Justify Widom Picture

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We can justify Widom picture by making a simple approximation. We assume that the density of water outside the solute core is the bulk density, as shown in Fig 1. Under this approximation, we can show that the results in our short solvent paper can be directly mapped to the Widom picture.

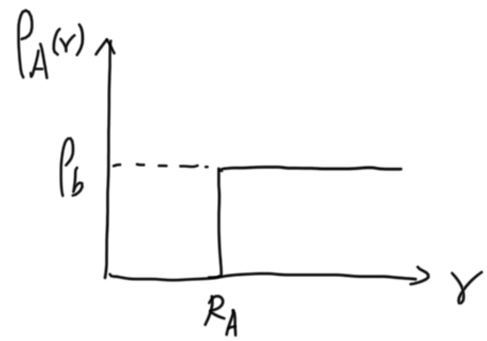

Figure 1: $\rho_{\mathrm{A}}(r)$ is the water density around solute A. ρ_b is the bulk water density. R_{A} is the radius of the solute.

In our short solvent paper we derived the following effective solute-solute pair potential that accounts for the long ranged vdw contribution to the solute-solute PMF:

$$
\begin{aligned}
&\mathsf{w}^{\mathrm{ss}}_{\mathrm{AB}}(r) = \mathsf{w}^{\mathrm{f}}_{\mathrm{AB}}(r) \\
&+\frac{1}{2}\int d\boldsymbol{r}'\Big(\delta\rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}}) + \delta\rho_{0,\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}})\Big)u_{1,\mathrm{BW}}(r'_{\mathrm{B}}) \\
&+\frac{1}{2}\int d\boldsymbol{r}'\Big(\delta\rho_{\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}}) + \delta\rho_{0,\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}})\Big)u_{1,\mathrm{AW}}(r'_{\mathrm{A}}) \\
&+\frac{1}{2}\int\int d\boldsymbol{r}'d\boldsymbol{r}''\Big(\delta\rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}})\delta\rho_{0,\mathrm{B}}(\boldsymbol{r}''_{\mathrm{B}}) \\
&+\delta\rho_{\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}})\delta\rho_{0,\mathrm{A}}(\boldsymbol{r}''_{\mathrm{A}})\Big)u_{1,\mathrm{WW}}(|\boldsymbol{r}''-\boldsymbol{r}'|)\,.
\end{aligned}
\tag{1}
$$

In Eq.(1) $\delta\rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}}) = \rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}}) - \rho_b$ is the perturbation of water density by solute A. We assume that in both the full and short solvent system the water density outside the solute is bulk density, which means that $\delta\rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}}) = \delta\rho_{0,\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}})$ and $\delta\rho_{\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}}) = \delta\rho_{0,\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}})$. Eq.(1) can thus be further simplified to

$$
\begin{aligned}
&\mathsf{w}^{\mathrm{ss}}_{\mathrm{AB}}(r) = \mathsf{w}^{\mathrm{f}}_{\mathrm{AB}}(r) \\
&+ \int d\boldsymbol{r}' \delta\rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}}) u_{1,\mathrm{BW}}(r'_{\mathrm{B}}) \\
&+ \int d\boldsymbol{r}' \delta\rho_{\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}}) u_{1,\mathrm{AW}}(r'_{\mathrm{A}}) \\
&+ \frac{1}{2} \int\int d\boldsymbol{r}' d\boldsymbol{r}'' \Big(\delta\rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}}) \delta\rho_{\mathrm{B}}(\boldsymbol{r}''_{\mathrm{B}}) \\
&+ \delta\rho_{\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}}) \delta\rho_{\mathrm{A}}(\boldsymbol{r}''_{\mathrm{A}}) \Big) u_{1,\mathrm{WW}}(|\boldsymbol{r}'' - \boldsymbol{r}'|) \,.
\end{aligned}
\tag{2}
$$

The first two integrals in Eq.(2) is the contribution of solute-water attraction to the AB PMF. The corresponding integrands are non-zero only in the blue and red region of Fig 2. Making using of this property, the two integrals can be simplified to

$$
\begin{aligned}
\text{first two integrals of Eq.(2)} &= -\int_{blue} d\boldsymbol{r}' \rho_b u_{1,\mathrm{BW}}(r'_{\mathrm{B}}) - \int_{red} d\boldsymbol{r}' \rho_b u_{1,\mathrm{AW}}(r'_{\mathrm{A}}) \\
&= -n_{blue} \frac{\int_{blue} d\boldsymbol{r}' u_{1,\mathrm{BW}}(r'_{\mathrm{B}})}{V_{blue}} - n_{red} \frac{\int_{red} d\boldsymbol{r}' u_{1,\mathrm{AW}}(r'_{\mathrm{A}})}{V_{red}} \\
&= -n_{blue} \left\langle u_{1,\mathrm{BW}} \right\rangle_{blue} - n_{red} \left\langle u_{1,\mathrm{AW}} \right\rangle_{red}
\end{aligned}
\tag{3}
$$

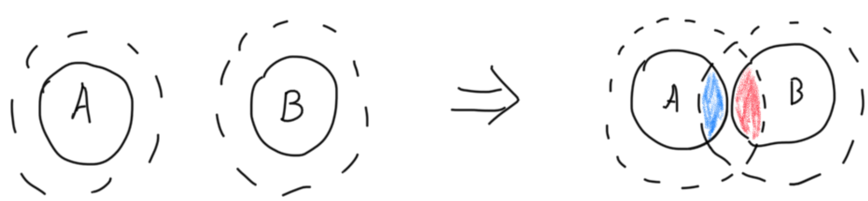

Figure 2: The dashed curve around the solute stands for the range of solute-water attraction. When A and B associate, the water in the blue and red region are depleted to the bulk.

In Eq.(3) n_{blue} and n_{red} are the number of water molecules in the blue and red region that are depleted to the bulk upon the association of A and B. $\left\langle u_{1,\mathrm{BW}} \right\rangle_{blue} = \frac{\int_{blue} d\boldsymbol{r}' u_{1,\mathrm{BW}}(r'_{\mathrm{B}})}{V_{blue}}$ is the average strength of BW attraction in the blue region, where V_{blue} is the volume of the blue region. $\left\langle u_{1,\mathrm{AW}} \right\rangle_{red}$ is defined similarly.

The result of Eq.(3) is exactly what is predicted by Widom's picture. When the two solutes associated, the water in the blue and red region are depleted to the bulk, thus no longer subject to the solute-water attraction. The corresponding free energy change is just what is given by Eq.(3).

The last integral of Eq.(2) is the contribution of water-water attraction, which can be further rewritten based on LMF potential:

$$\text{Last integral of Eq.(2)} = \frac{1}{2}\int d\boldsymbol{r}'\delta\rho_{\mathrm{A}}(\boldsymbol{r}'_{\mathrm{A}})\phi_{S,\mathrm{BW}}(r'_{\mathrm{B}}) + \frac{1}{2}\int d\boldsymbol{r}'\delta\rho_{\mathrm{B}}(\boldsymbol{r}'_{\mathrm{B}})\phi_{S,\mathrm{AW}}(r'_{\mathrm{A}}) \tag{4}$$

where $\phi_{S,\mathrm{BW}}(r'_{\mathrm{B}}) = \int d\boldsymbol{r}''\delta\rho_{\mathrm{B}}(\boldsymbol{r}''_{\mathrm{B}})u_{1,\mathrm{WW}}(|\boldsymbol{r}'' - \boldsymbol{r}'|)$ is the renormalized part of LMF potential around solute B. $\phi_{S,\mathrm{AW}}(r'_{\mathrm{A}})$ is defined similarly.

Note that the integrals in Eq.(4) are similar to the first two integrals of Eq.(2), with an additional prefactor $\frac{1}{2}$. We can connect Eq.(4) with Widom picture by following procedures analogous to what is shown in Eq.(3):

$$\text{RHS of Eq.(4)} = -\frac{1}{2}n_{green}\left\langle\phi_{S,\mathrm{BW}}\right\rangle_{green} - \frac{1}{2}n_{orange}\left\langle\phi_{S,\mathrm{AW}}\right\rangle_{orange} \tag{5}$$

where n_{green} and n_{orange} are the number of water molecules in the green and orange region that are depleted as shown in Fig 3. $\left\langle\phi_{S,\mathrm{BW}}\right\rangle_{green}$ is the average strength of $\phi_{S,\mathrm{BW}}$ in the green region. $\left\langle\phi_{S,\mathrm{AW}}\right\rangle_{orange}$ is the average strength of $\phi_{S,\mathrm{AW}}$ in the orange region.

Figure 3: The dashed curve around the solute stands for the range of $\phi_{S,\mathrm{AW}}$ and $\phi_{S,\mathrm{BW}}$ respectively. When A and B associate, the water in the green and orange region are depleted to the bulk.

Eq.(5) is consistent with Widom picture except for the $\frac{1}{2}$ prefactor. When the two solutes associate, the water in the green and orange region are depleted to the bulk, thus no longer subject to the renormalized part of LMF potential $\phi_{S,\mathrm{BW}}$ and $\phi_{S,\mathrm{AW}}$. Unlike the solute-water attraction $u_{1,\mathrm{BW}}$ and $u_{1,\mathrm{AW}}$ which can be viewed as external field, $\phi_{S,\mathrm{BW}}$ and $\phi_{S,\mathrm{AW}}$ are effective potentials coming from solvent-solvent pair attractions. Remember that one needs an $\frac{1}{2}$ prefactor when calculating the energy coming from pair interactions. That's why the $\frac{1}{2}$ shows up in Eq.(5).

To summarize, under the approximation that the water density outside the solute core is the bulk density, the result in the short solvent paper can be rewritten as

$$\begin{aligned}\mathsf{w}^{\mathrm{ss}}_{\mathrm{AB}}(r) = \mathsf{w}^{\mathrm{f}}_{\mathrm{AB}}(r) &- n_{blue}\left\langle u_{1,\mathrm{BW}}\right\rangle_{blue} - n_{red}\left\langle u_{1,\mathrm{AW}}\right\rangle_{red} \\ &- \frac{1}{2}n_{green}\left\langle \phi_{S,\mathrm{BW}}\right\rangle_{green} - \frac{1}{2}n_{orange}\left\langle \phi_{S,\mathrm{AW}}\right\rangle_{orange}\ ,\end{aligned} \tag{6}$$

which can be easily connected to Widom picture. The $\frac{1}{2}$ prefactor is due to the fact that $\phi_{S,\mathrm{BW}}$ and $\phi_{S,\mathrm{AW}}$ not an external field but generated by solvent-solvent pair interactions.