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## Structure and surface energy of the surfactant layer on the alveolar surface: inaccuracies and their correction

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**Abstract** The article of Kashchiev and Exerowa (Eur Biophys J 30:34–41) is shown to incorporate a number of inaccuracies that fit the categories “historical”, “anatomical”, and “biophysical”. These inaccuracies are corrected by reference to published research reports from 1978 to 1998. The monolayer-bilayer model proposed by Kashchiev and Exerowa may be thermodynamically correct *in vitro*, but has not been related to the structure of the alveolar surface *in vivo*, which is that of a foam (“the alveolar surface network”).

**Keywords** Alveolar surface structure · Alveolar surface energy · Monolayer-bilayer model · Intraalveolar bubbles · Alveolar surface network

### Introduction

The conformation and function of the fluid surface of mammalian alveoli has received considerable attention by biologists and physicists since the discovery of lung surfactants by Pattle (1955, 1958). That the phospholipid surfactants at the alveolar surface are fundamentally necessary for alveolar stability and alveolar liquid balance is well established (e.g., Scarpelli 1988). However, the specific molecular and interfacial conformations that affect these physiological equilibria continue to be problematic. My attention was drawn recently to the article by Kashchiev and Exerowa (2001) in which the structure and surface energy of the alveolar surfactant layer “is determined in the scope of a modification of the structural model of Larsson et al. (1999)” (Kashchiev and Exerowa 2001). Whereas the authors’ model is based on sound interfacial thermodynamics, its rele-

vance to the normal alveolar surface is in error from at least three perspectives, namely, historical, anatomical, and biophysical. Following is a brief discussion of each, with the errors corrected.

### Historical corrections

1. Kashchiev and Exerowa (2001) state that Scarpelli “introduced the hypothesis of intraalveolar bubble formation” in 1988 (Scarpelli 1988). This is incorrect on two counts. First, Scarpelli in fact discovered intraalveolar bubble formation as a natural, normal biological phenomenon *in vivo*. This was not a “hypothesis”, but an observable and universal fact. The year was 1978 (Scarpelli 1978) not “1988”. Second, the bubble agglomeration or foam, including bubble and foam films, was defined both chemically and morphologically. Again, not a “hypothesis”.
2. Kashchiev and Exerowa (2001) wrote that “... bubbles in the alveoli at birth was established by Scarpelli and Mautone (1994)”. The facts contradict this assertion. First, the discovery was made in neonates in 1978 (Scarpelli 1978) (above). Second, discovery of the same conformation (i.e., bubbles; bubble and foam films; foam) in adult lungs was first reported in 1983 (Scarpelli et al. 1983). Third, the original concept of the alveolar surface network was first presented in 1988 (Scarpelli 1988). Fourth, the article to which Kashchiev and Exerowa (2001) refer, i.e. Scarpelli and Mautone (1994), is in fact an *in vitro* study showing Clements’ “surface monolayer theory” to be incompatible with alveolar function *in vivo*.
3. Kashchiev and Exerowa (2001) state “... they proposed the closed lipid monolayer as a model...”. I have never, since 1978, considered the intraalveolar bubble “a model”, given that I have shown the bubbles to be the natural infrastructure of all normally aerated alveoli and given that the unit bubbles are easily recovered, intact, in the laboratory (see Scarpelli 1998).

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## Anatomical corrections

Kashchiev and Exerowa (2001) cite my monograph (Scarpelli 1988) as “morphological observations” in support of their monolayer-bilayer model. The facts are that my monograph supports the natural occurrence of intraalveolar bubbles. Indeed, included in the monograph (Scarpelli 1988; fig. 25) is a three-dimensional scanning electron micrograph showing alveolar bubble films in the lung of an adult rabbit! Kashchiev and Exerowa (2001) cite other “morphological observations” to support their model. These, however, are either *in vitro* preparations of questionable application to the morphology *in vivo* (see Scarpelli et al. 1997) or they are studies of lungs prepared for microscopy by the conventional processing methods. The unfortunate situation that all morphologists face is that, as we have shown (Scarpelli et al. 1997), all conventional processing methods – all that have been used throughout the years to evaluate the alveolar surface – distort and disrupt normal bubble/foam films *in situ*! Only when the fresh otherwise unperturbed lung is examined directly as it exists *in vivo* are these structures seen, including the “alveolar surface network” of bubble films (Scarpelli et al. 1996, 1997). In addition, we have developed a unique processing method (Scarpelli et al. 1997) that preserves the bubble/foam films for subsequent light and electron microscopy. Thus, Kashchiev and Exerowa (2001) need to address the alveolar surface network in order to evaluate the validity of their model. They did not.

## Biophysical corrections

At least two fundamental biophysical problems result from the failure of Kashchiev and Exerowa (2001) to recognize the normal foam configuration of the alveolar surfaces collectively. The first concerns the variety of appositions of unit bubble films. At least three foam film types have been described, including (1) appositions in which one monolayer is compressed and the other is at equilibrium, (2) both monolayers are compressed in the form of “classical” foam films, and (3) the compressed bubble film monolayer is apposed to either the cell surface or hypophase lipid structures (see Scarpelli 1998). The latter configuration may apply directly to the model of Kashchiev and Exerowa (2001). The second problem concerns hypophase hydrodynamics, which is influenced by cell topography, plateau border dynamics, and interstitial hydrostatic forces (see Scarpelli 1998). These factors, not addressed by Kashchiev and Exerowa (2001), are changing variables during the normal process

of breathing. Finally, it must be noted that the “tubular myelin” figures to which Kashchiev and Exerowa (2001) make corroborative reference are seen by the distorting conventional processing methods (above) as discontinuous short segments in the alveolar surface lining. This, if it exists *in vivo*, is not accounted for by the Kashchiev-Exerowa model. On the other hand, “tubular myelin”, if it exists *in vivo*, does not change the observable fact of the existence of the alveolar surface network (Scarpelli 1998).

## Conclusion

The article of Kashchiev and Exerowa (2001) is reviewed for its substantial inaccuracies in three areas, namely, historical, anatomical, and biophysical. Whereas their basic thermodynamic development of structure and surface energy of a lung surfactant monolayer-bilayer model is carefully drawn, its application to the alveolar surface *in vivo* is very much problematic because normal alveolar surface structure is not addressed. The difficulty resides fundamentally in the inaccuracies of the article, which are explained and corrected in this paper.

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