1}\overline{S}\right)\overline{S}.$

On the other hand, L.H.S. can be written as,

$\overline{r}^{3}\dot{\overline{Q}} = \left(\overline{r}_{1}+\overline{S}\right)^{3}\dot{\overline{Q}}_{1} \approx \overline{S}^{3}\dot{\overline{Q}}_{1}$.

Combining both L.H.S. and R.H.S., to get,

$$\overline{S}^{3}\dot{\overline{Q}}_{1} = -\overline{Q}_{1}\overline{S}^{2}-2\overline{H}_{1}\overline{T}_{0}\overline{S}^{3}-p\left(\overline{S}^{2}+2\overline{r}_{1}\overline{S}\right)\overline{S},$$

$$\Rightarrow \dot{\overline{Q}}_{1} = -\frac{\overline{Q}_{1}}{\overline{S}}-2\overline{H}_{1}\overline{T}_{0}-p\left(1+2\frac{\overline{r}_{1}}{\overline{S}}\right). \qquad 4.9a$$

2) $\dfrac{\dot{\overline{H}}}{\dot{\overline{\xi}}} = -\overline{Q}$

$\Rightarrow \dot{\overline{H}}\overline{r} = -\overline{S}\overline{Q}$,

plugging in the perturbed functions,

$\Rightarrow \dot{\overline{H}}_{1}\left(\overline{r}_{1}+\overline{S}\right) = -\overline{S}\overline{Q}_{1}$

$\Rightarrow \dot{\overline{H}}_{1}\overline{S} = -\overline{S}\overline{Q}_{1}$

$$\Rightarrow \dot{\overline{H}}_{1} = -\overline{Q}_{1} \qquad 4.9b$$

3) $\dfrac{\dot{\varphi}}{\dot{\overline{\xi}}} = -2\overline{H}-\dfrac{\sin\varphi}{\overline{r}}$,

$\Rightarrow \dot{\varphi} = -2\overline{H}\dot{\overline{\xi}}-\dfrac{\sin\varphi}{\overline{r}}\dot{\overline{\xi}}$,

$\Rightarrow \dot{\varphi} = -2\overline{H}\dfrac{\overline{S}}{\overline{r}}-\dfrac{\sin\varphi}{\overline{r}}\dfrac{\overline{S}}{\overline{r}}$,

$\Rightarrow \overline{r}^{2}\dot{\varphi} = -2\overline{H}\overline{S}\overline{r}-\sin\varphi\overline{S}$,

plugging in the perturbed functions,

$\Rightarrow \left(\overline{r}_{1}+\overline{S}\right)^{2}\dot{\varphi}_{1} = -2\overline{H}_{1}\overline{S}\left(\overline{r}_{1}+\overline{S}\right)-\sin\varphi_{1}\overline{S}$,

$\Rightarrow \overline{S}^{2}\dot{\varphi}_{1} = -2\overline{H}_{1}\overline{S}^{2}-\varphi_{1}\overline{S}$,

$$\Rightarrow \dot{\varphi}_{1} = -2\overline{H}_{1}-\frac{\varphi_{1}}{\overline{S}}, \qquad 4.9c$$

4) $\dfrac{\dot{\bar{r}}}{\dot{\bar{\xi}}} = \cos\varphi,$

$\Rightarrow \dot{\bar{r}} = \dot{\bar{\xi}}\cos\varphi,$

$\Rightarrow \dot{\bar{r}} = \dfrac{\bar{S}}{\bar{r}}\cos\varphi,$

$\Rightarrow \bar{r}\,\dot{\bar{r}} = \bar{S}\cos\varphi,$

plugging in the perturbed functions,

$\Rightarrow \left(\bar{r}_1 + \bar{S}\right)\left(\dot{\bar{r}}_1 + 1\right) = \bar{S}\cos\varphi_1,$

$\Rightarrow \bar{r}_1 + \bar{S} + \bar{S}\,\dot{\bar{r}}_1 = \bar{S},$

$\Rightarrow \dot{\bar{r}}_1 = -\dfrac{\bar{r}_1}{\bar{S}},$ 4.9d

5) $\dfrac{\dot{\bar{z}}}{\dot{\bar{\xi}}} = \sin\varphi,$

$\Rightarrow \dot{\bar{z}} = \dot{\bar{\xi}}\sin\varphi,$

$\Rightarrow \dot{\bar{z}} = \dfrac{\bar{S}}{\bar{r}}\sin\varphi,$

$\Rightarrow \bar{r}\dot{\bar{z}} = \bar{S}\sin\varphi,$

plugging in the perturbed functions,

$\Rightarrow \left(\bar{r}_1 + \bar{S}\right)\dot{\bar{z}}_1 = \bar{S}\sin\varphi_1,$

$\Rightarrow \dot{\bar{z}}_1 = \varphi_1,$ 4.9e

Hence, we have following system of equations,

$$\dot{\bar{Q}}_1 = -\frac{\bar{Q}_1}{\bar{S}} - 2\bar{H}_1\bar{T}_0 - p\left(1 + 2\frac{\bar{r}_1}{\bar{S}}\right)$$

$$\dot{\bar{H}}_1 = -\bar{Q}_1$$

$$\dot{\varphi}_1 = -2\bar{H}_1 - \frac{\varphi_1}{\bar{S}}, \qquad 4.9(a\text{-}e)$$

$$\dot{\bar{r}}_1 = -\frac{\bar{r}_1}{\bar{S}},$$

$$\dot{\bar{z}}_1 = \varphi_1,$$

Along with following boundary conditions,

1) at $\bar{S} = 0$,

$$\varphi = 0 \Rightarrow \varphi_1 = 0$$

$$\bar{Q} = 0 \Rightarrow \bar{Q}_1 = 0 \qquad 4.8(a\text{-}c)$$

$$\bar{r} = 0 \Rightarrow \bar{r}_1 = 0$$

2) at $\bar{S} = \bar{l}$,

$$\varphi = 0 \Rightarrow \varphi_1 = 0$$
$$\bar{z} = 0 \Rightarrow \bar{z}_1 = 0, \qquad 4.8(d\text{-}e)$$

Combined equation and comaprison with plate equation

Reviewing the governing equations,

$$\dot{\bar{Q}}_1 = -\frac{\bar{Q}_1}{\bar{S}} - 2\bar{H}_1\bar{T}_0 - p\left(1 + 2\frac{\bar{r}_1}{\bar{S}}\right)$$
$$\dot{\bar{H}}_1 = -\bar{Q}_1$$
$$\dot{\varphi}_1 = -2\bar{H}_1 - \frac{\varphi_1}{\bar{S}}, \qquad 4.9(a\text{-}e)$$
$$\dot{\bar{r}}_1 = -\frac{\bar{r}_1}{\bar{S}},$$
$$\dot{\bar{z}}_1 = \varphi_1.$$

Start with plugging in the eq. 4.9e into eq. 4.9c,

$$\ddot{\bar{z}}_1 = -2\bar{H}_1 - \frac{\dot{\bar{z}}_1}{\bar{S}} \Rightarrow \bar{H}_1 = -\frac{1}{2}\left(\ddot{\bar{z}}_1 + \frac{\dot{\bar{z}}_1}{\bar{S}}\right), \qquad 4.10$$

plugging eq. 4.10 into eq. 4.9b,

$$\bar{Q}_1 = -\dot{\bar{H}}_1 \Rightarrow \bar{Q}_1 = \frac{1}{2}\left(\dddot{\bar{z}}_1 + \frac{\ddot{\bar{z}}_1}{\bar{S}} - \frac{\dot{\bar{z}}_1}{\bar{S}^2}\right), \qquad 4.11$$

plugging eqs. 4.10 and 4.11 into eq. 4.9a,

$$\dot{\bar{Q}}_1 + \frac{\bar{Q}_1}{\bar{S}} + 2\bar{H}_1\bar{T}_0 = -p\left(1 + 2\frac{\bar{r}_1}{\bar{S}}\right),$$

$$\Rightarrow \frac{1}{2}\left(\ddddot{\bar{z}}_1 + \frac{\dddot{\bar{z}}_1}{\bar{S}} - 2\frac{\ddot{\bar{z}}_1}{\bar{S}^2} + 2\frac{\dot{\bar{z}}_1}{\bar{S}^3}\right) + \frac{1}{2}\left(\frac{\dddot{\bar{z}}_1}{\bar{S}} + \frac{\ddot{\bar{z}}_1}{\bar{S}^2} - \frac{\dot{\bar{z}}_1}{\bar{S}^3}\right) - \bar{T}_0\left(\ddot{\bar{z}}_1 + \frac{\dot{\bar{z}}_1}{\bar{S}}\right) = -p\left(1 + 2\frac{\bar{r}_1}{\bar{S}}\right),$$

$$\Rightarrow \frac{1}{2}\left(\ddddot{\bar{z}}_1 + 2\frac{\dddot{\bar{z}}_1}{\bar{S}} - \frac{\ddot{\bar{z}}_1}{\bar{S}^2} + \frac{\dot{\bar{z}}_1}{\bar{S}^3}\right) - \bar{T}_0\left(\ddot{\bar{z}}_1 + \frac{\dot{\bar{z}}_1}{\bar{S}}\right) = -p\left(1 + 2\frac{\bar{r}_1}{\bar{S}}\right),$$

$$\Rightarrow \frac{1}{\bar{S}}\frac{\partial}{\partial\bar{S}}\left[\bar{S}\frac{\partial}{\partial\bar{S}}\left\{\frac{1}{\bar{S}}\frac{\partial}{\partial\bar{S}}\left(\bar{S}\frac{\partial\bar{z}_1}{\partial\bar{S}}\right)\right\}\right] - 2\bar{T}_0\left[\frac{1}{\bar{S}}\frac{\partial}{\partial\bar{S}}\left(\bar{S}\frac{\partial\bar{z}_1}{\partial\bar{S}}\right)\right] = -2p\left(1 + 2\frac{\bar{r}_1}{\bar{S}}\right),$$

$$\Rightarrow \nabla^4_{\bar{S}}\bar{z}_1 - 2\bar{T}_0\nabla^2_{\bar{S}}\bar{z}_1 = -2p\left(1 + 2\frac{\bar{r}_1}{\bar{S}}\right). \qquad 4.12$$

Comparing this with the governing equation in the literature for a plate with pretension,

$$\nabla^4_{\bar{r}}\bar{w} - \bar{\sigma}_0\nabla^2_{\bar{r}}\bar{w} = \bar{q}, \qquad 4.13$$

where, $\bar{w}$ is the deflection in the plate,

$\bar{\sigma}_0$ is the pretension in the plate,

$\bar{q}$ is the load per unit area on the plate, and

$\bar{r}$ is the r coordinate of the system.

It can be shown that eqs. 4.12 and 4.13 are same equations. In order to do that, consider eq. 4.9d,

$$\dot{\bar{r}}_1 = -\frac{\bar{r}_1}{\bar{S}} \Rightarrow \frac{\partial \bar{r}_1}{\partial \bar{S}} = -\frac{\bar{r}_1}{\bar{S}} \Rightarrow \ln \bar{r}_1 + \ln \bar{S} = c \Rightarrow \bar{r}_1 \bar{S} = \mathrm{c}_1,$$

along with the boundary condition in eq. 4.8c, $\bar{r}_1\left(\bar{S}=0\right)=0$

$$\Rightarrow \bar{r}_1 \bar{S} = 0 \Rightarrow \bar{r}_1 = 0. \qquad 4.14$$

This also helps to conclude from eq. 4.7d,

$$\bar{r} = \bar{S}\ . \qquad 4.15$$

Hence, eq. 4.12 can be written down as,

$$\nabla^4_{\bar{r}} \bar{z}_1 - 2\bar{T}_0 \nabla^2_{\bar{r}} \bar{z}_1 = -2p. \qquad 4.16$$

On comapring eqs. 4.13 and 4.16,

$\bar{\sigma}_0 = 2\bar{T}_0$ and $\bar{q} = -2\bar{p}$.

5. Solution of Small deformation lipid membrane equation

The non-dimensionalised small deformation equation for an axis-symmetric flat lipid membrane can be written as,

$$\nabla^4 w(r) - 2T_0 \nabla^2 w(r) = -2p(r) \tag{5.1}$$

where,

$w(r)$, is the vertical deformation of the membrane at a given location r,

T_0, is the far field tension in the membrane, and

$p(r)$, is the pressure acting on the membrane at some given location r.

Making following replacements,

$\sigma^2 = 2T_0$ and $q(r) = -2p(r)$,

to get,

$$\nabla^4 w(r) - \sigma^2 \nabla^2 w(r) = q(r). \tag{5.2}$$

Making one more substitution of $\varphi(r) = \nabla^2 w(r)$ 5.3

to get,

$$\nabla^2 \varphi(r) - \sigma^2 \varphi = q(r). \tag{5.4}$$

For now, assuming that the pressure distribution is localized on a ring of radius r_0. Hence, we have,

$q(r) = \delta(r - r_0)$,

and it has the following integral result,

$$2\pi \int_0^\infty r\delta(r - r_0)\, dr = 1. \tag{5.5}$$

Solving for $\varphi(r)$

We solve eq 5.4 for $\varphi(r)$ and eventually solve for $w(r)$. Eq 5.4 can be solved two different ways, method 1 involves use of Hankel Transform and method 2 is standard ODE solving.

Method 1

Taking Hankel transform of eq 5.4,

$$-\xi^2\tilde{\varphi}(\xi)-\sigma^2\tilde{\varphi}(\xi)=\tilde{q}(\xi)=\int_0^\infty q(\rho)J_0(\rho\xi)\rho d\rho \ ,$$

where, $\tilde{f}(\xi)=\int_o^\infty f(r)J_0(r\xi)rdr$ denotes the Hankel transform of a function $f(r)$.

Further simplification gives,

$$\Rightarrow \tilde{\varphi}(\xi)=-\frac{1}{\sigma^2+\xi^2}\int_0^\infty q(\rho)J_0(\rho\xi)\rho d\rho \ .$$

Taking inverse Hankel transform and rearranging the order of integrals to get,

$$\Rightarrow \varphi(r)=-\int_0^\infty \frac{\xi J_0(r\xi)}{\sigma^2+\xi^2}\left[\int_0^\infty q(\rho)J_0(\rho\xi)\rho d\rho\right]d\xi,$$
$$\Rightarrow \varphi(r)=-\int_0^\infty \rho q(\rho)\left[\int_0^\infty \frac{\xi J_0(r\xi)J_0(\rho\xi)}{\sigma^2+\xi^2}d\xi\right]d\rho.$$

The integral in the [ ] brackets is a standard integral and can be written as follows,

$$\int_0^\infty \frac{\xi J_0(r\xi)J_0(\rho\xi)}{\sigma^2+\xi^2}d\xi=\begin{cases} I_0(\rho\sigma)K_0(r\sigma) & 0<\rho<r \\ K_0(\rho\sigma)I_0(r\sigma) & r<\rho \end{cases}.$$

Implementing this result in the integral, we get,

$$\Rightarrow \varphi(r)=-\int_0^r \rho q(\rho)I_0(\rho\sigma)K_0(r\sigma)d\rho-\int_r^\infty \rho q(\rho)K_0(\rho\sigma)I_0(r\sigma)d\rho,$$
$$\Rightarrow \varphi(r)=-K_0(r\sigma)\int_0^r \rho q(\rho)I_0(\rho\sigma)d\rho-I_0(r\sigma)\int_r^\infty \rho q(\rho)K_0(\rho\sigma)d\rho.$$

Now, plugging in the fact that q is a delta function to get a solution for φ

$$\Rightarrow \varphi(r)=-\frac{1}{2\pi}\begin{cases} I_0(r\sigma)K_0(r_0\sigma) & r<r_0 \\ K_0(r\sigma)I_0(r_0\sigma) & r>r_0 \end{cases}. \qquad 5.6$$

Method 2

Because of the delta function at $r = r_0$, in the region $r \in [0, \infty)$ excluding $r = r_0$, the solution of the eq 5.4 can be written down in terms of two arbitrary constants as follows,

$$\varphi(r) = \begin{cases} A\, I_0(\sigma r) & r < r_0 \\ B\, K_0(\sigma r) & r > r_0 \end{cases} . \tag{5.7}$$

From the inspection of eq 5.4, it can be observed that, the delta function on the right hand side originates from the $\nabla^2 \varphi(r)$ term, rather than $\varphi(r)$ term.

Integrating, both sides of eq 5.4, in the interval $r \in [r_0 - \varepsilon, r_0 + \varepsilon]$,

$$\int_{r_0-\varepsilon}^{r_0+\varepsilon} \left(\nabla^2 \varphi - \sigma^2 \varphi\right) r dr = \int_{r_0-\varepsilon}^{r_0+\varepsilon} q r dr,$$

$$\Rightarrow \int_{r_0-\varepsilon}^{r_0+\varepsilon} \left[\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial \varphi}{\partial r}\right) - \sigma^2 \varphi\right] r dr = \int_{r_0-\varepsilon}^{r_0+\varepsilon} r\delta(r - r_0) dr,$$

$$\Rightarrow \left(r\frac{\partial \varphi}{\partial r}\right)_{r_0-\varepsilon}^{r_0+\varepsilon} - \underbrace{\sigma^2 \left.\varphi\right|_{r_0-\varepsilon}^{r_0+\varepsilon}}_{\approx O(\epsilon)} = \frac{1}{2\pi},$$

$$\Rightarrow (r_0 + \varepsilon)\left.\left(\frac{\partial \varphi}{\partial r}\right)\right|_{r=r_0+\varepsilon} - (r_0 - \varepsilon)\left.\left(\frac{\partial \varphi}{\partial r}\right)\right|_{r=r_0-\varepsilon} - 0 = \frac{1}{2\pi},$$

$$\Rightarrow r_0\left[\left.\left(\frac{\partial \varphi}{\partial r}\right)\right|_{r=r_0+\epsilon} - \left.\left(\frac{\partial \varphi}{\partial r}\right)\right|_{r=r_0-\varepsilon}\right] = \frac{1}{2\pi}. \tag{5.8}$$

Apart from this, we have continuity condition for $\varphi(r)$ at $r = r_0$,

$$\left.\varphi\right|_{r=r_0+\epsilon} = \left.\varphi\right|_{r=r_0-\epsilon} . \tag{5.9.}$$

Using the expression of φ from eq 5.7 into the eqs 5.8 and 5.9, to get following set of equations,

$$r_0\left[-B\, K_1(\sigma r_0) - A\, I_1(\sigma r_0)\right] = \frac{q_0}{2\pi}, \tag{5.10}$$

$$A\, I_0(\sigma r_0) = B\, K_0(\sigma r_0) . \tag{5.11}$$

Solving eqs 5.10 and 5.11 for A and B,

$$A = -\frac{1}{2\pi\sigma r_0}\left[\frac{K_0(\sigma r_0)}{I_0(\sigma r_0)K_1(\sigma r_0) + K_0(\sigma r_0)I_1(\sigma r_0)}\right],$$

$$B = -\frac{1}{2\pi\sigma r_0}\left[\frac{I_0(\sigma r_0)}{I_0(\sigma r_0)K_1(\sigma r_0) + K_0(\sigma r_0)I_1(\sigma r_0)}\right].$$

Using the Wronskian property of modified Bessel functions,

$$I_0(\sigma r_0)K_1(\sigma r_0)+K_0(\sigma r_0)I_1(\sigma r_0)=\frac{1}{\sigma r_0},$$

into the expressions for A and B, to get,

$$A=-\frac{1}{2\pi}K_0(\sigma r_0),$$
$$B=-\frac{1}{2\pi}I_0(\sigma r_0).$$

Going back to eq 5.7, and plugging in the values of A and B to get,

$$\varphi(r)=-\frac{1}{2\pi}\begin{cases} I_0(\sigma r)K_0(\sigma r_0) & r<r_0 \\ K_0(\sigma r)I_0(\sigma r_0) & r>r_0 \end{cases}. \qquad 5.12$$

<u>Solving for</u> $w(r)$

Both methods of solving yielded the same result, as seen in eqs 5.6 and 5.12. Next step, is to solve for $w(r)$, in the equation,

$$\nabla^2 w(r)=\varphi(r)=-\frac{1}{2\pi}\begin{cases} I_0(\sigma r)K_0(\sigma r_0) & r<r_0 \\ K_0(\sigma r)I_0(\sigma r_0) & r>r_0 \end{cases}$$

$$\Rightarrow \frac{\partial^2 w}{\partial r^2}+\frac{1}{r}\frac{\partial w}{\partial r}=-\frac{1}{2\pi}\begin{cases} I_0(\sigma r)K_0(\sigma r_0) & r<r_0 \\ K_0(\sigma r)I_0(\sigma r_0) & r>r_0 \end{cases}. \qquad 5.13$$

The homogeneous solution of eq 5.13 is,

$$w(r)=C\ln r+D.$$

For a closed form w, $C=0$ and for the asymptotic solution of $w\to 0$, $D=0$. Hence, the solution of eq 5.13 only comprises of the particular solution.

Since, $I_0(\sigma r)$ and $K_0(\sigma r)$ are solutions to the following differential equation ,

$$\frac{\partial^2 y}{\partial r^2}+\frac{1}{r}\frac{\partial y}{\partial r}-\sigma^2 y=0\Rightarrow\frac{\partial^2 y}{\partial r^2}+\frac{1}{r}\frac{\partial y}{\partial r}=\sigma^2 y,$$

hence,

$$\frac{\partial^2 I_0(\sigma r)}{\partial r^2}+\frac{1}{r}\frac{\partial I_0(\sigma r)}{\partial r}=\sigma^2 I_0(\sigma r) \quad \text{and} \quad \frac{\partial^2 K_0(\sigma r)}{\partial r^2}+\frac{1}{r}\frac{\partial K_0(\sigma r)}{\partial r}=\sigma^2 K_0(\sigma r).$$

Using the above fact to obtain the particular solution,

$$\Rightarrow w(r) = -\frac{1}{2\pi\sigma^2}\begin{cases} I_0(\sigma r)K_0(\sigma r_0) & r < r_0 \\ K_0(\sigma r)I_0(\sigma r_0) & r > r_0 \end{cases}. \qquad 5.14$$

This solution of $w(r)$ in eq 5.14 is the Green's function of the eq 5.2 and can be written in the standard Green's function representation as,

$$G(r\,|\,\xi) = -\frac{1}{2\pi\sigma^2}\begin{cases} I_0(\sigma r)K_0(\sigma\xi) & r < \xi \\ K_0(\sigma r)I_0(\sigma\xi) & r > \xi \end{cases}, \qquad 5.15$$

and hence,

$$w(r) = 2\pi\int_0^\infty G(r\,|\,\xi)q(\xi)\xi d\xi,$$

$$w(r) = -\frac{1}{\sigma^2}\left[K_0(\sigma r)\int_0^r I_0(\sigma\xi)q(\xi)\xi d\xi + I_0(\sigma r)\int_r^\infty K_0(\sigma\xi)q(\xi)\xi d\xi\right].$$

Plugging in, the values of $q(\xi) = -2p(\xi)$ and $\sigma^2 = 2T_0$,

$$w(r) = \frac{1}{T_0}\left[K_0\left(\sqrt{2T_0}r\right)\int_0^r I_0\left(\sqrt{2T_0}\xi\right)p(\xi)\xi d\xi + I_0\left(\sqrt{2T_0}r\right)\int_r^\infty K_0\left(\sqrt{2T_0}\xi\right)p(\xi)\xi d\xi\right]. \qquad 5.16$$

<u>**Implementation in a numerical scheme**</u>

For a numerical scheme when the pressure $p(r_i)$ is provided at some discrete data point r_i. Apart from that the domain is also finite, hence the second integral instead of going to ∞ goes to some large value, l. Under these conditions, the deformation $w(r_i)$ can be written as,

$$w(r_i) = \frac{\Delta r}{T_0}\left[K_0\left(\sqrt{2T_0}r_i\right)\sum_{j=0}^{j=i}\left\{I_0\left(\sqrt{2T_0}r_j\right)p(r_j)r_j\right\} + I_0\left(\sqrt{2T_0}r_i\right)\sum_{j=i+1}^{j=n}\left\{K_0\left(\sqrt{2T_0}r_j\right)p(r_j)r_j\right\}\right]. \qquad 5.17$$